UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

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: 001-39620

PRAXIS PRECISION MEDICINES, INC.
(Exact Name of Registrant as Specified in its Charter)

Delaware	**47-5195942**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
99 High Street, 30th Floor Boston, MA	**02110**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: 617-300-8460

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.0001 per share	**PRAX**	**The Nasdaq Global Select Market**

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 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. ☒

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 common stock held by non-affiliates of the registrant, based on the closing price of a share of common stock on June 30, 2021 as reported by the Nasdaq Global Select Market on such date was approximately $761.0 million. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

As of February 18, 2022, the registrant had 45,487,614 shares of common stock, $0.0001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement relating to its 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2021 are incorporated herein by reference in Part III.

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SUMMARY OF THE MATERIAL RISKS ASSOCIATED WITH OUR BUSINESS

- We are a clinical-stage biopharmaceutical company and we have incurred significant losses since our inception. We anticipate that we will continue to incur significant losses for the foreseeable future.
- We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts.
- The development and commercialization of drug products is subject to extensive regulation, and the regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time-consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates on a timely basis if at all, our business will be substantially harmed.
- Preclinical and clinical drug development involves a lengthy, complex and expensive process, with an uncertain outcome. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA or comparable foreign regulatory authorities.
- Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following regulatory approval, if obtained.
- The markets for our product candidates may be smaller than we expect.
- We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.
- Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.
- We have entered into, and may enter into, license or other collaboration agreements that impose certain obligations on us. If we fail to comply with our obligations under such agreements with third parties, we could lose license rights that may be important to our business.
- Third-party claims of intellectual property infringement may prevent or delay our product discovery and development efforts.
- We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.
- Business interruptions resulting from COVID-19 or a similar pandemic, epidemic or outbreak of an infectious disease in the United States or worldwide may adversely affect our business.
- The price of our stock may be volatile, and you could lose all or part of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements contained in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the success, cost and timing of our product candidate development activities and clinical trials;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- the ability to license additional intellectual property relating to our product candidates from third parties and to comply with our existing license agreements and collaboration agreements;
- the ability and willingness of our third-party research institution collaborators to continue research and development activities relating to our product candidates;
- our ability to commercialize our product candidates, if approved, in light of the intellectual property rights of others;
- our ability to obtain funding for our operations, including funding necessary to complete further development and, if approved, commercialization of our product candidates;
- the commercialization of our product candidates, if approved;
- our plans to research, develop and, if approved, commercialize our product candidates;
- future agreements with third parties in connection with the commercialization of our product candidates, if approved, and any other approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and
- the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our ongoing and planned preclinical studies and clinical trials

In some cases, you can identify forward-looking statements by terminology such as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of

these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled “Risk Factors” and elsewhere in this Annual Report on Form 10-K. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K and have filed with the Securities and Exchange Commission as exhibits hereto completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this Annual Report on Form 10-K, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section titled “Risk Factors” and elsewhere in this Annual Report on Form 10-K.

PART I

Item 1. Business

BUSINESS

COMPANY OVERVIEW

We are a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system, or CNS, disorders characterized by neuronal excitation-inhibition imbalance. Normal brain function requires a delicate balance of excitation and inhibition in neuronal circuits, which, when dysregulated, can lead to abnormal function and disease. We are applying insights from genetic epilepsies to both rare and more prevalent neurological and psychiatric disorders, using our understanding of shared biological targets and circuits in the brain. We apply a deliberate and pragmatic precision approach, leveraging a suite of translational tools including novel transgenic and predictive translational animal models and electrophysiology markers, to enable an efficient path to proof-of-concept in patients. Through this approach, we have established a broad CNS portfolio with multiple programs, including product candidates across psychiatric disorders, movement disorders, epilepsy and other exploratory CNS indications, with three clinical-stage product candidates. Each of our clinical-stage product candidates is advancing in more than one indication and we anticipate expansion into additional indications. We expect multiple topline readouts from our clinical-stage programs and anticipate the launch of a fourth clinical development program in 2022. In addition, we have established a robust pipeline of preclinical stage programs through internal research and in-licensing.

Our broad portfolio of CNS programs is currently structured by therapeutic focus in three primary franchises – Psychiatry, Movement Disorders and Epilepsy. In addition, we are pursuing development in other exploratory CNS indications such as rare adult cephalgias. Within our Psychiatry franchise, our most advanced clinical candidate, PRAX-114, is being developed for the treatment of a broad range of patients suffering from major depressive disorder, or MDD and post-traumatic stress disorder, or PTSD. We expect to report topline results from the Aria Study, a Phase 2/3, placebo-controlled study evaluating PRAX-114 for monotherapy treatment of MDD, in the second quarter of 2022. We also expect to report topline results from the Acapella Study, a Phase 2, placebo-controlled, dose-ranging study evaluating PRAX-114 for treatment of MDD, in mid-2022. In addition, we have initiated a Phase 2, placebo-controlled study evaluating PRAX-114 for the treatment of PTSD and expect to report topline results in the second half of 2022.

Within our Movement Disorders franchise, our second clinical candidate, PRAX-944, is being developed for the treatment of Essential Tremor, or ET, and Parkinson's Disease, or PD. We anticipate reporting topline results from the second cohort of our ongoing Phase 2a trial evaluating PRAX-944 for the treatment of ET in the second quarter of 2022, including both open-label and placebo-controlled, randomized withdrawal period results. We have initiated a Phase 2b, placebo-controlled, dose-range finding trial, the Essential1 Study, to evaluate the tolerability, safety and efficacy of PRAX-944 in adults with ET and we expect to report topline results in the second half of 2022. We also expect to initiate a Phase 2, placebo-controlled, crossover study to evaluate the safety, pharmacokinetics, or PK, and efficacy of daytime dosing of PRAX-114 for the treatment of ET in the first quarter of 2022 and expect to report topline results in the second half of 2022. We expect to initiate a Phase 2, placebo-controlled trial to evaluate the safety, PK and efficacy of PRAX-944 as a non-dopaminergic treatment for the motor symptoms of PD in the second quarter of 2022.

Within our Epilepsy franchise, we expect to initiate a Phase 2 study with our third clinical-stage candidate, PRAX-562, in patients with rare pediatric Developmental and Epileptic Encephalopathies, or DEEs, in the second quarter of 2022. Our most advanced preclinical stage product candidate within our Epilepsy franchise, PRAX-222, is an antisense oligonucleotide, or ASO, designed to decrease the expression levels of the protein encoded by the gene SCN2A in patients with gain-of-function, or GOF, SCN2A mutations. We expect to initiate a seamless study of PRAX-222 in the second quarter of 2022, which would be our fourth program to reach clinical stage. We also expect to initiate a Phase 2 proof-of-concept, or POC, clinical trial evaluating PRAX-562 in patients with rare adult cephalgias in the first quarter of 2022. In addition, our preclinical pipeline consists of PRAX-628, a product candidate nominated in the fourth quarter of 2021 for focal epilepsy, a discovery program in development for KCNT1 related epilepsy, three ASOs targeting SCN2A in patients with loss-of-function, or LOF, mutations, PCDH19 and SYNGAP1, and three additional discovery programs for undisclosed targets in psychiatry, movement disorders and epilepsy.

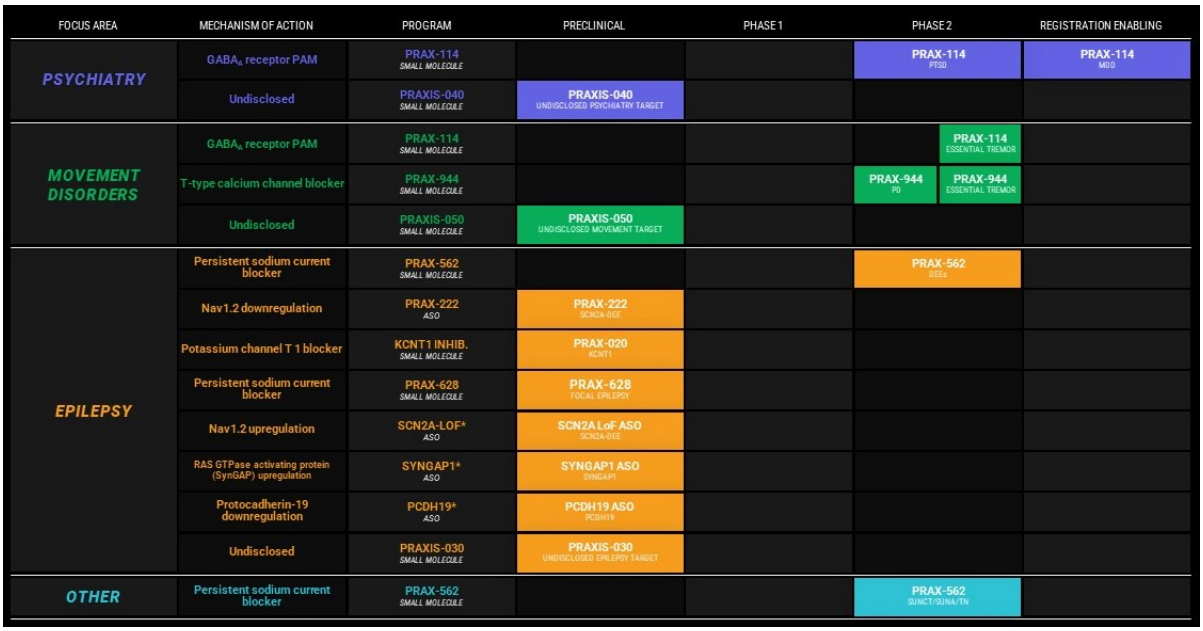
Our Approach

Each of our programs is based on four key principles that we believe will both increase the probability of success and allow us to efficiently translate insights into high-impact therapies for patients and society:

1. ***Focus on therapeutic targets identified through human genetics.*** Numerous CNS disorders are caused by an imbalance of excitation and inhibition in neuronal circuitry. By applying insights derived from the genetics of pediatric epilepsies, we have identified biological targets that we believe are implicated in determining neuronal excitability, not only in epilepsies, but also in a variety of rare and more prevalent CNS disorders. For example, human genetics points to the relevance of the GABAergic system where mutations in GABAA receptors are associated with a number of rare pediatric epilepsies. The GABAergic system is also implicated in MDD, where enhancing GABAA activity is believed to be beneficial. As our understanding of the genetic underpinning of these disorders evolves, we plan to continually apply learnings to expand and advance our portfolio.
2. ***Utilize translational tools to validate the potential of our targets and product candidates.*** We leverage a number of translational tools to both confirm pharmacodynamic effects of our product candidates in the brain and establish on-mechanism effects, which we believe will result in an increased probability of success in the clinic. Our programs utilize target-specific electroencephalogram, or EEG, endpoints to serve as robust markers of pharmacological engagement of the drug target and novel transgenic animal models to assess the therapeutic activity of our molecules. We expect these tools, along with rigorous preclinical PK and pharmacodynamic characterization of our molecules will position us to more efficiently translate preclinical findings into clinical utility.
3. ***Pursue efficient, rigorous clinical development paths to proof-of-concept in humans***. Our development strategies are focused on defining efficient paths to demonstrate the safety and therapeutic activity of our programs in humans. We select indications that we believe will enable the early demonstration of desired effect in a relatively small patient sample and we focus on clinical endpoints that both minimize inter-patient variability and offer a clear connection between pharmacodynamic effects and clinical measures that are meaningful to patients, physicians and regulatory agencies. Our global network of contract research organizations, or CROs, and scientists affords us the flexibility to conduct research and development activities in diverse geographic locations to accelerate our development timelines and limit geographic risks.
4. ***Apply patient-guided development strategies.*** We pursue the development of candidates that address the treatment needs of patients and the treating community, including targeting the underlying disease pathology versus just symptom management. We intend to develop therapies that provide patients long-term relief from their disorders and significantly reduce the overall burden to patients and caregivers. Our development strategies are tailored to demonstrate these benefits.

Our Portfolio

Below is a summary of our portfolio. We own global commercialization rights for all of our product candidates.



*SCN2A-LOF, SYNGAP1 and PCDH19 ASOs are being developed in collaboration with collaboration with The Florey Institute.

PSYCHIATRY

We are developing PRAX-114, an extrasynaptic GABAA receptor preferring positive allosteric modulator, or PAM, for the treatment of a broad range of patients suffering from MDD and PTSD. We believe that PRAX-114 has several advantages relative to currently available therapies and product candidates in the GABAA PAM therapeutic class, including the potential for rapid and durable antidepressant effect across MDD symptoms, a wider therapeutic window, simple nightly dosing with or without a meal via a tablet formulation and the potential for a differentiated tolerability profile. We have been diligently pursuing our strategy to advance PRAX-114 towards regulatory approval and commercialization to support a broad label in MDD that can be easily integrated into standard clinical practice. We intend to develop PRAX-114 as both a monotherapy and adjunctive therapy for MDD, and, if approved, commercialize it in the United States and explore opportunities to expand value in other countries. PRAX-114 is also being evaluated in a Phase 2 POC study for the treatment of PTSD. We believe that treatment of PTSD with a GABAA PAM has the potential to both address the underlying pathophysiology of the disorder more directly than standard of care treatments and address multiple unmet medical needs in this population. We intend to demonstrate POC for PRAX-114 for the treatment of PTSD and subsequently determine development and regulatory pathways. We are also assessing the potential development of PRAX-114 in additional indications.

PRAX-114 is currently in the registration-enabling phase of development for treatment of patients with MDD. We are conducting a Phase 2/3, placebo-controlled study, the Aria Study, to assess the efficacy and safety of 40mg of PRAX-114 for monotherapy treatment of MDD and expect to report topline results in the second quarter of 2022. The Aria Study is intended to serve as one of two trials required by the U.S. Food and Drug Administration, or the FDA, to demonstrate clinical efficacy to support registration of PRAX-114 for treatment of MDD. We are also conducting a Phase 2, placebo-controlled, dose-ranging study evaluating PRAX-114 for treatment of MDD, the Acapella Study, and expect to report topline results in mid-2022. The Acapella Study is intended to provide additional understanding of the dose range and to evaluate the safety and efficacy of PRAX-114 at doses of 10, 20, 40 and 60mg. We completed a multi-cohort, three-part Phase 2a clinical trial in Australia, in which Parts A and C of the trial treated patients with MDD while Part B focused on patients with perimenopausal depression, or PMD. For all parts of the trial, PRAX-114 was generally well-tolerated and demonstrated a rapid antidepressant effect that was maintained throughout the treatment period. We also observed improvements in menopausal and mood symptoms in patients with PMD and are assessing further development options based on this finding. In addition, we initiated a Phase 2, placebo-controlled study evaluating PRAX-114 for treatment of PTSD in the fourth quarter of 2021 and expect to report topline results in the second half of 2022.

Major Depressive Disorder

MDD is a chronic psychiatric condition causing severe impairments that interfere with the ability to carry out life activities. An MDD episode is characterized by a period of at least two weeks of persistent depressed mood and/or the loss of interest or pleasure in activities, accompanied by sleep and appetite disturbance, fatigue, concentration difficulty, cognitive impairment, feelings of guilt, psychomotor retardation or agitation and suicidal ideation. MDD is one of the most prevalent psychiatric disorders. In the United States, approximately 19 million adults, or seven percent of the adult population suffer from an episode of MDD every year, with episodes lasting on average six to eight months. It is estimated that MDD affects more than 300 million people worldwide. Moreover, the prevalence of depression has increased during the COVID-19 pandemic in the United States and globally. In the United States, depression symptoms have increased by more than 3-fold overall during the COVID-19 pandemic. The most dramatic increases are reported in moderate, moderately severe and severe depression symptoms, with a 2.6-fold, 3.7-fold, and 7.5-fold rise, respectively, relative to a pre-COVID-19 pandemic period.

MDD is a recurrent psychiatric condition that frequently requires long-term treatment, with the ultimate goal of achieving remission. MDD is associated with an elevated risk of suicide, underscoring the need for rapid and effective treatment. The most explored pharmacological mechanisms for treating MDD target monoamine neurotransmitters. Drugs in this class include selective serotonin reuptake inhibitors, or SSRIs, serotonin and norepinephrine reuptake inhibitors, or SNRIs, bupropion and atypical antipsychotic medications. SSRIs and SNRIs are associated with significant side effects, including weight gain, sexual dysfunction, drowsiness, nausea, insomnia and discontinuation syndrome. Atypical antipsychotics indicated for adjunctive treatment of insufficient clinical response are associated with weight gain, sexual dysfunction, metabolic syndrome and movement disorders. The side effect profile of current antidepressant standard of care negatively impacts treatment outcomes, quality of life and adherence in MDD patients.

Approximately 70% of MDD patients fail to achieve remission with first line treatment. Further, those patients that are responsive typically require approximately six to eight weeks of treatment to show a clinically meaningful response. Slow onset of action is a substantial unmet need in MDD, with some of the most commonly prescribed antidepressants showing a reduction in the Hamilton Depression Scale, or HAM-D, of approximately 6- to 8-points and a difference from placebo of approximately 1-2 points at Week 2. The HAM-D is one of the most widely-used clinical rating scales for depression and includes 17 items used for scoring over a wide range of symptoms typically found with depression including mood, suicidal thoughts, insomnia, anxiety, loss of appetite and weight loss. Patients with more severe depression have higher scores. Moreover, approximately 40% of patients on therapy discontinued treatment due to either a loss of response or adverse side effects. Finally, 33% of patients failed to respond after treatment with three or more different standard of care therapies.

Among the MDD patients who experience a response to treatment, the majority do not achieve remission. Even for patients deemed responsive, disease burden often persists through the presence of residual depression symptoms that lead to an ongoing negative impact on home, interpersonal and occupational functioning, as well as a significantly increased risk of relapse of the full depressive syndrome and worse comorbid outcomes, including suicide.

Despite the numerous and long-standing antidepressant treatment options, there continues to be an unmet need for antidepressants that provide rapid onset of effect, higher remission rates, efficacy throughout the depressive episode and an improved tolerability profile that is aligned with the clinical care and the course of MDD and its accompanying comorbid symptoms.

GABAA in depression

Gamma-aminobutyric acid, or GABA, is the principal neurotransmitter mediating neuronal inhibition in the brain. Neurons that produce GABA, known as GABAergic neurons, are present throughout the brain, representing between 20% and 40% of all neurons depending on the region. Their primary role is to balance and fine tune excitatory neurotransmission of various neuronal circuits. Whole-exome sequencing has identified GABAA receptor mutations as an important cause in a range of neurological conditions, underscoring their importance as central regulators of excitatory and inhibitory balance in the brain.

It is well established that GABAergic signaling is impaired in patients with MDD and other stress-related mood disorders. GABA levels, levels of the GABA synthesizing enzyme GAD67, as well as GABAA receptor levels, have been shown to be reduced in brains of patients with MDD. In addition, decreased GABAergic neuron function, most notably in the prefrontal cortex, has been documented in MDD patients and in preclinical animal models of depression. Endogenous neuroactive steroids, or NAS, such as allopregnanolone and pregnanolone or synthetic derivatives thereof, such as PRAX-114, have been shown to potentiate the activity of GABAA receptors. Both

human and animal data reveal an important role for NAS in these GABAergic deficits and levels of endogenous NAS are decreased in individuals with MDD.

Of particular relevance to PRAX-114 is the more recently established link between GABAergic signaling, neuroactive steroid levels and stress—a well-established risk factor for MDD and other mood disorders. In preclinical models, exposure to chronic stress leads to reduced neuroactive steroid biosynthesis and reduced GABAergic inhibition in depression-relevant brain circuits. This ultimately results in increased anxiety and depression-like behaviors. In particular, it has been shown that stress causes long-lasting loss of GABAergic inhibition in the amygdala, a brain region central to the stress response involved in controlling emotions. This reduced inhibition causes increased activity of the amygdala and is associated with an exaggerated stress hormone response.

We believe that enhancing modulation of GABAA receptors in patients with depression and anxiety has the potential to restore normal function in these circuits, leading to broad applications in mood and anxiety disorders.

Post-Traumatic Stress Disorder

PTSD is a chronic disorder occurring after direct or indirect exposure to psychological trauma. PTSD is characterized by re-experiencing aspects of the original trauma, avoidance of trauma reminders, anhedonic or dysphoric mood states, and/or negative thoughts or feelings that began or worsened after the trauma and trauma-related hyperarousal and hypervigilance. Problems with sleep onset and maintenance are common and may be associated with nightmares, safety concerns, or a generalized elevated arousal that interferes with sleep. PTSD is frequently associated with impairment in many aspects of daily functioning, including self-care, home functioning, relationships, and social interactions. Common occupational impacts include higher rates of sick leave, failure to return to work and reduced work performance that is correlated with PTSD symptom severity. Failure to achieve remission of PTSD is associated with ongoing functional impairment as well as subjective distress. Even with effective medication or psychotherapy treatment, hyperarousal symptoms such as irritability/anger, insomnia and nightmares often persist even when other symptoms have been adequately treated, with greater than half of patients reporting these residual symptoms even when they no longer meet diagnostic criteria. Continued sleep disruption can prolong other PTSD symptoms and increase risk of conditions frequently comorbid with PTSD such as severe chronic insomnia disorder, MDD and substance use disorders.

Despite the prevalence and negative impact of PTSD, there are few available pharmacotherapies for this disorder and their efficacy has substantial limitations. Only two medications are approved by the FDA for PTSD treatment (paroxetine and sertraline), and only a few additional medications (including fluoxetine and venlafaxine) have shown at least modest efficacy in the treatment of the disorder. The rate of response to SSRIs is at most 60%, and only 20 to 30% of those treated achieve symptomatic remission following pharmacotherapy. Achieving maximal improvement (even to incomplete response) with available medications can take months. In addition to the slow onset of efficacy for core PTSD symptoms, these treatments have adverse event, or AE, profiles including the potential to increase insomnia and anxiety symptoms during treatment initiation. The slow onset of efficacy and potential for increasing insomnia and anxiety symptoms lead a substantial proportion of patients to discontinue treatment. We believe this highlights the unmet medical need for a rapid onset treatment that can improve insomnia and anxiety symptoms both to ease subjective distress and support adherence with treatment.

GABAA in PTSD

Based on findings from third party studies, we believe there is a compelling rationale for alterations in GABAergic transmission associated with the pathophysiology of PTSD. These findings include reduced levels of plasma and cortical GABA seen in the insula and anterior cingulate cortex of veterans exposed to trauma. Additionally, in military service members with PTSD, lower brain levels of GABA in the parieto-occipital cortex were negatively correlated with and mediated by scores on the Insomnia Severity Index. Using transcranial magnetic stimulation, paired-pulse short- latency intracortical inhibition (an effect believed to reflect GABAA-mediated inhibition) was decreased in patients with PTSD relative to matched healthy controls.

PTSD has also been associated with alterations in NAS that positively allosterically modulate GABA action at GABAA receptors. These findings include reductions in allopregnanolone levels in cerebrospinal fluid that correlate negatively with PTSD and negative mood symptoms in both women and men. PTSD in women has been associated with a deficit in neurosteroid synthesis that in turn was associated with a deficit in extinction memory that plays a role in the development and maintenance of PTSD symptoms. Additionally, two neurosteroid GABAA receptor antagonists, dehydroepiandrosterone and dehydroepiandrosterone sulphate, have been shown to be elevated relative to controls in combat-associated PTSD, constituting an additional negative influence on GABAergic signaling. Taken together, these findings support our hypothesis that treatment of PTSD with a NAS GABAA PAM

has the potential to address the underlying pathophysiology of the disorder more directly than standard of care treatments and address multiple unmet medical needs in this population.

GABAA receptors: The target of PRAX-114

PRAX-114 is a small molecule neuroactive steroid that acts as a positive allosteric modulator of GABAA receptors. PAMs are substances that bind to a receptor, such as GABAA, to enhance that receptor's response to its endogenous ligand (or endogenous agonist). GABAA PAMs bind to a distinct site from endogenous GABA, an allosteric binding site, and do not activate the receptor in the absence of the GABA. Allosteric modulators are believed to have improved safety profiles and are less likely to result in tachyphylaxis, or decreasing drug response, as compared to agonists. GABA exerts its effects through binding to two types of GABAA receptors, synaptic and extrasynaptic receptors, which differ in their protein subunit composition, physical location on the cell surface and functional role in modulating neuronal circuits.

GABAA receptors are composed of five subunits which include two alpha, two beta and a fifth subunit (either gamma or delta) that is dependent on the type of receptor. Synaptic GABAA receptors, which are located in the synapse of neurons, contain a gamma subunit while GABAA receptors located outside of the synapse, referred to as extrasynaptic GABAA receptors, contain a delta subunit. Molecules that act as PAMs of only the synaptic GABAA receptor, such as benzodiazepines, bind to sites situated at the interface between the alpha and gamma subunits. Molecules that act as PAMs of both synaptic and extrasynaptic GABAA receptors, such as the NAS allopregnanolone and PRAX-114, bind to sites situated at the interface between the alpha and beta subunits present in both types of receptors. Figure 1 below displays the synaptic binding site for drugs such as benzodiazepines, and the distinct extrasynaptic and synaptic binding sites for NAS, such as allopregnanolone and PRAX-114.

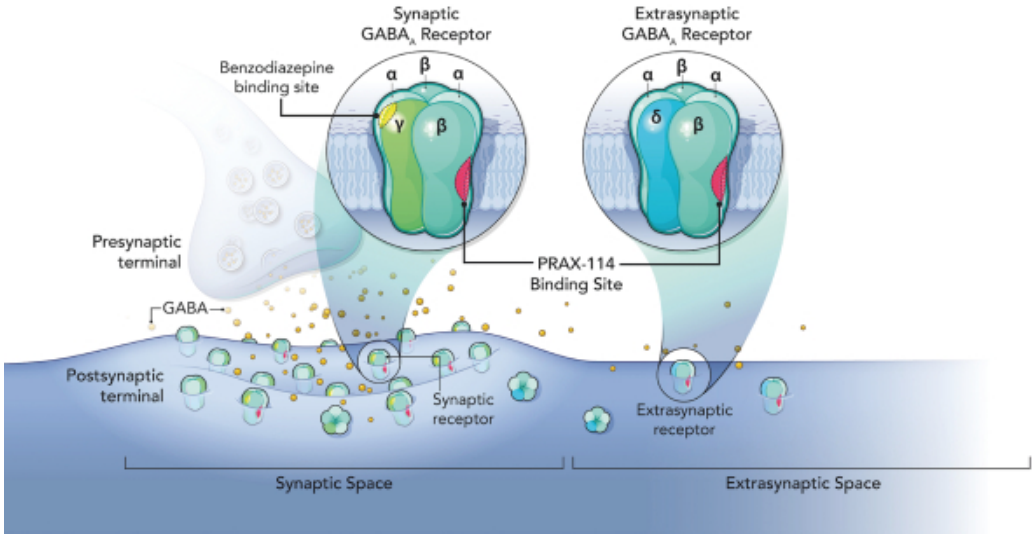


Figure 1. GABAA synaptic and extrasynaptic receptors differ in structure and function.

Synaptic and extrasynaptic GABAA receptors have distinct functions. Synaptic GABAA receptors are responsible for short-lasting, or phasic, inhibition of neurons in response to GABA release at the synapse. By contrast, extrasynaptic GABAA receptors drive continuous, or tonic, low-level inhibition of neurons in response to lower ambient levels of GABA outside of the synapse. While synaptic receptors can respond quickly to stimulation and network demand, extrasynaptic receptors have a broader modulatory role, serving to continuously modulate the overall excitability of neurons.

Molecules that act as PAMs of only the synaptic GABAA receptor, such as benzodiazepines and barbiturates, are used for sedation, sleep induction and anxiolysis, and have anticonvulsant and muscle relaxant properties. These drugs have potent and rapid onset of activity but have not demonstrated antidepressant effects.

Allopregnanolone is an endogenous neuroactive steroid and a PAM of both the extrasynaptic and synaptic GABAA receptors, which has been associated with antidepressant activity. However, allopregnanolone also has

shown significant dose-limiting sedative activity, which we believe is likely mediated at least partially by its effects on synaptic GABAA receptors. Despite this limitation, a formulation of allopregnanolone has been approved and is marketed as Zulresso™ to treat post-partum depression.

The distinct effects mediated by these classes of GABAA PAMs suggest that modulation of extrasynaptic GABAA receptors is responsible for the antidepressant effects demonstrated by allopregnanolone. One of the goals for a next generation neuroactive steroid, such as PRAX-114, is to preferentially modulate extrasynaptic GABAA receptors while minimizing the sedative impact from modulation of synaptic GABAA receptors.

PRAX-114 preference for extrasynaptic GABAA receptors

In preclinical studies, we assessed the relative potency *in-vitro* of PRAX-114-mediated GABAA receptor activation for synaptic and extrasynaptic receptors by measuring the peak current induced by a low concentration of GABA (2 µM) in the presence of increasing concentrations of PRAX-114 in Chinese Hamster Ovary, or CHO, cells expressing either extrasynaptic (α4ß3δ) or synaptic (α1ß2γ2) human GABAA receptors. In this model, PRAX-114 potentiated the GABA-activated current of both extrasynaptic and synaptic GABAA receptors but was approximately 6.4-fold more potent in potentiating the extrasynaptic form of the receptor than the synaptic form based on the concentration that gave half-maximal response, or EC50. At a concentration that activated extrasynaptic GABAA receptors to the equivalent of full activation by the endogenous ligand GABA (~260 nM, 300% potentiation of 2µM GABA), PRAX-114 led to 10.5-fold greater potentiation of extrasynaptic GABAA receptors than synaptic GABAA receptors (29%).

In the same assay, at the same level of extrasynaptic GABAA receptor potentiation (300%), other GABAA receptor PAM NAS in development, or on the market, demonstrated only 0.4 to 2.6-fold greater potentiation of extrasynaptic GABAA receptors, which compares unfavorably to the 10.5-fold observed for PRAX-114. Based on these assay conditions, we believe that the differentiated preference at extrasynaptic GABAA receptors by PRAX-114 will allow it to achieve high levels of extrasynaptic GABAergic activation with improved tolerability.

PRAX-114 for the treatment of MDD and PTSD

We believe that PRAX-114 has several potential advantages:

- **Wider Therapeutic Window**. In preclinical studies, PRAX-114 showed approximately 10-fold more selectivity for PAM of the extrasynaptic form of GABAA receptors compared to the synaptic form. In clinical studies in healthy volunteers, we have observed PRAX-114 markedly increased quantitative electroencephalography, or qEEG, power in the alpha and beta-frequency bands—unlike GABAA receptor PAMs that only modulate synaptic GABAA receptors, such as benzodiazepines, or that are equipotent at synaptic and extrasynaptic receptors, such as allopregnanolone, which has been shown to decrease power in the alpha frequency band. We believe these data suggest that PRAX-114 has a differentiated pharmacological profile in relation to other GABAA PAMs at therapeutic doses due to the relatively selective activation of extrasynaptic GABAA receptors. By preferentially modulating extrasynaptic GABAA receptors, we believe PRAX-114 is able to uniquely activate the GABAergic target and has the potential to mediate antidepressant and anxiolytic activity without the significant sedation observed with less selective NAS.
- **Simple Nightly Dosing With or Without Food**. We believe the ability to administer PRAX-114 and achieve targeted exposures, with or without food, is key for clinical and commercial success in MDD. We believe this type of dosing regimen is also critical for a patient-guided therapy because many patients with depression suffer from appetite disturbances. We have observed fast absorption of PRAX-114 within one to three hours of dosing and predictable PK results across multiple trials. In clinical studies completed to date, PRAX-114 achieved reproducible overall exposure (*i.e.*, area under the concentration curve, or AUC) across a wide range of administration conditions, demonstrating consistent exposure when administered with or without food and at different times of day, whereas other GABAA PAM NAS may require food to achieve therapeutic levels. While AUC is unaffected by administration conditions, nightly dosing has been shown to reduce blunted maximum drug concentration, or Cmax, thereby enhancing the potential for improved tolerability.
- **Sustained Administration**. After consultation with the FDA and other stakeholders in MDD therapy, we designed the Aria Study to include 28-day nightly dosing to evaluate patients at 14 days to assess the rapidity and robustness of response and 28 days to measure initial durability of effect. We believe that having a dosing paradigm consistent with the duration of depressive episodes and easily integrated into standard clinical practice will provide the most substantial benefit to patients in controlling their disease, further differentiating PRAX-114 from other GABAA PAMs.

PRAX-114 clinical development in depression

We are conducting a Phase 2/3, placebo-controlled study for monotherapy treatment of MDD, the Aria Study, and expect topline results in the second quarter of 2022. The Aria Study is intended to serve as one of two trials required by the FD, to demonstrate clinical efficacy to support registration of PRAX-114 for monotherapy treatment of MDD. We also are conducting a Phase 2, placebo-controlled, dose-ranging study for treatment of MDD, the Acapella Study, and expect topline results in mid-2022. The Acapella Study is intended to provide additional understanding of the dose range and to evaluate the safety and efficacy of PRAX-114 at doses of 10, 20, 40 and 60mg.

Phase 2/3 Aria Study

Patients in the Aria Study are randomized 1:1 to receive nightly bedtime doses of 40mg PRAX-114 or placebo for 28 days in a fully outpatient setting, with two-weeks of additional follow up after the end of the active treatment period. Patients are required to be between the ages of 18 and 65, have a diagnosis of MDD with a current episode of at least 8 weeks and not more than 24 months in duration, have a HAM-D total score of 23 or higher consistent with moderate-to-severe MDD, and have had at least one prior episode of MDD. Participants are excluded if they are currently being treated with an antidepressant, have demonstrated an inadequate response to antidepressant treatment in the current episode or have treatment resistant depression, or if they have comorbid medical or psychiatric conditions that could interfere with the scientific objectives or safety of the trial. The primary efficacy endpoint is change in the HAM-D total score from baseline at Day 15. A key secondary endpoint is change in the HAM-D score after 28 days of treatment to assess the durability of effect of 40mg PRAX-114, and we also plan to evaluate changes in other depression-related assessments.

We selected a dose of 40mg in tablet formulation for the Aria Study based on the safety and efficacy results we observed from the 45mg suspension formulation in the Phase 2a clinical trial of PRAX-114 described below. We anticipate the 40mg dose in tablet formulation to yield exposures consistently or slightly higher than what we observed with the 45mg dose in suspension formulation.

Our clinical trial design and study conduct applies several best practices to support evaluation of clinical effects in MDD, including but not limited to:

- Enrollment of patients with moderate-to-severe MDD and at least one prior episode of MDD because recurrent depression has been associated with a lower placebo response rate;
- A two-level subject and data quality process that includes independent clinical interviews confirming eligibility through the SAFER process and conducting audio confirmation of HAM-D clinical assessments at key timepoints with ongoing rating assessment quality feedback;
- Using sites with a known track-record of high quality data generation and drug-placebo separation in the conduct of MDD trials;
- Integration of a placebo control reminder script at every visit and screening for potential duplicate subjects via a dedicated clinical trial registry; and
- Inclusion of the AiCure smartphone-based adherence monitoring system with structured site intervention to address participant adherence issues.

Phase 2 Acapella Study

In parallel with the Aria Study, we are conducting the Acapella Study to evaluate additional PRAX-114 doses for inclusion in pivotal Phase 3 studies in patients with MDD. Given that comparable improvement in the HAM-D was observed in all doses (45, 60 and 80mg) evaluated in the Phase 2a MDD study, this trial is designed to evaluate the efficacy of lower doses of PRAX-114 to determine the optimal dose range to include in future Phase 3 trials. The population for this study is both treatment naïve (monotherapy) MDD participants and MDD participants who have demonstrated an insufficient response to standard of care antidepressant treatment (adjunctive).

Patients in this study will be randomized to receive 10, 20, 40, or 60mg PRAX-114 or placebo in a 1:1:1:1:1 ratio for 28 days, with 2 weeks of additional follow up after the end of the active treatment period. This trial is expected to enroll approximately 125 patients between the ages of 18 and 65 who are experiencing a current major depressive episode of at least 12 weeks and not more than 24 months in duration, have a HAM-D total score of 20 or higher, and who have had at least one prior episode of MDD responsive to antidepressant treatment. Adjunctive participants must be currently treated with an antidepressant at a stable dose for at least eight weeks prior to Day 1 and have demonstrated an insufficient clinical response to one or two adequate trials of antidepressant treatment in the current episode. Exclusion criteria will be similar to the Aria Study with the exception of allowing for adjunctive patients under the criteria described above. The primary objective is to assess the presence of a dose-response

signal for PRAX-114 in MDD using the primary efficacy endpoint of the change from baseline in HAM-D total score at Day 15. Secondary objectives will include evaluating the efficacy for each dose of PRAX-114 in MDD and the effect of PRAX-114 on the HAM-D scores after 28 days of treatment and impact on other depression-related assessments. This trial will employ the full set of clinical trial quality interventions summarized above for the Aria Study.

Phase 2a trial in patients with depression

Prior to the initiation of the Aria Study and the Acapella Study and based on the pharmacology observed in the Phase 1 trials described below, we conducted a three-part, open-label, Phase 2a trial in Australia to assess the safety and efficacy of PRAX-114 in patients with moderate-to-severe MDD or PMD.

Part A results

Part A of the open-label trial included two weeks of treatment and was designed to evaluate the timing and magnitude of the antidepressant effects of PRAX-114 across a range of doses in patients with MDD. Patients were required to be between the ages of 18 and 65 and to have moderate-to-severe MDD for at least one month as defined by a HAM-D score of 22 or higher. The effect of PRAX-114 was measured by the change in the HAM-D score relative to baseline. Patients who had previously failed to respond to a standard of care antidepressant in their current episode were eligible for inclusion. In addition to HAM-D, other scales used included the Montgomery–Åsberg Depression Rating Scale, or MADRS, the Hamilton Anxiety Rating Scale, or HAM-A, and the Symptoms of Depression Questionnaire, or SDQ. MADRS is a 10 item rating scale designed to assess the severity of symptoms in a depressive illness. HAM-A is a 14 item scale widely used to measure the severity of anxiety symptoms, including both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety). SDQ is a 44 item self-reported scale designed to measure the severity of symptoms across several subtypes of depression, including irritability, anger attacks and anxiety.

We selected an initial target dose of 45mg daily of PRAX-114 suspension formulation that was expected to achieve exposures demonstrating full clinical improvement based on the Phase 1 data and qEEG findings. Two additional cohorts were subsequently conducted to assess higher daily doses of 60mg and 80mg PRAX-114 due to the generally well-tolerated profile at 45mg. The first week of treatment was conducted in an inpatient setting to facilitate daily efficacy and safety assessments and then patients were discharged and treated as outpatients for the second week. Patients were instructed to take PRAX-114 at 4:00 PM on Day 1 to support collection of post-dose PK samples and then nightly at 9:30 PM on Days 2-14. Patients were not required to take PRAX-114 with food. Compliance was carefully monitored throughout the duration of the trial, including inpatient and outpatient periods, with a customized version of the AiCure smartphone adherence monitoring system.

Thirty-three patients were enrolled and completed Part A before the COVID-19 pandemic began impacting clinical trial conduct globally. At baseline, patients had a mean HAM-D total score of 25, ranging from 20 to 33, consistent with moderate-to-severe MDD. Twenty-six of the thirty-three participants had previously received an antidepressant during the current depressive episode but still had moderate-to-severe MDD. This failure to respond to initial antidepressant treatment has been associated with more severe and refractory depression. The remaining patients were not being treated with any antidepressant for the current episode before enrolling in the trial.

Dosing with PRAX-114 led to a marked improvement in the HAM-D score (Figure 2) within two weeks of treatment. After one week of treatment, least squares, or LS, mean improvements of 15 to 19 points from baseline were noted across the three dose groups. After two weeks of treatment, all 3 dose levels showed improvements from baseline of greater than 13 points with mean improvements from baseline of 14 to 16 points. Across all dose levels, two-thirds of patients were responders (defined as a >=50% reduction in HAM-D) or were clinically in remission (HAM-D<=7) at the end of the 14 day treatment period. Changes in MADRS, HAM-A and SDQ were consistent with the changes in HAM-D. While the study was not powered to show differences between dose levels, there was no notable dose response observed, which is common amongst trials of antidepressants.

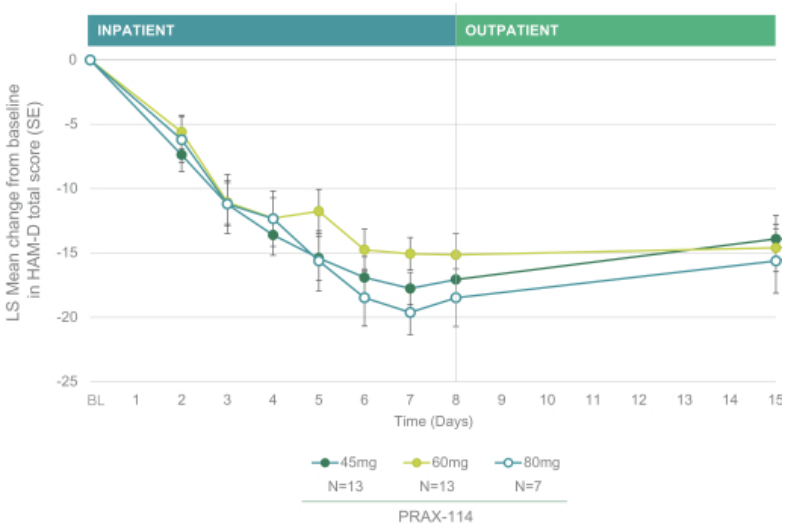


Figure 2. Reduction in HAM-D total score observed in MDD patients treated with PRAX-114 in Part A.

After 14 days of treatment, patients were monitored for an additional 14 days. During this monitoring period, the core mood symptoms measured by the HAM-D generally remained stable with a slight increase in the insomnia item scores post-treatment.

While our Phase 2a trial was not placebo controlled, prior randomized placebo-controlled MDD trials provide important context for the interpretation of the clinical response. The marked improvements in HAM-D scores seen in MDD patients in Part A within two weeks of treatment compares favorably to published reports on changes in HAM-D scale in clinical trials of approved antidepressants such as vortioxetine and duloxetine, among others, which commonly took approximately six to eight weeks to reach a maximal efficacy and often failed to differentiate from placebo at two weeks. Moreover, mean HAM-D changes from baseline at Day 14 for the placebo group of these randomized controlled antidepressant trials were most often between 4-8 points. Even at the first post-dose assessment on Day 3, patients dosed with PRAX-114 had a mean decrease of over 11 points on the HAM-D scale, which compares favorably with the average changes reported in the placebo groups at Day 14 from randomized studies completed for recently approved antidepressants (Figure 3), and other common antidepressants after several weeks of dosing. The clinical data that we have generated to date, and that we expect to generate in the future, from our clinical studies will constitute the bulk of the data needed to support an application for marketing approval of PRAX-114. Unless we conduct head-to-head studies of PRAX-114 against other molecules as part of our future clinical trials and elect to include the resulting data in an application for regulatory approval, we would not expect to rely upon PRAX-114's potential differentiation from any other molecules in connection with submissions to the FDA or other regulatory agencies, as applicable, for approval or otherwise. As the data presented above is based on a cross-trial comparison and not a head-to-head clinical trial, such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or other benefits of PRAX-114 compared to other product candidates that may be approved or that are or were in development for MDD.

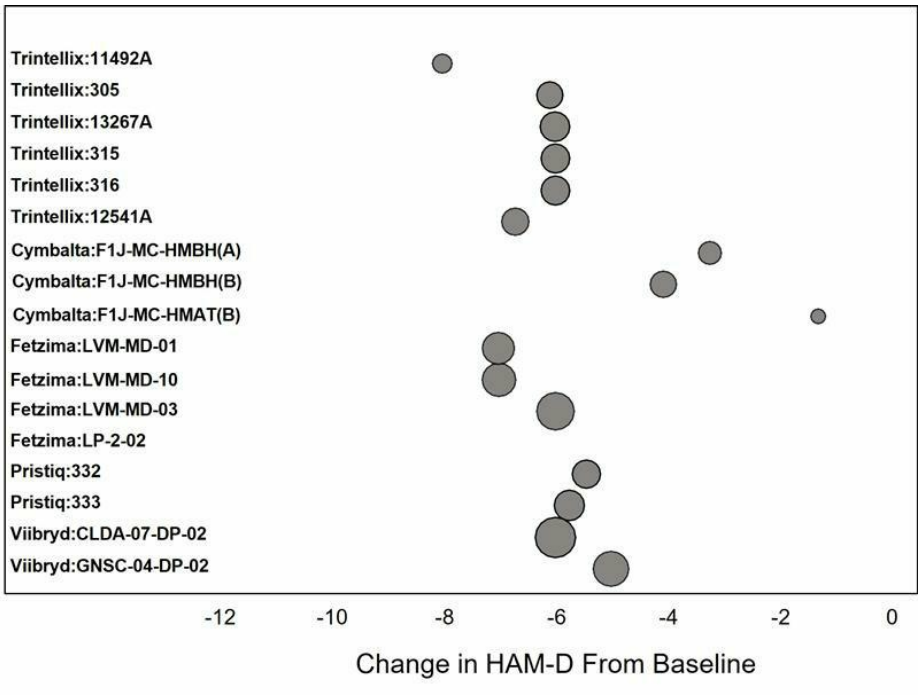


Figure 3. Change from baseline to Day 14 in HAM-D total score for the Placebo arm of selected randomized placebo-controlled studies of recently approved antidepressants. Bubble size is proportional to the sample size of the placebo group in each study. Across studies, the sample size in the placebo group ranged from 89 to 277.

Part B results

Part B of this trial assessed the effect of PRAX-114 on menopausal and mood symptoms in PMD patients. Six participants with PMD received 60mg of PRAX-114 nightly at 9:30PM for 14 days on an outpatient basis. The dose for this part of the trial was selected based on the data from Part A. Inclusion criteria for Part B were similar to Part A and C, except that Part B required participants to be females of 40 years of age or older with irregular menses and a minimum of four hot flushes per day averaged over the week prior to PRAX-114 dosing.

Daily treatment of PRAX-114 in Part B showed a rapid and marked decrease in menopausal symptoms throughout the 14-day treatment period. Treatment with PRAX-114 resulted in mean decreases from baseline at Day 15 of 60% in frequency of moderate-to-severe hot flashes and 68% in the total score of the Perimenopausal Depression Questionnaire, or Meno-D, a 12-item, self-reported questionnaire assessing the presence and severity of symptoms of PMD. At Day 28, two weeks following discontinuation of treatment, frequency of moderate-to-severe hot flashes and Meno-D total score trended toward baseline.

Daily treatment of PRAX-114 in Part B showed a rapid and marked decrease in mood symptoms throughout the 14-day treatment period. Treatment with PRAX-114 resulted in mean decreases from baseline at Day 15 of 47% in the HAM-D total score. Changes in MADRS, HAM-A and SDQ were consistent with the changes in HAM-D, and similar to the observations with hot flushes and the Meno-D, the HAM-D total score trended toward baseline at Day 28, two weeks following discontinuation of treatment.

Part C results

The goal of Part C was to evaluate the safety of four-week outpatient dosing with PRAX-114, similar to the study duration of our ongoing Aria Study, and the treatment effect from Day 15 to Day 28.

Inclusion criteria and symptom assessments were the same as Part A. However, due to restrictions imposed by the COVID-19 pandemic, we changed to the use of telehealth administered clinical efficacy assessments, mailed self-report assessments, and courier delivery of study drug to participants, which supported consistent site and participant adherence to study procedures and study drug administration through completion of Part C. We used our experience from Part C to inform the design and operationalization of the Aria Study.

A total of thirteen participants were enrolled and completed a nightly 9:30 PM dose of PRAX-114 at 60mg for four weeks. At baseline, patients had a mean HAM-D total score of 25, that ranged from 22 to 30, indicating moderate-to-severe MDD. Eight of the thirteen participants had previously received an antidepressant during the current depressive episode but still had moderate-to-severe MDD. This failure to respond to initial antidepressant treatment has been associated with more severe and refractory depression. The remaining patients were not being treated with any antidepressant for the current episode before enrolling in the trial.

Dosing with PRAX-114 for four weeks led to a rapid and marked improvement in the HAM-D score (Figure 4) within two weeks of treatment, and LS Mean improvement of 11 points at Day 15 remained stable through the end of the active treatment period.

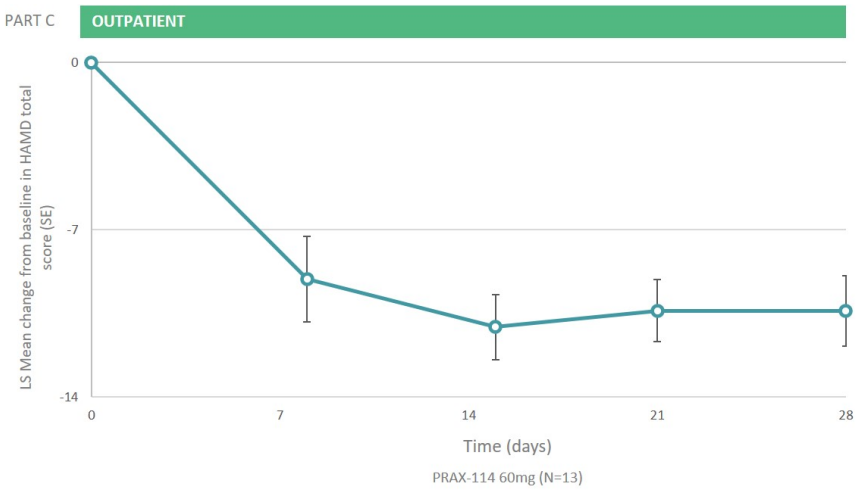


Figure 4. Reduction of HAM-D total score observed in MDD patients treated with PRAX-114 in Part C.

Overall, dosing with PRAX-114 led to a marked reduction in HAM-D score during the treatment periods in Parts A, B and C, with symptom improvement evident upon follow-up in the MDD populations in Parts A and C and trending toward baseline in Part B. Changes in MADRS, HAM-A and SDQ (and menopausal symptom assessments in Part B) were consistent with the changes in HAM-D. More than 70% of participants from all parts of the study had previously received an antidepressant during the current depressive episode but still had moderate-to-severe MDD. We also observed in each part of the Phase 2a trial that greater than 50% of patients were responders at two weeks.

Combined Safety Results Summary (Parts A, B and C)

In the Phase 2a study overall, PRAX-114 suspension formulation was generally well-tolerated across the dose range in 52 participants with MDD and PMD, including at the highest 80mg dose in Part A. Treatment-emergent adverse events, or TEAEs, were generally mild to moderate (Table 5). There were no serious adverse events, or SAEs, and study drug cessation at the end of the treatment period was generally well-tolerated. There was one discontinuation from the study due to AEs in a Part B participant of moderate daytime sedation and mild feeling abnormal. The most common AEs were headache, somnolence, and dizziness.

Rates of somnolence, which is characterized by sleepiness or drowsiness, increased with dose, demonstrating a pharmacological effect which was somewhat mitigated by dosing at night versus the morning. With night-time dosing, 17 out of 52 patients (33%) noted somnolence post-dosing, which was generally time-limited, not experienced during the daytime.

Preferred Term	45 mg* (N=13)	60 mg (N=32)	80 mg* (N=7)	Overall (N=52)
Headache	7 (53.8%)	12 (37.5%)	3 (42.9%)	22 (42.3%)
Somnolence	2 (15.4%)	12 (37.5%)	3 (42.9%)	17 (32.7%)
Dizziness	0 (0.0%)	5 (15.6%)	4 (57.1%)	9 (17.3%)
Fatigue	3 (23.1%)	2 (6.3%)	1 (14.3%)	6 (11.5%)
Feeling abnormal	1 (7.7%)	4 (12.5%)	1 (14.3%)	6 (11.5%)
Nausea	0 (0.0%)	5 (15.6%)	1 (14.3%)	6 (11.5%)

*Includes participants from Part A only.

In Part A, PRAX-114 was administered at daytime of Day 1, nighttime of Days 2-14.

Table 5. TEAEs reported in ≥10% of participants across all parts of the PRAX-114 Phase 2a study (Parts A, B and C).

Phase 1 trials in healthy volunteers

Phase 1 SAD clinical trial

We conducted a Phase 1 randomized, double-blind, placebo-controlled single ascending dose, or SAD, trial of PRAX-114 suspension formulation in healthy volunteers to evaluate safety and tolerability of PRAX-114. This trial enrolled 36 volunteers who were randomized into cohorts dosed with 1mg, 3mg, 10mg, 30mg or 60mg of PRAX-114 or placebo. In this trial, we observed fast absorption of PRAX-114 within one to three hours of dosing and approximately dose-proportional increases in peak concentration and total drug exposure. PRAX-114 was generally well-tolerated and no SAEs were reported in this trial.

Phase 1 MAD clinical trial

We subsequently conducted a Phase 1 randomized, double-blind, placebo-controlled multiple ascending dose, or MAD, trial in healthy volunteers in Australia to evaluate the safety, tolerability and PK of PRAX-114 suspension formulation and to assess the effect of food on drug exposure. Thirty-six volunteers were randomized to receive daily doses of 15mg, 30mg or 60mg of PRAX-114 or placebo for 14 days. Ten additional volunteers in a food effect cohort received 30mg doses of PRAX-114 when they were in a fasted state or with a high-fat meal.

As part of this trial, we evaluated the effect of PRAX-114 on qEEG to understand the potential pharmacodynamic effect of PRAX-114 on GABAA receptor activation. An EEG is a real-time, non-invasive measure of electrical activity of neurons in the brain. The frequency and amplitude of the detected electrical signals provide insights into brain function and brain state (*e.g.*, awake, deep sleep, etc). qEEG is a quantitative measure of the changes in brain activity in specific EEG frequency bands in response to treatment with a brain-active compound. Changes in power in the beta frequency band, specifically, are used as a pharmacodynamic biomarker of GABAA receptor activation in response to a brain active compound.

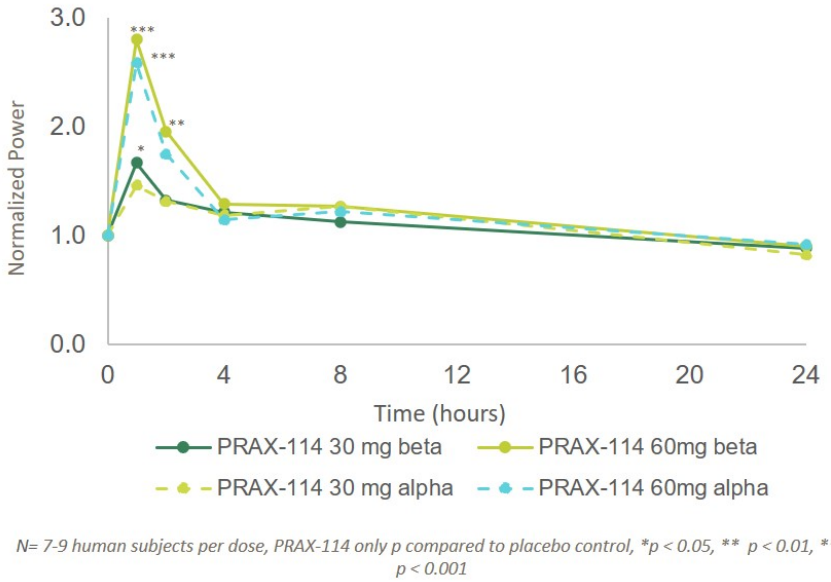
In this trial, we observed fast absorption of PRAX-114 within one to three hours of dosing and approximately dose-proportional increases in peak concentration and total drug exposure. The half-life of the drug was between 12.2 and 14.8 hours, consistent with a once-daily dosing regimen. Little or no accumulation of the drug was observed over the ranges of doses tested.

We believe that the potentially simple nightly administration of PRAX-114 with or without food is key for clinical, and, if approved, commercial success in MDD, as many patients struggle with adherence to medication and forcing a dietary regimen would impose further complications in this vulnerable population. In the food effect cohort of the MAD trial, overall drug exposure as measured by AUC of PRAX-114 increased by only 1.17-fold in the fed state versus in the fasted state. The primary effect caused by food intake was observed in the Cmax, which was 0.64-fold of that observed under fed conditions. These findings indicate that PRAX-114 may not need to be taken with food to achieve therapeutic exposures, which we believe could create a potential competitive advantage over drugs that may require administration with food to achieve consistent target exposures, and could allow flexibility to adjust to the comorbid changes in appetite and preferences of MDD patients.

We measured changes in qEEG power in our Phase 1 MAD volunteers to assess the effect of PRAX-114 on GABAA receptors in the brain on Days 1 and 14 of this trial. PRAX-114 produced marked increases in the power of the alpha and beta-frequency bands. Increases in the beta-frequency band are correlated with GABAergic activation, as previously shown by the marketed GABAA PAMs. We believe the qEEG measurements observed for

PRAX-114 were consistent with its extrasynaptic GABAA receptor preference and differentiated pharmacological profile relative to benzodiazepines and other GABAA PAMs in the class.

Moreover, the increases in alpha and beta-frequency were strongly correlated with dose and PRAX-114 levels in the blood. In these healthy volunteers at one hour post-dose on Day 1, PRAX-114 30mg resulted in an average increase in qEEG alpha and beta power of approximately 1.5-fold and 1.6-fold compared to baseline, and 60mg resulted in an increase in this measure of 2.6-fold and 2.8-fold compared to baseline, respectively (Figure 6). These increases on the qEEG alpha and beta power were sustained at Day 14. These data show that PRAX-114 engaged GABAA receptors in the brain and produced consistent increases on qEEG within the first hour after dosing with similar increases on Days 1 and 14. This finding was also consistent with the pharmacologic activity and qEEG data from our preclinical studies, where a 1.6-fold increase in beta power was associated with robust activity in animal models of anxiety and depression and was used to inform dose selection in subsequent clinical trials. Notably, PRAX-114 showed increases in beta power up to 2.8-fold without achieving a MTD or demonstrating any SAEs.



*N= 7-9 human subjects per dose, PRAX-114 only p compared to placebo control, *p < 0.05, ** p < 0.01, *** p < 0.001*

Figure 6. PRAX-114 (30mg and 60mg) showed a robust dose-dependent qEEG signal and target activation that was sustained over 14 days of dosing.

In this trial, PRAX-114 was generally well-tolerated, with no SAEs reported. The reported TEAEs were mild to moderate and were consistent with those expected for the potential mechanism of action. The most common TEAE was somnolence, which is characterized by sleepiness or drowsiness, and all events of somnolence were mild in severity. Increases in sleepiness as measured by the Stanford Sleepiness Scale occurred between one- and three-hours post-dosing, consistent with the period of peak drug concentrations; sleepiness ratings at the 60mg dose were similar to placebo within 4 hours post-dose. Other common TEAEs were dizziness and hypoaesthesia, or a diminished sense of touch. TEAEs observed in more than one subject were euphoric mood, hyperhidrosis, or excessive sweating, muscle twitching, skin irritation and fatigue. In the placebo group, we observed fatigue in 22.2% of subjects. TEAEs appearing to be dose-related were somnolence, dizziness headache, euphoric mood and hypoaesthesia. We did not observe a maximally tolerated dose, or MTD. We believe the tolerability results observed of PRAX-114 suggest the potential for a wider therapeutic window, increased adherence and a wider dose range for MDD patients.

Phase 1 pharmacokinetics bridging study

In preparation for our randomized, placebo-controlled trials in MDD, we conducted a clinical PK bridging study in which PRAX-114 was administered as a solid dose (*i.e.*, tablet) formulation in single ascending doses of 40mg, 60mg and 80mg or placebo in seventeen participants and compared to PRAX-114 suspension formulation administered at the 60mg dose. The PK of the tablet formulation was found to be comparable to the suspension formulation at the 60mg dose level. Overall, PRAX 114 showed demonstrated consistent drug exposure across a wide range of administration conditions and demonstrated a consistent AUC when administered with or without food and at different times of day, which we believe could enable once daily administration at bedtime without the need for additional patient instructions.

PRAX-114 clinical development in PTSD

We are conducting a Phase 2, placebo-controlled study evaluating PRAX-114 for the treatment of PTSD and expect to report topline results in the second half of 2022, which will guide decision making for subsequent development of PRAX-114 in the PTSD population.

Patients in the Phase 2 trial will be randomized 1:1 to receive nightly bedtime doses of PRAX-114 or placebo for 28 days in an outpatient setting, with two-weeks of additional follow up after the end of the active treatment period. Dose selection was based on similar considerations to those that informed dose selection for the Aria Study and the Acapella Study. Since it is not known whether there may be dose response differences between MDD and PTSD with this drug mechanism, a flexible-dose approach in the range that showed positive results in the Phase 2a MDD study was included in the design of this study.

Participants treated with PRAX-114 will receive 40mg on Days 1 to 14; on Day 15, those PRAX-114 participants not achieving at least a 20% reduction in PTSD symptoms, as measured by the Clinician-Administered PTSD Scale for DSM-5, or CAPS-5, total score, will receive an increase to 60mg from Days 15 to 28 unless tolerability concerns preclude a dose increase. CAPS-5 is a 30-item structured interview that is the gold standard in PTSD assessment, with versions that can be used to make a current diagnosis of PTSD and to assess PTSD symptoms over the past week. Patients will be required to be between the ages of 18 and 65, have a diagnosis of PTSD with a duration of at least six months, have a CAPS-5 total score of 30 or higher consistent with moderate-to-severe PTSD, and either currently not treated with psychiatric medications or taking no more than one antidepressant within the labeled prescribing dose range for a minimum of three months prior to screening, with the intent to remain on a stable dose throughout the trial. Participants will be excluded if they have comorbid medical or psychiatric conditions that could interfere with the scientific objectives or safety of the trial. The primary efficacy endpoint in this study is the change from baseline in the CAPS-5 total score after 28 days of treatment. A key secondary endpoint will be change from baseline in the CAPS-5 score after 14 days of treatment to assess the rapidity of onset of the treatment effect of PRAX-114 in PTSD. We expect to employ similar clinical trial quality interventions to those summarized above for the Aria Study and the Acapella Study.

PRAX-114 preclinical data

In our preclinical studies of PRAX-114, we evaluated translational pharmacodynamic biomarkers to inform clinical development. In our rat translational biomarker model, we administered PRAX-114 to wild-type rats at doses ranging from 1 to 20mg/kg to assess the impact on power in the beta frequency band. We found that PRAX-114 dose-dependently increased the power in the beta frequency band and these changes correlated with changes in plasma pharmacokinetics. This EEG biomarker was used to inform dose-selection for PRAX-114 clinical studies. In our preclinical studies, doses (and plasma/brain concentrations) that induced a 1.6-fold increase in the beta frequency power in rats were associated with both robust preclinical activity in animal models of depression and

anxiety and good tolerability. Specifically, the PRAX-114 dose was estimated to induce a 1.6-fold increase in EEG beta power activity in rats led to activity in the rat WKY model of depression and the window between that dose that increased beta power by 1.6-fold increase in EEG and the dose that caused a 50% reduction of spontaneous locomotion in the sLMA sedation assay, or ED_{50}, was ~11-fold, based on brain concentrations. In addition, at this brain concentration, PRAX-114 showed activity and was generally well-tolerated in animal models of anxiety including conditional emotional response, or CER, punished drinking, or Vogel, and elevated plus maze, or EPM (Figure 7).

In the figure below, the lower bound of the preclinical activity in animal models and EEG bars are determined by the brain exposure at the lowest dose at which significant activity was observed ($p < 0.05$). The lower bound of the tolerability bar represents the TC_{50} in the brain. The upper bound represents the mean brain concentration at the highest dose tested in a given assay.

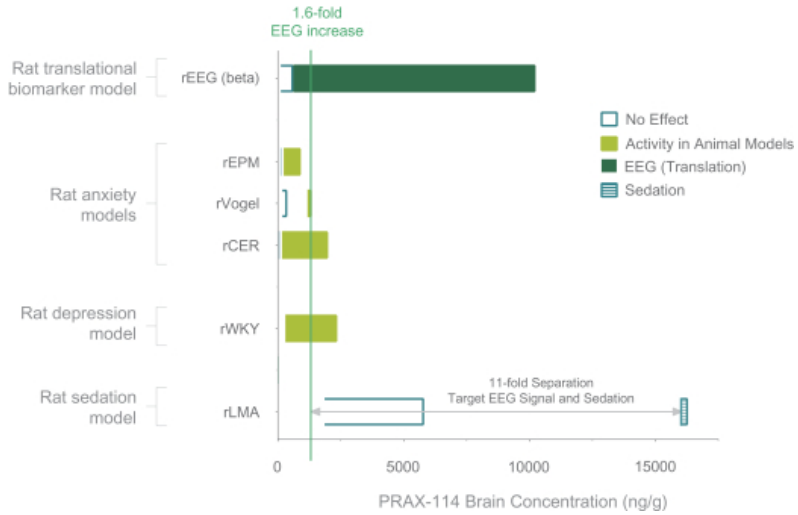


Figure 7. Summary of PRAX-114 preclinical data.

MOVEMENT DISORDERS

Our Movement Disorders franchise is currently focused on the two most prevalent movement disorders, ET and PD. We are developing PRAX-944, a potentially differentiated selective small molecule inhibitor of T-type calcium channels, and PRAX-114 for the treatment of ET, with the goal of allowing patients to fit the right therapy to their needs and on an as-needed or chronic basis. ET is the most common movement disorder, affecting up to seven million patients in the United States, and is a disease associated with debilitating action tremors triggered when a patient voluntarily attempts to move. There is a high unmet need for patients given limited treatment options, with only one approved pharmacotherapy that offers limited efficacy and poor tolerability.

For PRAX-944, there is a large body of clinical, preclinical and genetic evidence that points to the involvement of T-type calcium channels in the cerebello-thalamo-cortical, or CTC, circuit, as a main driver of ET. We have designed our development program to include clinical endpoints assessing how a patient feels and functions, a modified release formulation designed to provide a blunted Cmax for tolerability and sustained exposures throughout the day, and dose titration strategy to optimally reach therapeutic levels. We believe the design of PRAX-944, coupled with its modified release formulation, positions it for development as a differentiated therapy in ET. We intend to initiate a registrational study for PRAX-944 for the treatment of ET, pending receipt of positive topline results from the Phase 2b randomized controlled dose-range finding Essential1 Study, which are expected in the second half of 2022. For PRAX-114, the GABA neurotransmitter system is hypothesized to play an important role in ET, and several available treatment options appear to work via GABAergic mechanisms directly or indirectly (primidone, topiramate, propranolol). In the PRAX-114 Phase 2 placebo-controlled, crossover study for the treatment of ET, we intend to evaluate whether there is an appropriate dose of PRAX-114 for daytime administration that enables reduction in tremor without somnolence or sedation that will guide decision making for subsequent development of PRAX-114 in the ET population.

We are also developing PRAX-944 as a potential non-dopaminergic therapy for PD. T-type calcium channels in the CTC are also implicated in the modulation of motor circuits in PD and there is preclinical evidence which suggests blocking T-type calcium channels may support improvement of motor activity in PD models. We intend to initiate a Phase 2 POC study of PRAX-944 for the treatment of PD in the second quarter of 2022 to evaluate motor function improvement in patients and subsequently determine development and regulatory pathways. Because of the gatekeeper role of T-type calcium channels in regulating neuronal firing patterns in multiple neuronal circuits, we believe PRAX-944 is suitable for potential development across a wide range of indications and potentially sizable expansion opportunities in addition to ET.

For the treatment of ET with PRAX-944, we have evaluated the safety and tolerability in approximately 200 healthy volunteers and patients in seven completed and two ongoing studies. We are conducting the Essential1 Study to evaluate the tolerability, safety and efficacy of PRAX-944 in adults with ET. We have also completed enrollment in a two-part open-label Phase 2a proof-of-concept trial in ET patients. Data from six patients from Part A showed tremor reduction and that PRAX-944 was generally well-tolerated at one and two weeks in patients dosed up to 40 mg once daily, which compared favorably to historical placebo response. Based on the Part A data and the observed safety results in the healthy volunteer titration study, we added a second cohort, Part B, to the Phase 2a trial in which patients are being titrated to a dose of up to 120mg/day of PRAX-944. We have also included a randomized, double-blind, placebo-controlled withdrawal phase to Part B, during which participants will either be maintained on their final open-label dose or switched to placebo. Preliminary open-label data as of December 10, 2021 from nine evaluable subjects in Part B showed favorable trends in tremor reduction and activities of daily living, or ADLs, in doses up to 120mg/day. We plan to report topline results for Part B in the second quarter of 2022, including both open-label and placebo-controlled, randomized withdrawal results. We have also studied the safety of PRAX-944 modified release formulation with titration up to 120mg/day and no MTD has been identified.

We expect to initiate a Phase 2 study evaluating daytime administration of PRAX-114 in ET patients in the first quarter of 2022. The objective of this trial is to evaluate the safety, tolerability, PK and efficacy of PRAX-114 in the treatment of adults with ET. The trial is comprised of two parts: Part A and Part B. Part A is a randomized, double-blind, placebo-controlled, three-period crossover design where all participants will receive a single dose of 10mg of PRAX-114, 20mg of PRAX-114, and matching placebo across three dosing days. Part B is an open-label design where participants from Part A may receive either 10mg PRAX-114 for 28 days, or 10mg PRAX-114 for 14 days and then 20mg PRAX-114 for 14 days. Topline results are expected to be reported in the second half of 2022. The doses of 10mg and 20mg PRAX-114 were chosen based on pharmacological activity observed in clinical trials with healthy participants and clinical experience, to balance the known impact of GABAergic molecules on somnolence and sedation in older patients with ET. Our PK-PD modeling predicts pharmacodynamic activity at concentrations resulting from daily administration of 10 and 20mg PRAX-114, hypothesized to be predictive of efficacy in ET based on preclinical harmaline-induced tremor data. Additionally, data in healthy volunteers at 20mg during the day suggested a tolerable profile when assessed using the Stanford Sleepiness Scale, or SSS. Thus, the selected dose levels present a favorable benefit/risk profile in ET based on the overall interpretation of the preliminary preclinical efficacy data, clinical PK and safety data (including safety AEs, SSS and EEG), qEEG biomarker data, and nonclinical safety data.

Essential Tremor

ET is characterized by involuntary rhythmic movement in the upper limbs, with or without tremor in other body locations such as the head, vocal cords, or legs. ET is a daytime disease associated with debilitating tremors triggered when a patient voluntarily attempts to move. These tremors significantly disrupt daily living and are progressive in nature, with increases in tremor severity and amplitude commonly observed over the course of the disease. ET is a heterogeneous disease with a range of patient characteristics including a variety of comorbidities, range of age, severity, and impact on daily living including psychosocial aspects.

Despite the prevalence and significant disease burden of ET, only approximately two million people in the United States are diagnosed with ET and only approximately one million are actively treated, based on U.S. healthcare claims data as of 2019. We believe that the low treatment rate is due to limitations in efficacy and tolerability of the existing treatment options, and that the treated population could increase with the availability of new therapies with improved efficacy and tolerability that allow for patients to stay on therapy longer and more patients to start therapy sooner. There have been no approved pharmacotherapy products designed to treat ET and the two current products commonly used offer limited efficacy and poor tolerability, resulting in treatment delays and high discontinuation rates. Propranolol, approved by the FDA in 1967, remains the only approved therapy for ET in the United States. A non-selective beta blocker, propranolol is contraindicated for individuals with certain respiratory or cardiac issues, which are common comorbidities in the age group affected by ET. Primidone, an anticonvulsant, is used off-label and can cause sedation and balance issues while accelerating osteoporosis with long-term use.

As a last line therapy, several thousand ET patients in the United States opt for invasive surgery each year. Interventions include gamma knife and focused ultrasound thalamotomy, where part of the thalamus involved in the CTC circuit is ablated, or deep brain stimulation, or DBS, where an electrode is implanted into the brain. These procedures are generally effective, but are associated with significant side effects and risk. Therefore, many patients who are eligible for surgical therapies elect to not have these procedures.

Genetics of Essential Tremor

Our rationale for approaching ET through inhibition of T-type calcium channels is rooted in the genetics of epilepsy. CACNA1G, a gene that encodes for a particular isoform of T-type calcium channels, is one of the most significantly associated genes for generalized genetic epilepsy, or GGE. Some of these epilepsy patients also suffer from comorbid movement disorders such as tremor and ataxia. The odds of observing a T-type calcium channel mutation in the GGE population is nine times of that of the healthy population. This supports the key role of T-type calcium channels in maintaining excitation and inhibition balance.

Additional human genetic data provide evidence for the role of T-type calcium channels in movement disorders. Whole exome sequencing of early-onset familial ET patients also identified mutations in CACNA1G that segregated with the tremor phenotype in multiple family pedigrees. The importance of T-type Ca++ channels to the function of the CTC circuit is highlighted by variants in the CACNA1G gene which are associated with rare cases of pediatric cerebellar atrophy. Additionally, mutations in the T-type calcium channel have also been reported as causative of a form of spinocerebellar ataxia. We believe this genetic link, along with the preclinical and clinical evidence, support the role of T-type calcium channels in the pathophysiology of ET.

Role of T-type calcium channels in ET

T-type calcium channels function as the gatekeepers of neuronal firing patterns, controlling the switch between tonic and burst firing in the CTC circuit. The CTC circuit is a series of brain nuclei or neuron clusters, including the inferior olivary nucleus, cerebellar Purkinje cells, deep cerebellar nuclei, ventral motor thalamus and motor cortex, which work together in regulating coordinated movements and when disrupted generate tremor. All nuclei in this circuit contain pacemaker cells with inherent burst firing capability and express T-type calcium channels, which are known drivers of oscillatory burst firing.

T-type calcium channels are low voltage activated channels that respond to weak depolarization of neuronal membranes and are quickly inactivated (a closed state where the channel cannot be reopened for some time). The opening of T-type calcium channels leads to membrane depolarization, which activates voltage-activated sodium channels, leading to the formation of an action potential and neuronal firing. When only a small number of T-type calcium channels are activated, leading to small T-type calcium channel mediated membrane depolarizations, the neuron generally generates unitary action potentials, also called tonic firing. When the activity of T-type calcium channels is increased, either due to genetic mutations or other changes in network activity that recruit more T-type calcium channels, a longer lasting depolarization is generated, resulting in high-frequency clusters of sodium channel driven action potentials, also called burst firing, as illustrated in Figure 8 below.

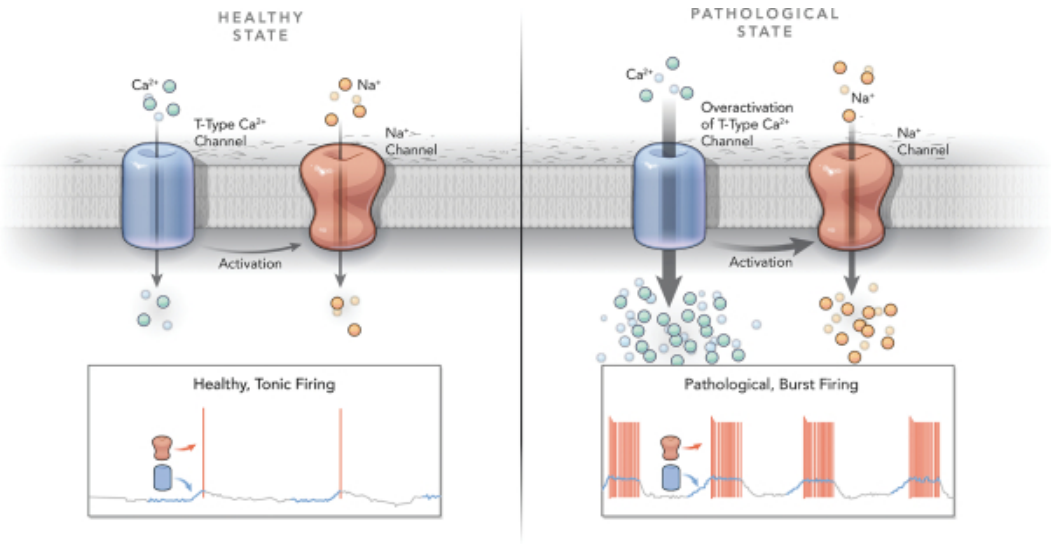


Figure 8. T-Type calcium channels are gatekeepers of neuronal firing patterns.

Neuroimaging and neurophysiology studies in ET patients have consistently demonstrated that individual nuclei along the CTC circuit oscillate at the same frequency as the tremor and with strong coherence among the brain regions and movement in the affected muscles. Further, intraoperative real-time single-unit recordings of action potentials of individual neurons in the ventral motor thalamus of severe ET patients receiving DBS implants, in periods with and without tremors, further substantiates the central role of the CTC circuit and T-type calcium channels in ET. When no tremor was observed at rest, tonic firing was recorded in neurons of the ventral motor thalamus. During tremor, the same neurons fire in rhythmic bursts that are highly coherent with tremor activity. Furthermore, the emergence of action tremors coincided with the emergence of burst firing. Lesioning or DBS of the ventral motor thalamus has been shown to silence the oscillatory burst firing activity in the CTC circuit, resulting in significant tremor reduction. The strong temporal coordination between the tremors and burst firing, a neuronal firing pattern frequently gated by T-type calcium channel activity, strongly suggest that pharmacological inhibition of these channels may represent an effective pharmacological approach in ET.

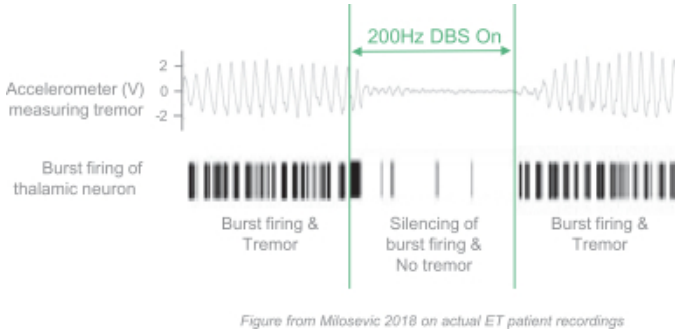


Figure 9. Thalamic neuron burst firing correlated with tremor activity in ET patients.

The role of the CTC circuit and T-type calcium channels has been further observed in animal models. A known pharmacological tremor model utilizes administration of harmaline, an alkaloid toxin, to animals. Harmaline, on administration to experimental animals such as rodents, induces an acute action tremor as well as rhythmic burst-firing activity in the CTC circuit similar to that observed in ET patients. We believe this model carries clinically predictive value, as compounds that improve tremor in ET patients clinically (*e.g.*, propranolol, primidone) have also been shown to reduce harmaline-induced tremor preclinically; in contrast compounds that worsen tremor in patients (*e.g.*, caffeine) also worsen tremor in this model. Similar to observations in ET patients, normalizing oscillatory

activity in the CTC circuit, for example with DBS, reduces harmaline induced tremor in rodents. Pharmacological inhibition or genetic knockout of T-type calcium channels led to resistance to harmaline-induced tremor.

Role of GABAA in ET

The GABA neurotransmitter system is hypothesized to play an important role in ET, and several available treatment options appear to work via GABAergic mechanisms directly or indirectly (primidone, topiramate, propranolol). Studies in patients with ET have shown a reduction in GABA receptor binding capacity using positron imaging that also correlated with disease severity and a loss of GABAergic cerebellar Purkinje neurons in postmortem tissue that contributes to overall reduced inhibitory output from the cerebellum. In animal models of harmaline-induced ET, the hypothesized reduction of GABAergic activity can be reversed with GABAA receptor modulation using benzodiazepines and other compounds that act at both synaptic and extrasynaptic GABAA receptors as well as NAS GABAA-PAMs that activate both synaptic and extrasynaptic GABAA receptors. In addition, extrasynaptic GABAA receptor activation using highly selective agonists like THIP/gaboxadol, has been demonstrated to reduce tremor in the same model. These data suggest that therapeutics that possess preferential extrasynaptic GABAA receptor activity, like NAS, may have greater efficacy in ET than molecules that primarily activate synaptic receptors (*e.g.*, benzodiazepines).

Parkinson's Disease

PD is a debilitating neurodegenerative disorder with about one million diagnosed patients in the United States and about 10 million worldwide. Approximately 60,000 patients are diagnosed with PD each year in the United States alone.

PD is characterized by slow movement (bradykinesia), in combination with either rest tremor and/or rigidity. Symptoms progress over time in severity and eventually affect both sides of the body, often impairing ADLs such as dressing and eating. Non-motor symptoms, such as impaired smell, sleep disorders, gastrointestinal symptoms and psychiatric disorders like depression also play a pivotal role in the daily life of PD patients.

Degeneration of dopaminergic neurons in the mid-brain (specifically pars compacta of the substantia nigra, or SNc) results in loss of dopaminergic output. Thus, the cornerstone of treatment for PD has been dopaminergic replacement therapy. L-dopa, or levodopa, a formulation of replacement dopamine, is considered the standard treatment of PD. Levodopa has been shown to be highly effective in improving symptoms of bradykinesia and rigidity, but has a variable impact on tremor. Other common PD medications mainly reduce dopamine metabolism or are dopamine receptor agonists. As the neuronal degeneration progresses, higher and more frequent levodopa is required due to diminishing responses to dopaminergic medication and an inability to store excess dopamine.

While chronic dopaminergic therapy is effective, it can result in distressing side effects of motor fluctuations (wearing off) and levodopa-induced dyskinesias, impulse control disorders, and psychosis. These side effects are disabling and, at times, more severe and distressing than the PD symptoms themselves. Patients may also opt for a more invasive procedure to deliver continuous dopamine stimulation with levodopa-carbidopa enteral suspension to continuously control motor fluctuations and dyskinesias. Thus, symptom management using non-dopaminergic therapeutics that have a better safety and tolerability profile are needed. Adjunctive therapies that alleviate PD symptoms could also indirectly reduce the need for dose escalations of dopaminergic therapies and thus lower the risk of side effects.

Advanced therapies, such as DBS, can be very effective for treating for tremors and motor complications by modifying basal ganglia function downstream of the nigrostriatal pathway. Depending on the patient’s specific symptoms, DBS electrodes can be placed in either the globus pallidus interna, or gPi, nucleus ventralis intermedius, or VIM, of the thalamus, or the subthalamic nucleus, or STN, and may be affecting aberrant burst firing in these areas.

DBS is typically reserved for those patients who respond to dopaminergic therapy like levodopa but have residual symptons despite best medical management . Further, DBS carries significant risks associated with brain surgery, including intracerebral hemorrhage, infection, hemiparesis and cognitive decline. The prospect of neurosurgery in later years is often overwhelming or contraindicated (*e.g.*, due to presence of cognitive impairment), and many patients are not treated with DBS. Thus, we believe there is a clinical need for a pharmacological therapy that could mimic the effects of DBS and modulate burst firing downstream of SNc.

Role of T-type calcium channels in PD

Animal models and human PD patient data from third-party studies demonstrate that degeneration of nigral dopaminergic neurons converts the subthalamic nucleus, or STN, from a tonic firing to an aberrant bursting phenotype. This bursting activity drove symptoms of bradykinesia and rigidity in animal models and excessive

activation of T-type Ca2+ channels has been shown to underlie this phenotype. T-type Ca2+ channels are expressed widely throughout the brain, including in the STN. Eliminating this burst firing through blockade of T-type Ca2+ channels has been shown to improve motor function in a 6-hydroxydopamine (6-OHDA) rat model of PD. Thus, we believe an inhibitor of T-type Ca2+ channels could offer a non-surgical and non-dopaminergic treatment option to alleviate motor symptoms in PD.

PRAX-944 in Essential Tremor

We believe that our PRAX-944 program has several potential advantages in development for ET:

- **Wide Therapeutic Window**: We are currently studying PRAX-944 across a wide range of doses, ranging from 5mg to 120mg. Our goal is to find the appropriate dose(s) to meet the needs of different patients and help address a larger market by tailoring PRAX-944 to the key unmet need in ET as well as individual patient needs. Importantly, no MTD has been identified to date.
- **Simple Daytime Dosing**: We believe the ability to administer one-time daily dose is important for reducing the burden for ET patients that are treated chronically. These patients are typically older and with multiple comorbidities where simplicity is important when adding medications.
- **Modified Release Formulation**: We believe that PRAX-944 has the potential to provide a more attractive treatment option for ET patients due to its modified release, or MR, formulation, along with a wide potential therapeutic window that could allow for up-titration. We have observed that the MR formulation, which released approximately 80% of the drug product over seven hours in vitro, reduced the maximum plasma concentration and delayed the tmax without meaningfully impacting the overall AUC. We have also observed that this formulation resulted in improved tolerability relative to an immediate release, or IR, formulation and sustained targeted concentrations throughout the day.

PRAX-944 clinical development in ET

Phase 2b Essential1 Study in patients with ET

We are conducting the Essential1 Study to evaluate the safety and efficacy of titration to PRAX-944 20mg, 60mg or 100mg with the objective of identifying the dose for a registrational study. Participants in the Essential1 Study will be randomized to receive either 56 days of treatment with one of three PRAX-944 dose levels or placebo every morning. Fixed titration regimens will be used. The primary objective of this trial is to assess for the presence of a tolerability dose-response signal over 56 days of dosing in ET participants with moderate-to-severe tremor. A secondary objective is to identify a potential dose-response profile for PRAX-944 with respect to efficacy outcomes. This trial will also assess innovative approaches to objectively measure tremor in ET participants and will include a sub-study with a wearable device. Together, these data, if supportive, are expected to enable dose selection for subsequent Phase 3 trials. Topline data from this trial is expected to be reported in the second half of 2022.

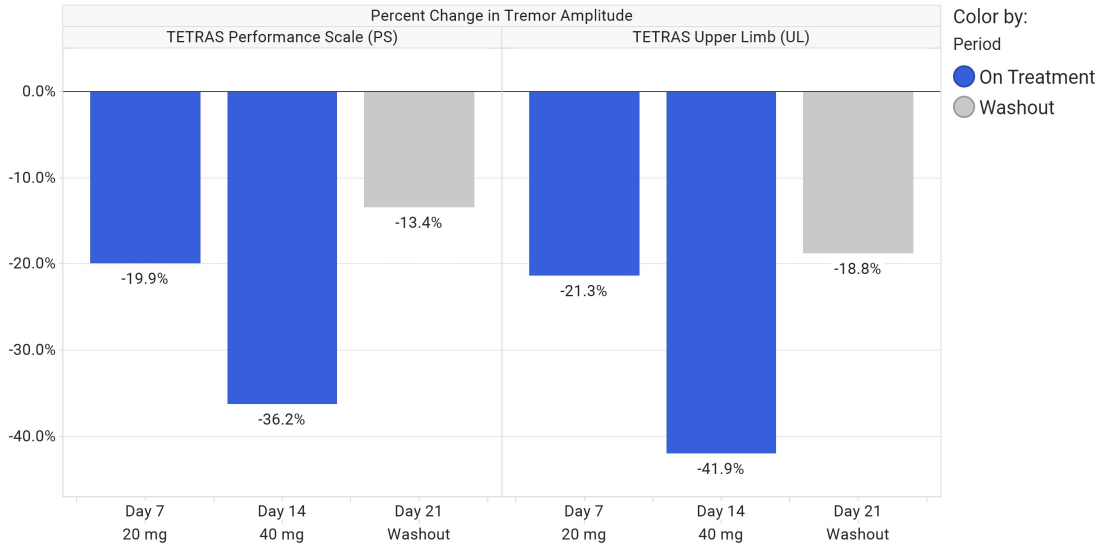
Phase 2a trial in patients with ET

We are currently in the second of two cohorts of our Phase 2a POC open-label trial evaluating safety and efficacy in patients titrated up to 120mg per day. In the first cohort, Part A, participants received 20mg daily dosing of PRAX-944 for one week followed by 40mg daily dosing for the second week, taken in the morning. We have completed enrollment in an additional cohort, Part B, of ET patients dosing up to 120mg for up to 42 days.

We are measuring changes in tremor with different, complementary approaches including components of the Essential Tremor Rating Scale, or TETRAS, Performance Scale and accelerometry. We are using change from baseline in the rating of upper limb, or UL, items of the TETRAS as the primary efficacy outcome in this proof-of-concept trial because all ET patients suffer from UL tremor. As the UL items drive most of the score on the overall TETRAS and are more reliably rated than other items on the scale, we expect them to have the best signal to noise ratio. UL items have also been the basis of the most recent regulatory approval of neurosurgical treatments for severe ET. We have established rigorous procedures for training and for blinded scoring of efficacy, including using centralized video assessment as an exploratory endpoint, with randomization of the videos and masking to allow for rating concordance. We have also included the overall TETRAS performance scale, or TETRAS-PS, (both site and central video rating) and Kinesia ONE accelerometer (an objective measure of tremor), clinical global impression of severity and improvement, or CGI-S and CGI-I, respectively, and the patient global impression of change, or PGI-C, as secondary endpoints to assess consistency of response across different endpoints.

In this trial, we are enrolling participants with well-established ET, as defined by the Movement Disorders Society Task Force for Tremor as an isolated tremor syndrome of bilateral UL action tremor with at least three years' duration. In Part A, tremor severity was evaluated before drug administration, after daily morning dosing of

PRAX-944 20mg for seven days (Day 7), following daily administration of PRAX-944 40mg for seven additional days (Day 14) and one week after administration of PRAX-944 has been stopped (Day 21). Data available from six participants who completed Part A of the trial and received PRAX-944 doses of 20mg followed by 40mg each for seven days is shown in Figure 10 below. Preliminary site (primary endpoint measure) and central video assessments of participants TETRAS-PS in this cohort showed generally stable tremor severity between screening and baseline visits. The primary endpoint change suggests dose dependent tremor reduction on the TETRAS-UL, and this change was consistent with the central video assessment. Importantly, five of the six participants remained on propranolol in this study, suggesting that PRAX-944 could also be developed as an adjunctive treatment. Similar patterns of improvement were also observed in the full TETRAS-PS, and Kinesia ONE accelerometry scores. The site and central ratings were strongly correlated on the TETRAS-UL and TETRAS-PS with r values of 0.8 and 0.83, respectively.



*As TETRAS PS items are rated on a logarithmic scale, the Weber-Fechner law was used to calculate the percent change in tremor amplitude according to the equation presented in Elble (2018).

Figure 10. Percent change from baseline in tremor amplitude as measured by site ratings of the TETRAS PS and Upper Limb subscale in Part A of the ET OL study (N=6).

In Part A, the dose levels were generally well-tolerated. No SAEs and no severe AEs were observed. The majority of AEs were mild, transient and resolved without intervention. Six out of seven participants completed dosing per protocol. One participant discontinued on Day 8 due to anxiety. This participant was also non-compliant with the protocol, stopping propranolol on Day 3 of dosing without consulting study staff. Due to this protocol deviation which would have impacted this participant's TETRAS scores, this participant was included in the safety analysis but not in efficacy analysis. No clinically significant ECG or laboratory abnormalities were reported.

We are currently conducting Part B of the Phase 2a clinical trial, titrating up to 120mg in an open-label fashion for 42 days following by a randomized, double-blind, placebo-controlled withdrawal phase, where participants will either be maintained on their final open-label dose or switched to placebo. The goals of the randomized withdrawal are to obtain blinded evidence of any potential effect from the open-label titration and to assess for durability of any such effect. In addition, the TETRAS activities of daily living sub-scale was added to the efficacy endpoints. In December 2021, preliminary data from twelve participants in Part B were presented. Figure 11 shows preliminary open-label data from nine evaluable subjects in Part B demonstrating favorable trends in tremor reduction in doses up to 120mg/day as of December 10, 2021, as measured by percent change from baseline in UL tremor amplitude measured with the TETRAS scale.

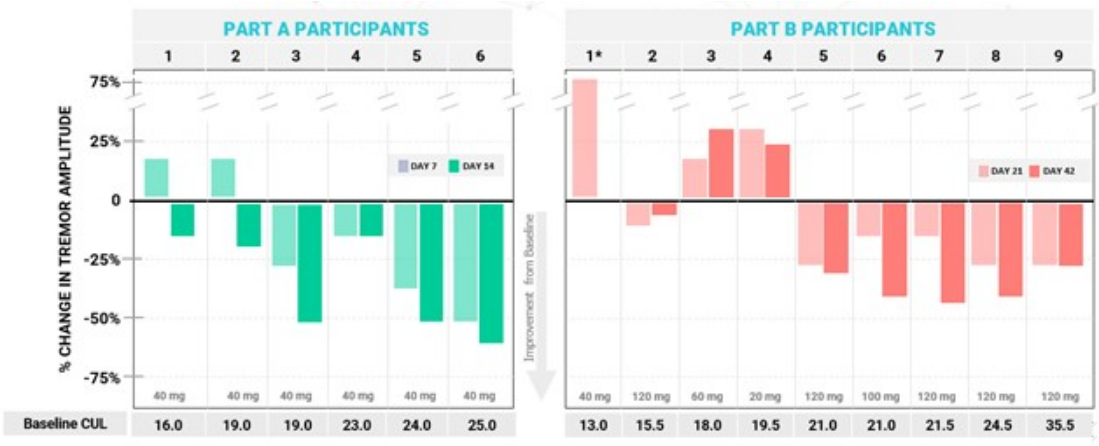


Figure 11. Individual participant percent change from baseline in UL tremor amplitude in Part A (left panel) and the open-label component of Part B (right panel).

Moreover, participants in Part B who had a reduction in their UL tremor as of December 10, 2021 were generally noted to have improvements on the TETRAS activities of daily living subscale (Figure 12). Participants with more severe tremor at baseline generally showed greater improvement in both tremor and ADLs with PRAX-944 treatment, which was consistent with the floor effects seen in the TETRAS scale and challenges with visual estimation of tremor.

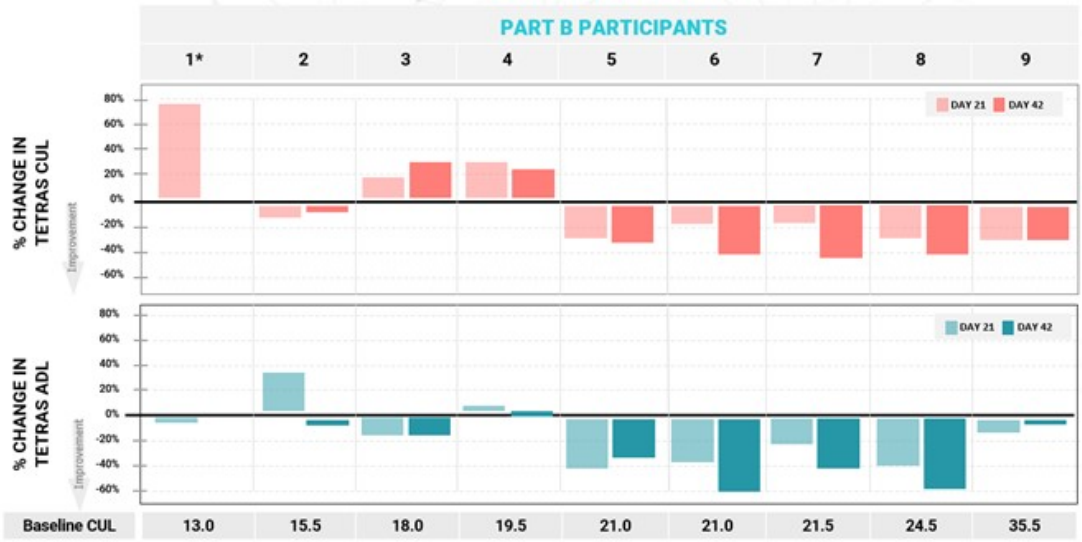


Figure 12. Individual participant percent change from baseline in UL tremor amplitude (upper panel) and activities of daily living subscale (lower panel) in the open-label component of Part B.

PRAX-944 was generally well-tolerated with no SAEs and no physical exam, laboratory, ECG or CSSRS abnormalities as of December 10, 2021. In Part B, one participant discontinued at 20mg due to an AE, one participant withdrew after Day 21 assessment at 40mg due to an AE, and two participants at the same site discontinued at 20mg but had protocol violations related to eligibility. Additionally, in Part B, there were four AEs leading to dose down-titration. TEAEs leading to dose down-titration or discontinuation were mild-moderate. Participants not tolerating dose escalation have been able return to a lower dose level and continue the study.

Phase 1 trials in healthy volunteers using MR formulation

We conducted a Phase 1 multiple dose trial of the MR formulation of PRAX-944 in England. Doses of 20mg and 40mg were generally well-tolerated over 8 days. AEs were transient and occurred at a rate similar to placebo. The most common TEAEs were somnolence, headache, dizziness, fatigue, hot flashes, and nausea. We also observed ECG application site rash, EEG application site skin reaction, blurred vision, thermal burn (accidental), euphoric mood, vomiting, and dry throat. All TEAEs were mild to moderate.

A single dose of 60mg was not tolerated in the single dose trial due to reports of nausea in five of six subjects and vomiting in three of six subjects. In the multiple dose 20mg and 40mg groups, three subjects reported nausea with one subject also reporting vomiting; these events were mild in severity and resolved on Day 1 of dosing. No subjects reported nausea or vomiting after Day 1 of dosing. While a single dose of 60mg was not well-tolerated, the average peak drug levels (138ng/mL) observed in the 40mg group after eight days of treatment were greater than those seen with the single 60mg dose (130ng/mL) on Day 1 (Figure 13). Improved tolerability observed at higher concentrations following repeated dosing suggests that titration to higher doses might be a viable strategy to further improve the tolerability profile.

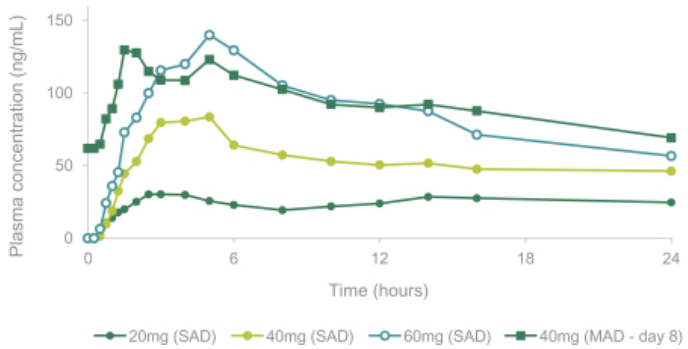


Figure 13. Sustained exposures were observed for the MR formulation of PRAX-944.

Quantitative EEG studies in healthy volunteers were used to assess the pharmacodynamic effect of PRAX-944 on T-type calcium channels in the brain. One frequency band known to be driven by T-type calcium channel activation is the sigma frequency band (11 to 15 Hz) during non-rapid eye movement sleep, or NREM sleep. T-type calcium channels expressed in thalamic neurons are critically involved in the generation and modulation of these rhythmic thalamocortical oscillations during NREM sleep.

In our preclinical studies, dosing of normal rats with PRAX-944 led to robust and dose-dependent changes in EEG activity. Because similarly robust sigma frequency band changes after dosing with PRAX-944 were observed during NREM sleep in rats and humans, our hypothesis is that the inhibition of this EEG signal can be used as a pharmacodynamic biomarker. Because the doses at which EEG changes observed in rats were similar to those that demonstrated activity in a preclinical model of essential tremor, or the harmaline model, we believe that this EEG biomarker can be used to estimate the dose of PRAX-944 that we believe will be most likely to produce a therapeutic effect in patients with ET.

In our Phase 1 trial, 20mg and 40mg doses of PRAX-944 administered to healthy volunteers produced changes in the qEEG recordings of the sigma frequency band during NREM sleep consistent with those observed in rats (Figure 14). These results suggested that PRAX-944 reached target levels in the brain needed to inhibit T-type calcium channels. Based on the overlap of these EEG changes with drug levels showing activity in the preclinical harmaline model, we believe that 20mg and 40mg doses of PRAX-944, which were generally well-tolerated in healthy volunteers without titration, have the potential to reduce tremor in patients with ET.

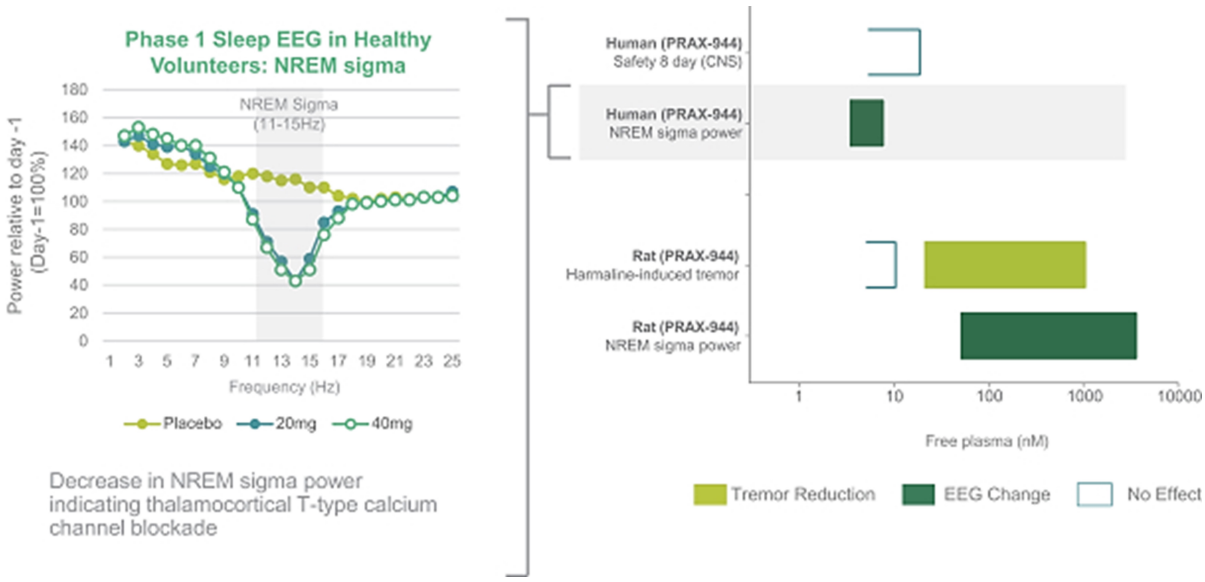


Figure 14. Exposures of PRAX-944 that decreased sigma band activity were generally well-tolerated in healthy volunteers and were associated with harmaline tremor reduction.

Titration trial in healthy volunteers

Considering that improved tolerability is the key unmet need in ET and that existing data suggest that titration is a viable strategy to improve PRAX-944's tolerability, we explored titration in a two-part healthy volunteer study. In Part A, a 5mg PRAX-944 tablet was assessed for low-dose pharmacodynamic effects in an open-label titration paradigm from 5mg up to 20mg daily. In Part B, PRAX-944 was titrated from 20mg up to 120mg daily, to assess the safety, tolerability and pharmacodynamic activity of higher doses. Participants were randomized to PRAX-944 or placebo in a 3:1 ratio, starting at 20mg daily in the morning and titrated at 20mg increments up to 120mg daily with up to one week in between each dose increment to achieve steady-state plasma concentrations and for the collection of safety data. The total dosing duration was 31 days.

The safety data demonstrated that with titration, PRAX-944 was generally well-tolerated up to 120mg daily. There were no SAEs and no severe AEs. The majority of AEs were mild, transient and resolved without intervention (Figure 15). There were no treatment-related ECG or EEG abnormalities. Safety laboratory values were generally within normal limits and there were no dose dependent excursions from the normal range. One of 12 participants randomized to PRAX-944 discontinued due to a TEAE. This participant dropped out after one dose (20mg) due to symptoms the participant described as similar to a prior panic attack (not reported at screening). Vital signs, physical examination, clinical laboratory tests, and ECG parameters were all within normal limits for this participant. The symptoms self-resolved.

Importantly, no MTD was identified. Analyses showed pharmacodynamic changes consistent with those seen in the previous Phase 1 trial described above, and showed similar changes in sigma EEG power during NREM sleep across the dose range up to 120mg/day (Figure 16).

MedDRA Preferred Term	Placebo (N=4) n (%)	PRAX-944 20mg qAM (N=12) n (%)	PRAX-944 40mg qAM (N=11) n (%)	PRAX-944 60mg qAM (N=11) n (%)	PRAX-944 80mg qAM (N=9) n (%)	PRAX-944 100mg qAM (N=8) n (%)	PRAX-944 120mg qAM (N=8) n (%)	PRAX-944 Overall (N=12) n (%)
Participants with at least 1 TEAE	**3 (75.0%)**	**5 (41.7%)**	**3 (27.3%)**	**5 (45.5%)**	**2 (22.2%)**	**6 (75.0%)**	**2 (25.0%)**	**12 (100%)**
Dizziness	0	0	2 (18.2%)	0	1 (11.1%)	0	0	3 (25.0%)
Medical device site dermatitis	2 (50.0%)	1 (8.3%)	0	1 (9.1%)	0	1 (12.5%)	1 (12.5%)	3 (25.0%)
Chest discomfort	0	1 (8.3%)	1 (9.1%)	0	0	0	0	2 (16.7%)
Dry throat	0	0	1 (9.1%)	0	1 (11.1%)	0	0	2 (16.7%)
Feeling drunk	0	2 (16.7%)	0	0	0	0	1 (12.5%)	2 (16.7%)
Headache	2 (50.0%)	1 (8.3%)	0	1 (9.1%)	0	0	0	2 (16.7%)
Palpitations	0	2 (16.7%)	0	0	0	0	0	2 (16.7%)

Source: PRAX-944-105, Draft Table 14.3.1.3.2
Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities; TEAE=treatment emergent adverse events
Note: 4 participants randomized to PRAX-944 group did not complete the planned dosing. Only 1 out of these four dropped out due to a treatment related AE. 1 participant had an unrelated AE and 2 dropped out for non-safety reasons

Figure 15. TEAEs Occurring in at least two participants in a dose group or overall.

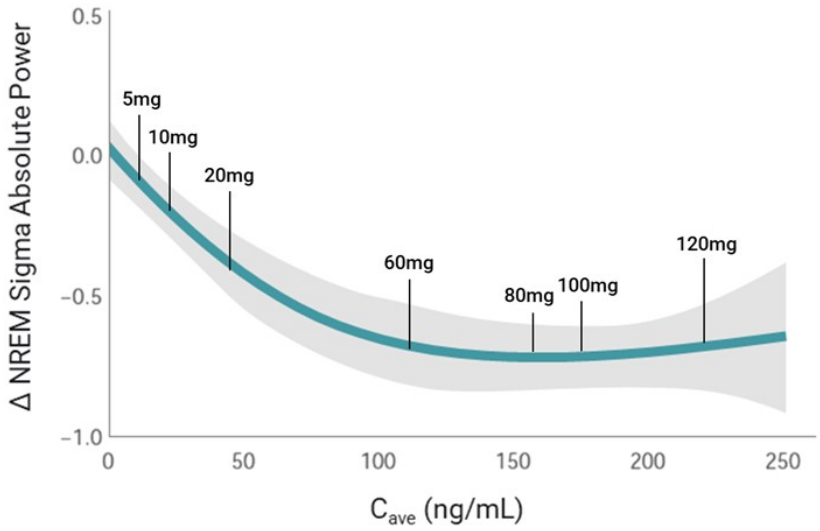


Figure 16. Dose and concentration dependent pharmacodynamic effects on sigma band (11-15 HZ) EEG power in the PRAX-944-105 study.

Phase 1 study to explore shorter titration schemes

We completed a single-center, multi-part, Phase 1, randomized, double-blind, placebo-controlled clinical trial in which we assessed the safety, tolerability, and PK of a more rapid PRAX-944 titration scheme up to 120mg in healthy male and female participants aged 18 to 54 years (Part A) and 55 to 75 years (Part B). We observed no new safety signals and PK results were consistent with what we previously reported.

Preclinical support for advancing PRAX-944

In preclinical studies, PRAX-944 inhibited all three human T-type calcium channel isoforms, CaV3.1, CaV3.2 and CaV3.3, and has demonstrated high selectivity against L and N-type calcium channels, or CaV1.2 and CaV2.2, respectively, and other key ion channels important for normal physiology, such as the cardiac potassium channel human Ether-à-go-go-Related Gene, or hERG, and the voltage gated sodium channel NaV1.5. Robust selectivity and potency have been demonstrated across both exogenously expressed recombinant channels in a human cell line and naïve channels in isolated dorsal root ganglion, or DRG, neurons from rats using electrophysiological techniques.

Consistent with the gatekeeper role of T-type calcium channels in neuronal firing patterns, a gain of function mutation of the T-type calcium channel CaV3.2 leads to pathological burst firing in thalamic neurons in a rat model known as the GAERS model. Administration of PRAX-944 resulted in complete suppression of the pathological burst-firing in thalamic neurons derived from the GAERS model.

We evaluated the therapeutic potential of PRAX-944 to treat ET using the harmaline-induced tremor model in rats. Administration of harmaline triggers ET-like tremors in experimental animals as well as pathological burst firing throughout the CTC circuit. We observed a large and dose-dependent decrease of harmaline-induced tremor in rats treated with PRAX-944 as compared to vehicle-treated animals, when measured as percent increase of tremor from pre-harmaline baseline. We believe this result served to both support the potential of PRAX-944 in ET and provide independent evidence of the potential role of T-type calcium channels in tremor reduction.

EEG as a pharmacodynamic biomarker for dose selection

PRAX-944 robustly and dose-dependently decreased EEG power in the sigma frequency band during NREM sleep in rats. We believe the effect of PRAX-944 on the EEG observed in rats when dosed with PRAX-944 suggests its potential to mediate the blockade of T-type calcium channels in the thalamocortical circuit, and further suggesting that this result may provide a pharmacodynamic biomarker for PRAX-944. Because the doses at which the EEG changes were observed were similar to those that led to tremor reduction in the harmaline model, we believe that this potential biomarker could be used to estimate a dose that could be effective in treating ET.

EPILEPSY

Epilepsy is a common neurological disorder that affects all age groups, can lead to significant disability and social impact to the patient, family and caregivers, and is characterized by brain excitation-inhibition, or E/I, imbalance. Hyperexcitability can lead to abnormal synchronization of neurons and neuronal circuits, which is the electrical basis of a seizure. It is estimated that over 70 million people are living with epilepsy globally and a significant number of them are refractory to current pharmacotherapy. In the United States, the number of people living with epilepsy is estimated to be approximately three million, of which approximately 30% are characterized as refractory to treatment despite the availability of over 20 antiseizure medications.

The mechanisms of action for most of the currently available epilepsy treatments are poorly understood. Nevertheless, fundamentals of brain electrophysiology and mechanisms dictating seizure genesis are conserved across species and, consequently, animal models of seizures and epilepsy enable a clinically predictive and therefore efficient drug development path in this therapeutic area. Moreover, the existence of rapid POC clinical designs and established regulatory pathways for epilepsy drug approvals, together with the significant unmet need, make the epilepsy market attractive.

Recent investigations have led to the identification of over 500 genes that are causal or present risk factors for different forms of epilepsy. We believe this understanding unlocks opportunities for disease mechanism-targeted drug discovery that can more precisely meet the needs of people with epilepsy by addressing such fundamental mechanisms. We have utilized this approach to identify genes that are well-positioned to impact not only rare epilepsies but also the more common forms of epilepsy, as well as other CNS conditions. Our pipeline is being developed in recognition that through better understanding of validated targets, we may be able to maximize the impact our product candidates have on people with epilepsy, mood disorders, movement disorders and potentially other excitability disorders. Discovery and development for rare epilepsies is therefore a key driver and catalyst for optimization of our pipeline and meeting the needs of the broader CNS patient populations we seek to serve.

Underpinning this approach is continual assessment and evaluation of computational, discovery, development, formulation and delivery technologies that can further optimize the speed and quality of the delivery of our pipelines. Whether through in-house developments or via key strategic collaborations, we will explore ways to enhance successful delivery of new products to market and do so time and time again.

A subset of epilepsy, DEEs, are rare neurologic diseases characterized by early onset (< 2 years of age), frequent seizures, abnormal epileptiform electroencephalographic activity, developmental impairment and resistance to available antiepileptic drugs. Furthermore, DEEs are associated with a high mortality rate and comorbidities such as developmental delay in addition to behavioral disorders, movement disorders, pain and sensory dysfunction and sleep disruptions. The understanding of the etiology of DEEs has been revolutionized by recent whole-exome sequencing initiatives that showed over 60 genetic causes of epilepsy. An underlying pathologic feature of many DEEs is the dysregulated neuronal activity leading to hyperexcitability, seizures and associated comorbidities. This phenomenon is observed in many pediatric DEEs with an identified genetic cause, such as SCN8A, SCN2A, KCNT1, KCNQ2, KCNQ1, STXBP1 and SYNGAP1, as well as epilepsies in which a genetic cause remains unclear, such as Lennox Gastaut Syndrome, or Doose Syndrome. Up to 40% of DEEs are caused by single gene mutations, enabling precision medicine approaches. Given the overlapping biology, phenotypic presentation and clinical execution considerations, we believe that developing a portfolio of drugs to treat DEEs will create a distinct body of knowledge and operational synergies across our rare disease portfolio, positioning us as a leader in developing meaningful therapies for this group of patients with devastating unmet clinical needs.

Within our Epilepsy franchise, we expect to initiate a Phase 2 study with our third clinical-stage candidate, PRAX-562, in patients with rare pediatric DEEs in the second quarter of 2022. Our lead product candidate to treat epilepsy is PRAX-222, an ASO designed to lower the expression levels of the protein encoded by the gene SCN2A in patients with GOF mutations in SCN2A, the underlying cause of SCN2A-GOF DEE. PRAX-222 has completed IND-enabling toxicology studies, and we expect to initiate a seamless study in the second quarter of 2022. In January 2022, we exercised our option to in-license PRAX-222 from Ionis Pharmaceuticals, Inc., or Ionis.

We intend to develop PRAX-628, a small molecule with unique NaV channel binding kinetics that favor inhibition of pathological neuronal activity underlying aberrant brain function, such as that seen in our initial indication of focal onset seizures. We anticipate use in other common forms of epilepsy and CNS excitability disorders more generally. PRAX-628 is currently in IND-enabling toxicology studies.

We have also entered into a research collaboration with The Florey Institute of Neuroscience and Mental Health to develop three novel ASO therapies for the treatment of patients with SCN2A loss-of-function, or LOF, mutations and two additional rare epilepsy targets, SYNGAP1 and PCDH19. We believe this collaboration positions us at the forefront in rare epilepsy drug development with six distinct programs for the treatment of six different rare epilepsies.

PRAX-562

Standard of care sodium channel blockers, such as Tegretol (carbamazepine), Lamictal (lamotrigine), Dilantin (phenytoin) and many others are an important class of medicines in neurology and psychiatry. All standard of care sodium channel blockers modulate neuronal activity by targeting peak sodium current, which can reverse the pathological neuronal hyperexcitability that underlies many CNS conditions, but simultaneously affects the physiological cellular action potential firing required for a functioning nervous and cardiovascular system. Hence, this class is widely used for the treatment of epilepsy, pain, migraine and bipolar disorder. However, the efficacy of sodium channel blockers is generally limited by side effects, many attributable to on-target toxicological effects.

PRAX-562 is a preferential, persistent sodium current blocker that is designed to reduce pathological neuronal hyperexcitability and to provide an improved tolerability profile. PRAX-562 is in development for the treatment of a broad range of rare, devastating CNS disorders, such as severe pediatric epilepsies and adult cephalgias. We are pursuing proof of concept clinical data in a subset of rare cephalgias, initially Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing, or SUNCT, Short-lasting Unilateral Neuralgiform headache with Autonomic symptoms, or SUNA, and Trigeminal Neuralgia, or TN.

We completed a Phase 1 trial of PRAX-562 in Australia to evaluate the safety, tolerability, PK and effects on an exploratory EEG biomarker in up to 129 adult healthy volunteers. We completed the dosing and safety follow-up period for the single ascending dose and multiple ascending dose cohorts up to 150mg and 120mg, respectively. PRAX-562 was well-tolerated, with no clinically significant safety findings. In this study, we used auditory steady state response, or ASSR, as an exploratory EEG biomarker to determine the doses required to achieve pharmacological blockade of persistent sodium current, which we believe is a potential indicator of efficacy in patients. Dose-related changes were observed in the ASSR biomarker with a reduction of greater than 50% in Phase Locking Factor, or PLF, after 14 days of daily dosing of PRAX-562 (120mg), as compared to baseline. These data suggest that PRAX-562 appeared to be achieving brain exposures needed to modulate cortical E/I balance.

Based on the observed signal in the ASSR biomarker in the Phase 1 trial, we have started dosing patients in the United States in a Phase 1, placebo-controlled, two-cohort study to further evaluate the observed ASSR signal

and to evaluate 28-day dosing. We expect to report topline data in the second quarter of 2022. The study is designed to evaluate ASSR as a potential biomarker for the PRAX-562 program to further support selection of doses to evaluate in Phase 2 studies. The clinical development plan for PRAX-562 encompasses exploring the broad potential for the mechanism of action in rare diseases through conducting proof-of-concept clinical trials in rare adult cephalgias, then expanding its development into a range of rare pediatric DEEs.

The FDA granted both orphan drug and rare pediatric disease designations for PRAX-562 for the treatment of SCN2A and SCN8A developmental and epileptic encephalopathies, or SCN2A-DEE and SCN8A-DEE, respectively, and the EMA Committee for Orphan Medicinal Products granted orphan drug designation for PRAX-562 for the treatment of SCN2A-DEE and SCN8A-DEE.

Voltage-gated sodium channels, persistent sodium current and neuronal excitability

Voltage-gated sodium channels, or VGSCs, are transmembrane proteins that are required for electrical signaling and therefore communication in neurons. VGSCs respond to changes in the membrane potential and are tightly regulated by their biophysical properties. Upon opening of VGSCs, sodium ions can move into the cell leading to a depolarization and therefore excitation of the neuron. This sodium current is the initiator and driver of neuronal action potentials, or APs, the primary means of electrical signal propagation along the neuron's axon.

The family of VGSCs consists of nine highly related isoforms (NaV1.1 – NaV1.9) with differential tissue distributions and functions. NaV1.1, 1.2 and 1.6 are the major sodium channels expressed in the central nervous system.

Isoform	Gene	Expression
NaV1.1	SCN1A	CNS
NaV1.2	SCN2A	CNS
NaV1.3	SCN3A	CNS/Pancreas
NaV1.4	SCN4A	Muscle
NaV1.5	SCN5A	Heart
NaV1.6	SCN8A	CNS/PNS
NaV1.7	SCN9A	PNS
NaV1.8	SCN10A	PNS
NaV1.9	SCN11A	PNS

CNS: Central Nervous System, PNS: Peripheral Nervous System

Table 17. Sodium Channel Isoforms and tissue distribution.

VGSCs undergo a structural change that alter their ability to conduct sodium ions (Table 17) and are triggered to open upon excitation, or depolarization, of the cell membrane allowing sodium ions to enter the neuron. Sodium influx further excites, or depolarizes, the neuron, leading to the opening of even more sodium channels. This series of events can lead to a large peak sodium current underlying the initiation and propagation of neuronal action potentials, or APs, the primary means by which neurons propagate information in the nervous system. To prevent overexcitation of neurons, or hyperexcitability in the form of excessive high frequency AP firing, the majority of sodium channels only open very briefly after activation (1-2ms), followed by a refractory period of inactivation or non-responsiveness.

However, at membrane potentials below the AP firing threshold, a small subset of sodium channels can remain open for hundreds of milliseconds, carrying the so-called persistent sodium current. Persistent sodium current is present under physiologic conditions where it modulates excitability of neurons and can be significantly increased in pathologic states (Figure 18).

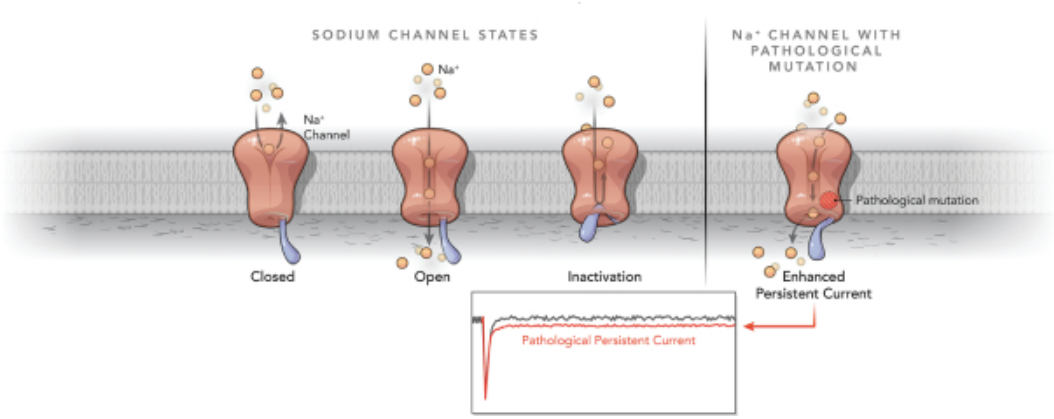


Figure 18. Impact of a pathological mutation on sodium channels.

There are currently more than 15 sodium channel blockers in the market commonly used to treat diseases such as epilepsy, bipolar disorder and pain. While standard of care sodium channel blockers, such as carbamazepine, lamotrigine and phenytoin, inhibit persistent sodium current, they likely also block peak sodium current at therapeutic concentrations, which can cause significant AEs such as ataxia, drowsiness and dizziness, and therefore have a very narrow Therapeutic Index, or TI.

Genetics of persistent sodium current

In published whole-exome sequencing studies of diverse patient populations, mutations in all voltage gated sodium channel subtypes have been reported as a likely cause of disease. Furthermore, gain-of-function mutations that are associated with disease can cause an increase of persistent sodium current, raising the idea that this might be a critical driver of hyperexcitability in neurologic disorders.

The specific disease that a patient develops depends on both the sodium channel subtype and where the affected sodium channel is expressed. Gain-of-function mutations in SCN2A, or NaV1.2, and SCN8A, or NaV1.6, two of the major sodium channels in the brain, cause early onset epileptic encephalopathies with frequent seizures and developmental delay. Gain-of-function mutations in NaV1.1, NaV1.4, NaV1.5 and NaV1.7 cause familial hemiplegic migraine, myotonia, cardiac arrythmia and severe pain disorders, based on their primary expression in the CNS, muscle, heart and pain pathways, respectively. These channelopathies demonstrate the important role persistent sodium current plays as a modulator of cellular excitability.

PRAX-562 preclinical data

PRAX-562 preclinical studies were designed to test our belief that the block of persistent sodium current is sufficient to demonstrate robust activity in animal models of hyperexcitation and that the selective block of persistent sodium current over physiological peak current could lead to an improved TI.

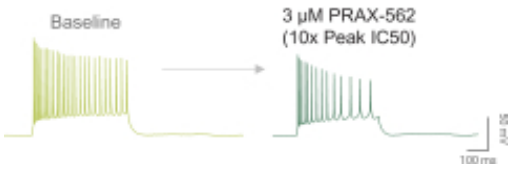
Selective inhibition of persistent sodium channels

PRAX-562 showed potent inhibition of persistent sodium current as measured in cell-based assays, in which sodium channel isoforms were heterologously expressed and channel activity was measured via patch clamp electrophysiology. Using electrophysiological voltage protocols, the effect of compounds on a specific channel state (*e.g.*, peak current vs persistent current) can be measured. When compared to other approved sodium channel inhibitors for various neurological indications, PRAX-562 showed hundreds of times greater potency in inhibiting persistent sodium current. PRAX-562 had an IC_{50} of 141 nM compared to SOC sodium channel blockers lamotrigine and carbamazepine which had an IC_{50} of 78,530 nM and 77,520 nM, respectively – a potency difference of over 500-fold. PRAX-562 also potently inhibited persistent I_{Na} expressed by the SCN8A-DEE mutant $hNa_V1.6$-N1768D (IC_{50} 75 nM). PRAX-562 was ~60 fold selective for inhibiting persistent current over peak current.

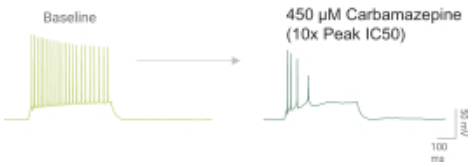
The selective block of persistent sodium current reduces neuronal hyperexcitability without affecting the action potential, or AP, amplitude, which is required for normal neuron function. In mouse brain slice experiments, a hyperexcitable state can be mimicked by artificially depolarizing the neuron using the patch clamp method, which elicits high frequency AP firing. PRAX-562 reduced the neuronal AP firing frequency, an indicator of neuronal excitability, without a significant effect on AP amplitude, an indicator of normal neuronal function, suggesting reduction of hyperexcitability without impacting the ability of the neuron to respond to physiologic stimuli. In

comparison, carbamazepine, a SOC sodium channel blocker, at comparable concentrations (relative to the potency in cells heterologously expressing $Na_V1.6$), excessively decreased AP firing almost completely and reduced the amplitude of APs, indicating impairment of normal function.

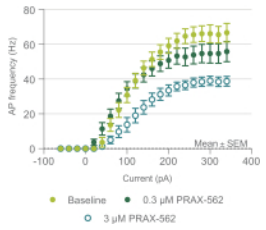
PRAX-562 Representative AP Traces



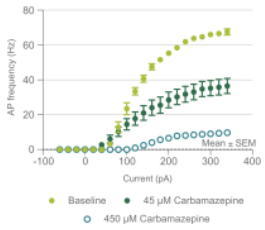
Carbamazepine Representative AP Traces



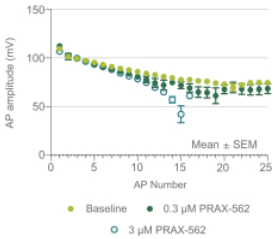
PRAX-562 Average AP Frequency During Increasing Current Steps



Carbamazepine Average AP Frequency During Increase Current Steps



PRAX-562 Average AP Amplitude During Current Step



Carbamazepine Average AP Amplitude During Current Step

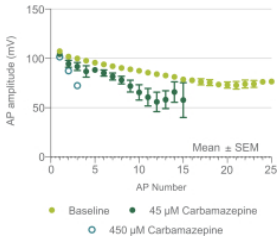


Figure 19. PRAX-562 reduced neuronal hyperexcitability (AP frequency) without impairing normal function (minimal effect on AP amplitude). In contrast, carbamazepine significantly reduced the AP amplitude suggesting impairment of normal function.

Preclinical in vivo pharmacological activity, tolerability and EEG pharmacodynamic biomarker

We investigated the preclinical activity of PRAX-562 in the maximal electroshock model of epilepsy, or MES model, that has shown good predictive validity for clinical anti-convulsant activity, and compared it to the effects of SOC sodium channel blockers carbamazepine and lamotrigine. To determine how well PRAX-562 was tolerated in this study, we compared its effects on spontaneous locomotor activity, or sLMA, to the effects of carbamazepine and lamotrigine.

PRAX-562 was able to block seizures completely in mice at a dose that did not impair locomotor function (10mg/kg). In contrast, carbamazepine and lamotrigine only achieved full block of seizures in this model at doses that also showed impairment of locomotion. PRAX-562 at a dose of 2mg/kg (concentration in brain of 116ng/g and plasma of 90.1ng/mL), inhibited the epilepsy response to half of its maximum value, or ED50. Inhibition of sLMA required an estimated dose of 44mg/kg (concentration in brain of 1,899ng/g and plasma of 1,553ng/mL), to obtain 50 percent inhibition, or TD50.

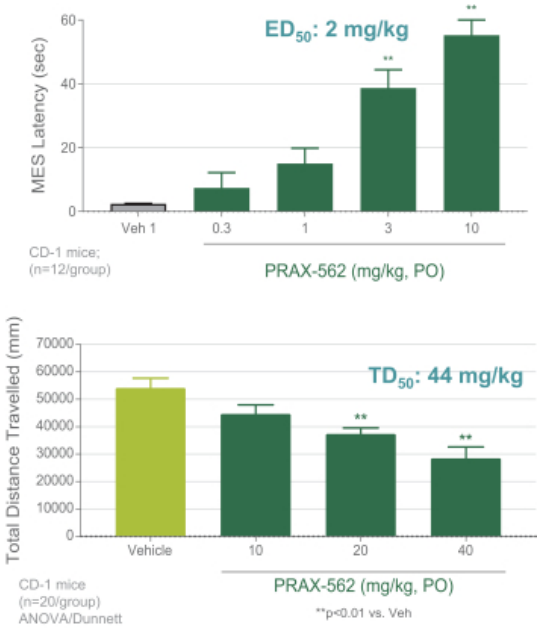


Figure 20. Doses of PRAX-562 resulting in potent anticonvulsant activity were associated with minimal effects on general locomotor activity.

We calculated the TI of each molecule as the preclinical tolerability/pharmacological activity ratio. This ratio is calculated by dividing the plasma and brain concentrations at the dose that reduces locomotion by 50% by the concentrations that reduce seizures by 50%. We found that PRAX-562 had a significantly improved TI of ~16 fold (based on brain concentrations) and ~17 fold (based on plasma concentrations) compared to the currently prescribed sodium channel blockers carbamazepine and lamotrigine, which had a much lower protective index of three to six-fold. Notably, standard sodium channel blockers, such as carbamazepine and phenytoin, show severe toxicity in humans at exposures that are only about 1.5 to 3 times the target therapeutic exposures, underscoring the need for modulators of sodium channels with an improved tolerability.

The ASSR is a non-invasive EEG measure of E/I balance in the brain. This response is elicited with short lasting (2sec) auditory stimuli that lead to brain activity changes that are measured as a 40Hz EEG signature and depend on network activity between excitatory and inhibitory cortical neurons. We believe that persistent current block has the potential to lead to reduced excitability of the network and will be measurable with this endpoint.

Consistent with this hypothesis, dosing normal mice with PRAX-562 led to a dose-dependent decrease in the ASSR amplitude (40Hz power). This decrease was greater at doses that showed robust anticonvulsant activity in the maximal electroshock model.

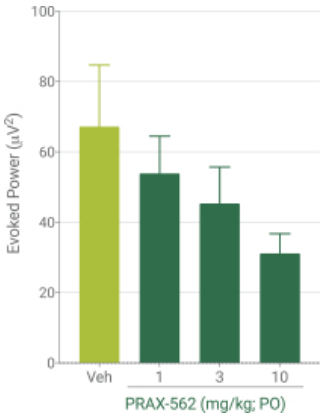


Figure 21. PRAX-562 dose-dependently reduced the 40Hz EEG power of the auditory steady state response in mice.

Together, our data suggest that PRAX-562 selectively affected hyperexcitable states without affecting normal neuronal function, which led to the robust preclinical reduction of seizures and improved tolerability in animal models. As shown below, exposures of PRAX-562 that led to biomarker change (ASSR amplitude reduction shown in top row) also demonstrated robust anticonvulsant activity (shown in middle row). Moreover, PRAX-562 has shown a ~16.4 fold protective index based on the spontaneous locomotor activity (shown in bottom row). In the figure below, the lower bound of the preclinical pharmacological activity range, EEG and tolerability bars is determined by the brain EC_{50} (preclinical seizure and ASSR assays) or TC_{50} (tolerability assay) in a given assay and the upper bound represents the mean brain concentration at the highest dose tested in a given assay.

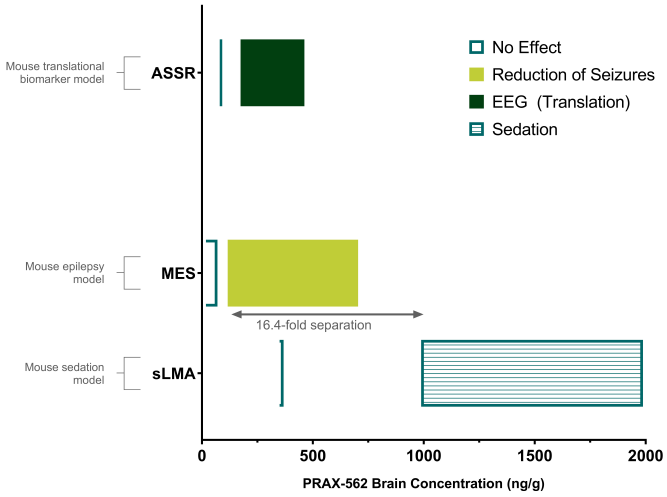


Figure 22. Summary of PRAX-562 preclinical data.

We believe that the preclinical results for PRAX-562 may support clinical development across several indications caused by underlying hyperexcitability where standard sodium channel blockers have shown efficacy, albeit with limited tolerability, such as rare pediatric epilepsies and cephalgias like SUNCT/SUNA and TN.

Preclinical in vivo pharmacological evaluation in mouse models of SCN2A and SCN8A Gain-of-Function Epilepsy

PRAX-562 also blocked seizures in two independent transgenic mice strains expressing mutant Na_V gene alleles which cause human seizure disorders and encode NaV channels with gain-of-function increases in persistent I_{Na}. Transgenic mice heterozygous for $Scn8a^{D/+}$ (encoding $Na_V1.6$-N1768D) exhibit symptoms observed in the human disease, including spontaneous seizures, audiogenic seizures, and sudden unexpected death. PRAX-562 resulted in dose-dependent inhibition of audiogenic seizures with an ED_{50} of 3.7 mg/kg (concentration in brain of 120 ng/g and plasma of 114 ng/mL). The $Scn2a^{Q54}$ mouse line is a model of $Na_V1.2$ gain-of-function where an engineered mutation (GAL879-881QQQ) results in increased persistent I_{Na}. Similar to patients, $Scn2a^{Q54}$ mice exhibit spontaneous early life seizures and premature death. PRAX-562 resulted in dose-dependent reduction of spontaneous seizure frequency in the $Scn2a^{Q54}$ mice with an ED_{50} of 0.73 mg/kg (concentration in brain of 51.0 ng/g and plasma of 17.8 ng/mL). These preclinical studies demonstrate a dose-dependent and complete prevention of seizures in two independent mouse models Na_V gain-of-function DEE.

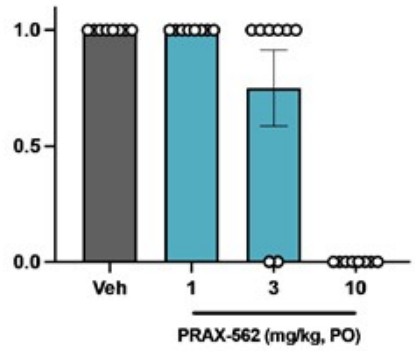


Figure 23. PRAX-562 protected against audiogenic seizures in Scn8a-N1768D (D/+) GOF Mice

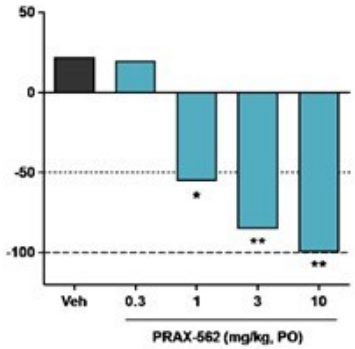


Figure 24. PRAX-562 protected against spontaneous seizures in $Scn2a^{Q54}$ GOF Mice

PRAX-222

PRAX-222 is an ASO for patients with SCN2A GOF epilepsy. The PRAX-222 program is ongoing under a three-way collaboration with Ionis and RogCon Inc., or RogCon. Under the terms of the collaboration agreement, Ionis was responsible for preclinical and IND-enabling toxicology studies and we are responsible for clinical development and commercialization. PRAX-222 has completed IND-enabling toxicology studies, and we expect to initiate a seamless study in SCN2A GOF patients in the second quarter of 2022. In January 2022, we exercised our option to in-license PRAX-222 from Ionis. The FDA has granted both rare pediatric disease and orphan drug designations for PRAX-222 for the treatment of SCN2A-DEE, and the EMA Committee for Orphan Medicinal Products has granted orphan drug designation for PRAX-222 for the treatment of SCN2A-DEE.

SCN2A is the gene that encodes the voltage-gated sodium channel NaV1.2 that is primarily found in excitatory neurons throughout the brain and which plays a critical role in action potential generation and signaling between neurons. Individuals with gain-of-function mutations in SCN2A develop early-onset epileptic encephalopathy with

severe seizures that begin within the first month of life that are often refractory to standard of care antiepileptic medications. SCN2A GOF DEE patients also suffer from significant intellectual disability, movement disorders and in some cases early death due to sudden unexpected death in epilepsy, or SUDEP. It is estimated that there are thousands of patients worldwide with gain-of-function changes in SCN2A leading to epileptic encephalopathy.

The PRAX-222 program is designed to directly target the cause of SCN2A disease by down-regulating NaV1.2 expression, an effect that has demonstrated disease-modifying activity in animal models of SCN2A epileptic encephalopathy. In transgenic mice carrying a human SCN2A GOF mutation, we observed a significant, dose-dependent reduction in seizures and increased survival of mice treated with a mouse ASO that is designed to down-regulate SCN2A. The survival benefit from the ASO was maintained with repeat dosing. We also observed survival benefits following administration of a mouse ASO to a group of mice after onset of disease and around the time of onset of mortality. This observation suggests that candidate ASOs of the PRAX-222 program may have the potential to provide clinical benefits for children after disease onset. The ASO-treated disease model animals demonstrated similar behavior and locomotor activity as wild type animals, suggesting SCN2A knockdown was generally well-tolerated and that the potential benefits could extend beyond seizure control alone.

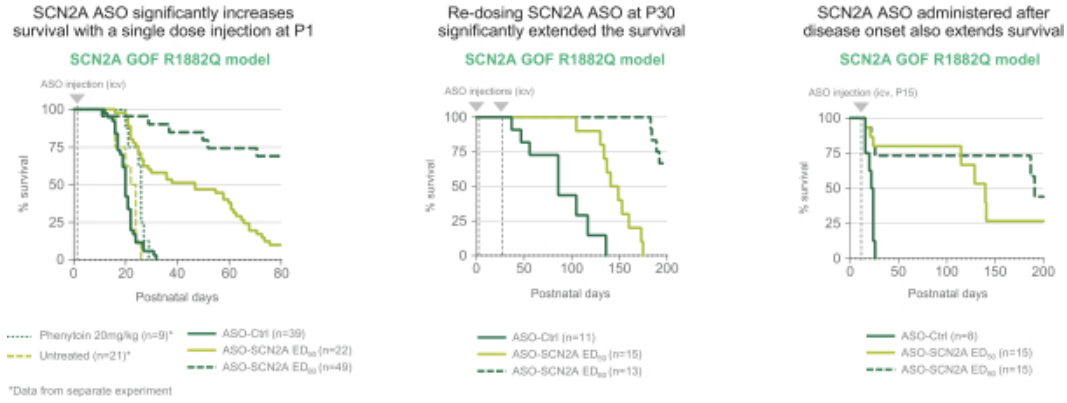


Figure 25. An SCN2A ASO increased survival in a SCN2A gain-of-function mouse model.

KCNT1 Program

We are currently identifying small molecule inhibitors of the sodium-activated potassium channel encoded by the gene KCNT1 for the treatment of KCNT1 GOF epilepsy. Potassium channels encoded by the KCNT1 gene play a key role in regulating neuronal AP firing. Gain-of-function KCNT1 mutations promote neuronal hyperexcitability, resulting in severe early onset epilepsy with continuous seizures and severe developmental delay, affecting thousands of patients worldwide. KCNT1 GOF epilepsy is often refractory to conventional treatment approaches. Anticonvulsants, such as stiripentol, benzodiazepines, levetiracetam and ketogenic diet, have all demonstrated limited efficacy.

Genetically lowering KCNT1 expression in transgenic mice carrying a KCNT1 human GOF mutation has been reported to result in disease modifying preclinical activity including seizure reduction, improved cognitive function and survival benefit. Through chemical optimization of the potency and pharmacokinetic properties of hits from a high-throughput screen, we have identified novel small molecule inhibitors of KCNT1. These inhibitors restored normal action potential firing *in-vitro* in KCNT1 GOF mutant neurons and reduce seizure and abnormal interictal spikes *in-vivo* in transgenic mice carrying a KCNT1 human GOF mutation, recapitulating the reported disease modifying preclinical activity demonstrated by genetic tools.

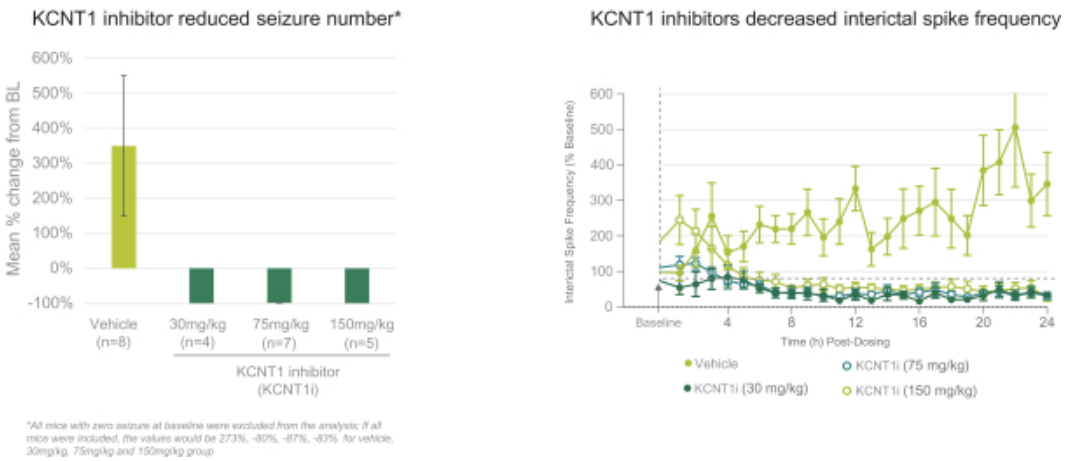


Figure 26. A KCNT1 inhibitor eliminated the occurrence of seizures in a KCNT1 transgenic mouse model and suppressed interictal spikes (or abnormal electrographic discharges observed between seizures) as detected by EEG

Development options based on ongoing preclinical work are under assessment and we expect to provide an update in the first half of 2022.

COMPETITION

The biopharmaceutical industry is characterized by rapidly advancing technologies, strong competition and an emphasis on proprietary products. While we believe that our technology, knowledge, experience and scientific personnel provide us with competitive advantages, we face substantial competition from many different sources, including large and small pharmaceutical and biotechnology companies, academic research institutions, governmental agencies and public and private institutions.

Any product candidates that we successfully develop and commercialize will compete with currently approved therapies and new therapies that may become available in the future. Key product features that would affect our ability to effectively compete with other therapeutics include the efficacy, safety, convenience, cost, effectiveness of promotional support and intellectual property protection of our products. Our competitors fall primarily into the following groups of treatment:

- GABAA receptor modulator programs in development targeting MDD, including that of SAGE Therapeutics, as well as other programs in clinical development targeting other mechanisms of action and approved therapies such as SSRIs.
- T-type calcium channel inhibitor programs in development targeting ET, including that of Jazz Pharmaceuticals and Neurocrine Biosciences, as well as other programs in clinical development targeting other mechanisms of action and approved therapies, such as propranolol, and off-label therapies, such as primidone.
- Sodium channel blocker or similar programs in development for DEEs, including those of SK-Pharma, Xenon Pharmaceuticals, Neurocrine Biosciences and Stoke Therapeutics, as well as other programs in clinical development targeting other mechanisms of action and approved therapies including other existing ion channel blockers.
- Treatments for TN include anticonvulsive medications, such as carbamazepine as well as various procedures or surgical interventions (vascular decompression or gamma knife). We are not aware of any development programs targeting SUNCT and SUNA, but we may face competition from off-label therapies such as intravenous lidocaine.

Many of our competitors have substantially greater financial resources, expertise and capabilities in research and development, the regulatory approval process, manufacturing and marketing than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through M&A activity and sizeable collaborative arrangements with established companies.

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 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 position in the field of neuroscience that may be important for the development of our business. We additionally may rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions, where available.

Patent expiration dates noted in the following paragraphs refer to statutory expiration dates and do not take into account any potential patent term adjustment or extension that may be available. Depending upon the timing, duration and specifics of FDA approval of our drug product candidates, some of our U.S. patents may be eligible for limited patent term extension. These patent term extensions permit a patent restoration term of up to five years as compensation for any patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the drug product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a New Drug Application, or NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark Office, or the USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration

GABAA receptor positive allosteric modulators

We own twelve patent families directed to GABAA receptor positive allosteric modulators. Several patent families disclose and claim salts and polymorphs of PRAX-114, including the current clinical candidate salt. Two patents are granted in the United States (U.S. 10,562,930 and U.S. 10,927,141), and patent applications are pending in other potentially commercially relevant jurisdictions, which expire in 2039. Other patent families are directed to alternative salt forms of PRAX-114 and deuterated forms of PRAX-114, which expire in 2041. Other patent applications cover formulations and processes for making related to PRAX-114, which expire in 2043. Several patent applications covers various methods of use, including treatment of major depressive disorder (the current lead clinical indication,) with PRAX-114, which expire in 2039. Other patent applications are directed to methods of treating various perimenopausal symptoms with PRAX-114 (which expire in 2040); methods of treating mood disorders (including depression) with combinations of GABA-PAMs (including PRAX-114) with NMDA antagonists, NMDA Negative Allosteric Modulators or NMDA partial agonists (which expire in 2040); methods of treating adjustment disorder with PRAX-114 (which expire in 2041); and methods of treating motor disorders (including essential tremor) and musculoskeletal conditions with PRAX-114 (which expire in 2042).

T-type Calcium channel blockers

We own six patent families directed to T-type Calcium channel blockers. One patent family discloses and claims compositions of matter of certain T-type calcium channel modulators, including PRAX-944. This patent family has issued in many major pharmaceutical markets and is pending in others, and expires in 2029. A second family is directed to methods of use of certain T-type calcium channel modulators, including PRAX-944, in treating disease such as epilepsy. This patent family is pending in the United States and expires in 2037. A third patent family is directed to certain pharmaceutical formulations of PRAX-944 and methods of use in treating disorders such as essential tremor. This patent family is pending in multiple jurisdictions of potential commercial interest, and expires in 2029. A fourth family is directed to titration methods of using PRAX-944, and expires in 2041 A fifth patent family is directed to certain analog compounds of PRAX-944, and expires in 2041. The sixth patent family is directed to the adjunctive use of a beta blocker and/or certain anticonvulsants with PRAX-944 and expires in 2043.

Persistent sodium current blockers

We own fifteen patent families directed to persistent sodium current blockers, including a patent family that relates to PRAX-562 and PRAX-1451, two additional patent families that relate to PRAX-562 program, and the remaining patent families related to other persistent sodium current blockers. One patent family discloses and claims certain persistent sodium current blockers, including PRAX-562 and PRAX-1451, and methods of use in treating diseases such as epilepsy (including pediatric epilepsy), as well as migraine and pain. In this patent family, PRAX-562 is covered by a patent that has granted in the United States (U.S. 11,014,931), and patent applications pending in other potentially commercially relevant jurisdictions, which expire in 2039. A second family discloses other persistent sodium current blockers and generically claims PRAX-562, as well as methods of treating diseases such as pediatric epilepsy. This patent family is pending in multiple jurisdictions, and expires in 2037. A third family

is directed to pharmaceutical formulations of PRAX-562, methods of use in treating diseases such as pediatric epilepsy, cephalgia, SUNCT and SUNA, and methods of making PRAX-562, and expires in 2040. The remaining patent families are directed to other persistent sodium current blockers of various core structures and methods of use in treating diseases such as pediatric epilepsy, expiring between 2037 and 2040.

SCN2A downregulation

We have exclusively in-licensed three patent families directed to our SCN2A program. Two of these patent families are owned by RogCon, and disclose and claim certain antisense oligonucleotides targeting SCN2A and methods of use in treating diseases such as epilepsy, including epilepsy having certain SCN2A mutations. One patent family is pending in the United States, and expires in 2038. A second patent family is directed to methods of treating SCN1A encephalopathy using antisense oligonucleotides targeting SCN2A, and expires in 2039.

The other in-licensed patent family is owned by Ionis, and is directed to compositions of matter of PRAX-222. It includes pending PCT and Taiwanese applications that expire in 2041.

We own two patent families directed to our PRAX-222 program. The first has claims directed to a method of treating SCN2A gain of function neurological diseases using certain antisense oligonucelotides. This patent family is pending in the United States, and expires in 2041. The second is directed to methods of treating SCN2A-related disorders using SCN2A inhibitors and expires in 2043.

KCNT1 blockers

We own eleven patent families directed to KCNT1 blockers including ten families related to our KCNT1 program and one family related to antisense oligonucleotides. Ten patent families disclose and claim small molecule KCNT1 blockers and methods of use in treating diseases such as epilepsy, including epilepsy having certain KCNT1 mutations, and expire between 2040 and 2042. One patent family is directed to certain antisense oligonucleotides and methods of use in treating diseases such as epilepsy, including epilepsy having certain KCNT1 mutations, and expires in 2039.

LICENSE AGREEMENTS

License Agreement with RogCon

In September 2019, we and RogCon entered into a Cooperation and License Agreement, or the RogCon Agreement, to collaborate to develop antisense oligonucleotides for the treatment of epilepsy caused by mutations of the SCN2A gene. RogCon had an existing collaboration arrangement with Ionis and as a result, we and Ionis negotiated a Research Collaboration, Option and License Agreement, or the Ionis Agreement, (described below) in order to complete the license agreement with RogCon. In December 2018, we entered into an agreement with RogCon to advance to them a fully refundable deposit of up to $1.0 million while the RogCon Agreement was being negotiated. Under the RogCon Agreement, RogCon granted us, subject to a concurrent license grant of certain rights to Ionis, an exclusive, worldwide license under RogCon's intellectual property to research, develop and commercialize products for the treatment of all forms of epilepsy and/or neurodevelopmental disorders in each case caused by any mutation of the SCN2A gene. Under the RogCon Agreement, we will conduct, at our own cost and expense, the research and development activities assigned to us under the research plan set out in the Research Collaboration, Option and License Agreement with Ionis. Under the terms of the RogCon Agreement, RogCon is eligible to receive a one-time milestone payment of $3.0 million as well as profit share payments as a percentage of net profits in the mid-teens. Profit share payments will be calculated and due quarterly on any net profits generated from a product commercialized under the RogCon Agreement. The $3.0 million milestone payment will become due when (i) the first profit share payment has become due and payable and (ii) the Additional Milestone, the Initial Interest Amount and the Second Interest Amount (each as defined within the Ionis Agreement as described below) have all become due and payable to Ionis under our collaboration agreement with Ionis. As part of the RogCon Agreement, we agreed to provide up-front consideration of $2.1 million, consisting of a $1.0 million deposit, $0.7 million in cash reimbursements for certain historical costs previously incurred by RogCon and $0.4 million for the retirement of existing loan balances as of September 11, 2019.

Subsequent to September 11, 2019, we will reimburse RogCon for its out-of-pocket costs incurred for activities performed under the RogCon Agreement. We expense these costs as incurred as research and development. We expensed $0.1 million and $0.2 million related to the reimbursement of RogCon's out-of-pocket costs in the years ended December 31, 2021 and 2020, respectively.

Additionally, RogCon has agreed to certain defined exclusivity obligations. The RogCon Agreement, unless earlier terminated, will continue until the latest of: (i) the expiration of all patent rights within RogCon patents, (ii) we certify we have abandoned the research, development and commercialization of product with no intention to re-

establish such activities and (iii) no third party is obligated to pay any amounts that comprise net sublicense revenue. Either party may terminate the RogCon Agreement for material breach or insolvency of the other party. Additionally, we may terminate for convenience with prior written notice to RogCon. Upon termination by either party, all rights and licenses granted by RogCon to us will revert back to RogCon.

Ionis Collaboration Agreement

In September 2019, we and Ionis entered into the Ionis Agreement to discover and develop antisense oligonucleotides to treat forms of epilepsy caused by mutations of the SCN2A gene. Pursuant to the Ionis Agreement, we and Ionis each conducted certain research activities and Ionis was responsible for identifying a development candidate and conducting an IND-enabling toxicology study. The design of the IND-enabling toxicology study was prepared and mutually agreed to by us and Ionis. We are obligated to reimburse any out-of-pocket costs incurred by Ionis related to research activities, identification of a development candidate and conducting IND-enabling studies. Ionis granted us an exclusive option to obtain the rights and license to further develop and commercialize a development candidate in the field of epilepsy and neurodevelopmental disorders, other than Dravet Syndrome, following the results of the IND-enabling toxicology study. We exercised this exclusive option in January 2022 and paid a $2.0 million license fee. Ionis is eligible to receive certain contingent payments from us relating to development and other milestones, interest payments, royalties as a percentage of net product sales worldwide in the low-20s and any potential sublicense fees calculated as a percentage of sublicense revenue using a rate in the low-to-mid double digits.

Development milestones of $5.0 million for each product developed under the agreement are due upon the completion of the first clinical trial for each product, or the Development Milestone. Ionis will be entitled to receive an additional one-time milestone payment of $5.0 million, or the Additional Milestone, upon the earliest to occur of the following (each, a Payment Trigger): (i) the first acceptance of an NDA filing for a product by the regulatory authority in a major market, (ii) we have both (a) received, in the aggregate, $300.0 million in cash since September 11, 2019 and (b) initiated the first clinical study with respect to a product or (iii) the closing of a change of control event affecting Praxis. In addition, upon the occurrence of a Payment Trigger, Ionis is also entitled to certain interest payments equal to (i) 10% simple interest per annum calculated from the effective date of the agreement on the Additional Milestone, or the Initial Interest Amount, plus (ii) 10% simple interest per annum calculated from the date the Additional Milestone is paid on the initial Interest Amount, or the Second Interest Amount, until the earliest to occur of the following: (i) aggregate net sales of $100.0 million has been received, (ii) a change in control event affecting Praxis occurs or (iii) the Ionis Agreement has been terminated. Upon the occurrence of one of these three payment triggers, both the Initial Interest Amount and Second Interest Amount are due and payable to Ionis.

The Ionis Agreement will continue in full force and effect until the expiration of all payment obligations to Ionis, unless terminated earlier by either party. Either party may terminate the agreement upon material breach or insolvency of the other party. Praxis is able to terminate the Ionis Agreement for convenience with prior written notice. Ionis may terminate if we fail to achieve certain performance milestones. Upon termination by us for convenience, we will stop selling all products, subject to certain wind-down provisions and all products will revert back to Ionis.

License Agreement with Purdue

In December 2017, we and Purdue Neuroscience Company, or Purdue, entered into a license agreement, or the Purdue Agreement, pursuant to which we were granted exclusive rights under certain Purdue know-how to research, develop and commercialize pharmaceutical products concerning a $GABA_A$ positive allosteric modulator. We are obligated to make future milestone payments based on the achievement of specified development and sales milestones up to $33.0 million. Additionally, under the Purdue Agreement, we were obligated to sell to Purdue $0.6 million of our Series B Preferred Stock in connection with our Series B financing. In addition, as consideration for the license obtained, we issued Purdue the anti-dilution obligation to ensure Purdue's ownership remained at a specified percentage throughout the Series B financing. Further, we are obligated to pay to Purdue a royalty percentage in the low single-digits of net sales of each licensed product for 12 years from the date of the first commercial sale of such product.

The Purdue Agreement will remain in effect until the expiration of our royalty obligation for all licensed products. Either us or Purdue may terminate the agreement in the event of a material breach by the other party and such party fails to cure such breach within a certain period of time. Either party may voluntarily terminate the agreement with prior notice. If the agreement is voluntarily terminated by Purdue, our license rights will survive such termination and such rights will become fully paid, perpetual and irrevocable. Purdue may also terminate in the event of our insolvency.

MANUFACTURING

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently source all of our non-clinical and clinical compound supply through third-party contract development and manufacturing organizations, or CDMOs.

For clinical supply, we rely on CDMOs to manufacture drug substance and drug product in accordance with the FDA's current Good Manufacturing Practices, or cGMP. We expect to rely on third parties for our manufacturing processes and the production of all clinical supply drug substance and drug product and currently expect to continue to do so for commercial supplies of our product candidates, if approved. We use additional contract manufacturers to fill, label, package, store and distribute our investigational drug products and currently expect to continue to do so for commercial supplies of our product candidates, if approved. It is our intent to identify and qualify additional manufacturers to provide active pharmaceutical ingredient and fill-and-finish services prior to submission of a new drug application, or NDA, to the FDA for any product candidates that complete clinical development.

GOVERNMENT REGULATION

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of prescription drugs, such as those we are developing. These agencies regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of drug products. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

U.S. regulation of drug products

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice regulations;
- submission to the FDA of an Investigational New Drug Application, or IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug product for each intended use;
- preparation and submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of potential FDA audits of clinical trial sites to assess compliance with GCPs and the integrity of the clinical data; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical studies

Before testing any product candidate in humans, the product candidate must undergo preclinical testing. Preclinical studies generally include laboratory evaluation of product chemistry, formulation and stability, as well as animal studies to assess potential toxicity, which support subsequent clinical testing. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical

data or literature and a proposed clinical protocol, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial. Additionally, the FDA will review any data from clinical trials conducted outside the United States when determining whether to allow an IND to proceed in the United States. Specifically, the FDA's acceptance of data from trials conducted outside of the United States is subject to certain conditions, including that the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with GCPs; the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful; and that the trials are conducted in compliance with all applicable U.S. laws and regulations. Clinical holds also may be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance.

Clinical trials

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study, and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries. Specifically, information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website. Information related to the product candidate, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in some cases for up to two years after the date of completion of the trial.

Human clinical trials are typically conducted in three phases, which may overlap or be combined. In Phase 1, the product candidate is introduced into healthy human subjects or patients with the target disease or condition to test for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early evaluation of effectiveness. In Phase 2, the product candidate is administered to a limited patient population with a specified disease or condition to evaluate possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for the specified disease or condition, and to determine dosage tolerance and optimal dosage. In Phase 3, the product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product candidate for approval, to establish the overall risk-benefit profile of the product candidate, and to provide adequate information for the labeling of the product candidate.

In some cases, the FDA may require, or sponsors may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies, may be conducted after initial marketing approval, and may be used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition or requirement of approval of an NDA.

Progress reports summarizing the results of clinical trials and nonclinical studies must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and investigators if serious and unexpected suspected adverse events occur, findings from other studies of the same or similar drug or from animal or *in vitro* testing suggest a significant risk, or there is an increased incidence of a serious suspected adverse reaction compared to that in the protocol or investigator brochure. Furthermore, 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. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution for a variety of reasons, including if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Concurrent with clinical trials, companies usually complete additional animal studies and also must 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 product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidates do not undergo unacceptable deterioration over their shelf life.

Marketing application submission and FDA review and approval

Assuming successful completion of the required clinical testing, the results of preclinical and clinical studies, 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 product for one or more indications. The submission of an NDA is subject to a substantial application user fee, unless a waiver or exemption applies.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be withdrawn and resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once an application is accepted for filing, the FDA has a goal of ten months from the date of "filing" to complete a standard review of an NDA for a drug that is a new molecular entity, and six months from the filing date to complete a priority review. The FDA does not always meet its goal dates, and the review process can be extended by FDA requests for additional information or clarification and a sponsor's process to respond to such inquiries. This FDA review process typically takes 12 months from the date the NDA is submitted to FDA (for a standard review) or eight months (for a priority review) inclusive of the 60 days to make a "filing" decision after the application is submitted. Once the submission is accepted for filing, the FDA begins an in-depth substantive review.

The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facilities in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity. Before approving an NDA, the FDA typically will inspect the facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites and/or the study sponsor to assure compliance with GCP requirements.

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

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan, if it determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks and to assure the safe use of the drug product. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS plan is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without a REMS, if required.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. The FDA must send a non-compliance letter

to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities, sponsor, and clinical trial sites, the FDA may issue either an approval letter or a complete response letter, or CRL. An approval letter authorizes commercial marketing of the drug with specific prescribing information and for specific indications. A CRL will describe all of the deficiencies in the NDA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the NDA in condition for approval, including requests for additional information or clarification. If a CRL is issued, the applicant may choose to either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. If those deficiencies have been addressed to the FDA's satisfaction, the FDA will issue an approval letter. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

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

Orphan drug designation and exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan drug designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same disease or condition for seven years. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or to provide a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee. Orphan product designation, however, does not convey any advantage in or shorten the duration of the regulatory review and approval process.

Rare pediatric disease designation and priority review vouchers

In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the United States within one year following the date of approval.

For purposes of this program, a "rare pediatric disease" is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years; and (b) rare

diseases or conditions within the meaning of the Orphan Drug Act. Congress has only authorized the Rare Pediatric Disease Priority Review Voucher program until September 30, 2024. Consequently, sponsors of marketing applications approved after that date will not receive the voucher unless Congress reauthorizes the program. If the program is not reauthorized, if a drug candidate receives Rare Pediatric Disease Designation before October 1, 2024, the sponsor of the marketing application for such drug will only be eligible to receive a voucher if the application for the designated drug is approved by the FDA before October 1, 2026.

Fast track, breakthrough therapy and priority review designations

The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation and priority review designation.

To be eligible for a fast track designation, the FDA must determine that a product candidate is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address unmet medical needs for the condition. Fast track designation provides opportunities for more frequent interactions with the FDA review team to expedite development and review of the product candidate. The FDA may also agree to review sections of the NDA for a fast track product candidate on a rolling basis before the complete application is submitted.

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

Finally, the FDA may designate an NDA for priority review if the product candidate treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the product candidate represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by, among other things, evidence of increased effectiveness, elimination or substantial reduction of a treatment-limiting drug 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 ten months to six months from the filing date for an NDA for a new molecular entity.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, fast track designation, priority review and breakthrough therapy designation do not change the standards for approval and may not ultimately expedite the development or approval process.

Accelerated approval pathway

A drug product may also be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and provides a meaningful therapeutic benefit over existing treatments. Such product candidates can be approved upon a determination that the product candidate has an effect on either a surrogate endpoint that is reasonably likely to predict clinical benefit or on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the disease or condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials to verify and describe the predicted effect on IMM or other clinical endpoint. The FDA may withdraw approval of a drug or indication approved under accelerated approval on an expedited basis if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product or the sponsor fails to conduct such confirmatory trials in a timely manner. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. In addition, all promotional materials for products approved under the accelerated approval program are subject to prior review by the FDA.

U.S. drug product marketing exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. For example, the FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an Abbreviated New Drug Application, or ANDA, or a 505(b)(2) NDA submitted by another company for a generic or follow-on version of the protected drug product, respectively, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

The FDCA also provides three years of marketing exclusivity when an NDA, or a supplement to an existing NDA, includes new clinical investigations, other than bioavailability studies, conducted or sponsored by the applicant that are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs or follow-on 505(b)(2) NDAs if the protected clinical data are not referenced. Five-year and three-year exclusivity will not delay the submission or approval of a stand-alone NDA submitted under section 505(b)(1) of the FDCA. However, an applicant submitting a stand-alone NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness, if applicable.

Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods. This six-month exclusivity may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued “Written Request” for such a trial.

Post-approval requirements

Following approval of a new prescription drug product, the manufacturer and the approved drug are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to monitoring and recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. 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 requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. After approval, most changes to the approved product, such as adding new indications or other labeling claims or changes to the manufacturing processes or facilities, are subject to prior FDA review and approval. There are continuing, annual program fee requirements for any marketed products.

Once an approval of a drug is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- Imposition of post-marketing studies or clinical trials to assess new safety risks, or restrictions under a REMS program;
- Restrictions on the marketing, manufacturing or distribution of the product, complete withdrawal of the product from the market or product recalls;
- Fines, warning letters, untitled letters or other enforcement-related letters or clinical 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;
- Consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- Mandated modification of promotional materials and labeling and the issuance of corrective information;

- Issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product;
- 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 must be promoted by a manufacturer and any third parties acting on behalf of a manufacturer only for the approved indications and in a manner consistent with the approved label for the product. 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. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested and approved by the FDA. The FDA does not regulate the behavior of physicians in their choice of treatments, but it does restrict the manufacturer's communications on the subject of off-label use of their products. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labeling.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or 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.

Healthcare laws and regulations

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states in which they conduct their business, which may constrain the financial arrangements and relationships through which these companies and their partners research, sell, market and distribute any products for which marketing approval is obtained. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims and transparency laws regarding drug pricing and payments and other transfer of value to physicians and other healthcare providers. If their operations are found to be in violation of any of such laws or any other governmental regulations that apply, they may be subject to penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of operations.

Current and future healthcare reform legislation

In the United States, there have been, and likely will continue to be, a number of legislative and regulatory changes regarding the healthcare system directed at broadening the availability of health care, improving the quality of health care and containing or lowering the cost of health care. For example, in March 2010 the Affordable Care Act, or ACA, was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjected biological products to potential competition by lower-cost biosimilars; expanded the types of entities eligible for the 340B drug discount program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations; established annual fees and taxes on manufacturers of certain branded prescription drugs; and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, or BBA, effective as of January 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been judicial, administrative, executive and legislative challenges to certain aspects of the ACA. On June 17, 2021 the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, President Biden issued an executive order to, among other things, instruct certain governmental agencies to review and reconsider their existing policies and rules that limit access to health care, including among others, reexamining Medicaid

demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013, and, due to subsequent legislative amendments, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Payment methodologies may also be subject to changes in healthcare legislation and regulatory initiatives. For example, Centers for Medicare and Medicaid Services may develop new payment and delivery models, such as bundled payment models. There also has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in 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 in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs.

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

Coverage, pricing and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. Sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such drug products. In the United States, third-party payors include federal and state healthcare programs, government authorities, private manage care providers, private health insurers and other organizations. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs.

Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. Such payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our product candidates, if approved, in addition to the costs required to obtain the FDA approvals. Nonetheless, our product candidates may not be considered medically necessary or cost-effective. Moreover, the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payor will pay for the drug product. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and could increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Regulation of drug products and healthcare laws and regulations outside of the United States

Our product candidates may be subject in the future to laws and regulations related to drug products and health care imposed by jurisdictions outside of the United States, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals. Outside of the United States, the provision of health care, including the pricing of pharmaceutical products, is subject to governmental control in many countries, and efforts to control prices and costs, including legislative action, will likely continue as countries attempt to manage healthcare expenditures.

Data privacy and security laws

Numerous state, federal and foreign laws govern the collection, dissemination, use, access to, confidentiality, and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws, including the Health Insurance Portability and Accountability Act, or HIPAA, and federal and state consumer protection laws and regulations that govern the collection, use, disclosure, and protection of health-related and other personal information could apply now or in the future to our operations or the operations of our partners. In addition, certain state and non-U.S. laws, such as the California Consumer Privacy Act of 2018, the California Privacy Rights Act of 2020, and the General Data Protection Regulation, or GDPR, and the UK GDPR, govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to make compliance efforts more challenging, and can result in investigations, proceedings, or actions that lead to significant penalties and restrictions on data processing.

Laws and regulations governing international operations

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

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

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

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

HUMAN CAPITAL

At Praxis, we are fiercely dedicated to our mission to translate genetic insights into the development of therapies for CNS disorders characterized by neuronal imbalance. We strive each day to innovate and adapt to deliver treatments that could potentially change the course of CNS disorders and to do so based on a culture built to attract, develop and retain a talent-dense workforce. We are committed to developing our culture and our employees through our company core values – ***Trust***, ***Ownership***, ***Curiosity*** and ***Results***.

It is the strength of our culture and our work environment that allow us to attract top talent to Praxis, which is how we were able to grow from 62 employees in 11 states at the end of 2020 to 139 in 22 states as of February 18, 2022.

We ***Trust*** each other's judgement, which is why we do not implement excessive policies. We value transparency among team members that leads to direct, clear, and timely feedback so we can all improve together. We commit to be one another's checks and balances. We respect all opinions and encourage diversity. Discrimination is never tolerated. Because we trust employees to have good judgment, there is a lot of freedom built into the way we operate. As an example, we do not have prescriptive policies on vacation, sick or personal time – we encourage employees to take that time as they need it and simply align with their manager about their plans.

We have adapted to new working methodologies that embrace a virtual and cooperative work environment while emphasizing personal ***Ownership*** for actions and outcomes. We want employees to own projects and stay engaged through communication, but we also make sure employees know that Praxis is not a nine-to-five culture. We are a culture where employees have real accountability as we all work towards a greater goal. Our headquarters is designated as a collaborative workspace where we gather in teams or as a company when practical and safe. Being able to own projects, while expressing when you need a break, is something we value. Allowing employees to best structure their days to their needs is one of the most important foundations we believe is necessary for having a sturdy organization.

Curiosity is at the center of innovation, and we are always asking how we can better help our patients. We love to learn. One day a month, we commit to what we call "Curiosity Day." We ask our employees to step away from the computer, meetings and calls for a single day to focus solely on being curious – whether that means catching up on professional articles or journals, diving deeper into a rare disease we do not currently support, challenging ourselves by exploring an area outside our comfort zone, perfecting a new skill, or even taking some time to safely enjoy the outdoors. These opportunities have a positive impact on our employees, and enables them to bring the new knowledge and learnings to the work they do and increase the ability to deliver on our mission.

As we pursue objectives to achieve the ultimate ***Results***, we challenge ourselves daily. Through trust, ownership and curiosity, our employees are positioned to leave lasting results that reach the communities we serve. At the end of the day, the magic we witness when employees put their minds together is what we are most proud of as a company.

To hold ourselves accountable for fulfilling our core values, we have established a unique social feedback system process that supports our agile, self-managed teams and is conducted on a regular schedule throughout the year. Each employee chooses approximately 10 colleagues to provide them with thoughtful and constructive feedback on performance and our Praxis values. Feedback givers are instructed to be candid but with positive intent, so that the feedback receiver has the opportunity to learn valuable lessons and identify development opportunities, both of which are crucial for our collective and individual growth. To promote a culture of openness and transparency, the feedback is not given anonymously and each employee sees the reviewer's ratings and comments. We feel the breadth of feedback helps ensure employees best understand what they do well, what they have improved on, where improvement is still needed and ultimately results in a high-performance culture.

In line with our core values, we are committed to providing a highly competitive total rewards package. Our compensation is a mix of salary, bonus, long-term equity and health and welfare benefits.

AVAILABLE INFORMATION

Our Internet address is http://praxismedicines.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act are available through the "Investors + Media" portion of our website free of charge as soon as reasonably practicable after we electronically

file such material with, or furnish it to, the 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 herein by reference. In addition, our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at http://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.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and in our other filings with the Securities and Exchange Commission, or SEC, before deciding to invest in our common stock. The risks described below are not the only risks facing our company. The occurrence of any of the following risks, or of additional risks and uncertainties not presently known to us or that we currently believe to be immaterial, could cause our business, prospects, operating results and financial condition to suffer materially. In such event, the trading price of our common stock could decline, and you might lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

Risks Related to Past Financial Condition

We are a clinical-stage biopharmaceutical company and we have incurred significant losses since our inception. We anticipate that we will continue to incur significant losses for the foreseeable future.

Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue to date, and we will continue to incur significant research and development and other expenses related to our clinical development and ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception. Since our inception, we have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and our clinical trials. Our financial condition and operating results, including net losses, may fluctuate significantly from quarter to quarter and year to year. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance. Additionally, net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' (deficit) equity and working capital. Our net losses were $167.1 million and $61.8 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $316.6 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 in our initial and potential additional indications as well as for other product candidates.

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

- continue to develop and conduct clinical trials, including in expanded geographies such as the United States or Europe, for our product candidates;
- initiate and continue research and development, including preclinical, clinical and discovery efforts for any future product candidates;
- seek to identify additional product candidates;
- seek regulatory approvals for our product candidates that may successfully complete clinical development;
- add operational, financial and management information systems and personnel, including personnel to support our product candidate development and help us comply with our obligations as a public company;
- hire and retain additional personnel, such as clinical, quality control, scientific, commercial and administrative personnel;
- maintain, expand and protect our intellectual property portfolio;
- establish sales, marketing, distribution, manufacturing, supply chain and other commercial infrastructure in the future to commercialize various products for which we may obtain regulatory approval;
- add equipment and physical infrastructure to support our research and development; and
- acquire or in-license other product candidates and technologies.

Our expenses could increase beyond our expectations if we are required by the U.S. Food and Drug Administration, or the FDA, or other 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.

Risks Related to Future Financial Condition

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

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to continue the preclinical and clinical development of our current and future programs. If we are able to gain marketing approval for our product candidates, we will require significant additional amounts of cash in order to launch and commercialize such product candidates to the extent that such launch and commercialization are not the responsibility of a future collaborator that we may contract with in the future. In addition, other unanticipated costs may arise in the course of our development efforts. Because the design and outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any product candidates we develop.

Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of researching and developing our current product candidates and other product candidates we may develop and pursue, including drug product manufacturing;
- the timing and uncertainty of, and the costs involved in, obtaining marketing approvals for our current product candidates, and other product candidates we may develop and pursue;
- the number of future product candidates that we may pursue and their development requirements;
- the number of jurisdictions in which we plan to seek regulatory approvals;
- if approved, the costs of commercialization activities for our product candidates for any approved indications, or any other product candidate that receives regulatory approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of regulatory approval, revenue, if any, received from commercial sales of our product candidates for any approved indications or any other product candidates;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications and maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property related claims; and
- the ongoing costs of operating as a public company.

We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Any of our current or future license agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements.

We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2023. Our estimate may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

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

We expect our expenses to increase in connection with our planned operations. Unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our future cash needs

through public or private equity offerings, debt financings, collaborations, licensing arrangements or other sources, or any combination of the foregoing. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, our existing stockholders' ownership interests may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect the rights of our stockholders. In addition, debt financing, if available, may result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

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

We are a clinical-stage biopharmaceutical company with a very limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.

We are a clinical-stage biopharmaceutical company, focused on translating genetic insights into the development of therapies for CNS disorders characterized by neuronal imbalance. We commenced operations in 2016, have no products approved for commercial sale and have not generated any revenue from product sales. Our operations have been focused on developing and conducting preclinical and clinical studies of our product candidates. To date, we have not initiated or completed a pivotal clinical trial, obtained marketing approval for any product candidates, manufactured a commercial scale product or arranged for a third party to do so on our behalf, or conducted 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 biopharmaceutical 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.

Drug development is a highly uncertain undertaking and involves a substantial degree of risk.

We have no products approved for commercial sale. To obtain revenues from the sales of our product candidates that are significant or large enough to achieve profitability, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing, and marketing our product candidates. Our ability to generate revenue and achieve profitability depends on many factors, including:

- initiating and successfully completing research and preclinical and clinical development of our product candidates;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials, if any;
- developing a sustainable and scalable manufacturing process for our product candidates, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and commercial demand of our product candidates;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- launching and successfully commercializing product candidates for which we obtain regulatory and marketing approval, if any, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;

- obtaining and maintaining an adequate price for our product candidates in the countries where our products are commercialized, if any;
- obtaining adequate reimbursement for our product candidates from payors;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- receiving milestone and other payments under any future collaboration arrangements;
- maintaining, protecting, expanding and enforcing our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the FDA or foreign regulatory agencies to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our future collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with launching and commercializing any approved product candidate and ongoing compliance efforts.

We may expend our limited resources on programs that do not yield a successful product candidate or fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We currently have three product candidates, PRAX-114, PRAX-944 and PRAX-562, in clinical trials, and intend to initiate a clinical study for PRAX-222 in 2022. Due to the significant resources required for the development of our programs and product candidates, we must focus our programs and product candidates on specific diseases and disease pathways and decide which product candidates to pursue and advance and the amount of resources to allocate to each. We are currently evaluating (i) PRAX-114 for the treatment of major depressive disorder, or MDD, post-traumatic stress disorder, essential tremor, or ET, and women with menopausal and mood symptoms, (ii) PRAX-944 for the treatment of ET and Parkinson's Disease, (iii) PRAX-562 for the treatment of a broad range of rare CNS disorders, including severe pediatric epilepsies and rare adult cephalgias; and (iv) PRAX-222 for the treatment of SCN2A development and epileptic encephalopathy, or SCN2A-DEE. Our drug development strategy is to clinically test and seek regulatory approval for our product candidates in indications in which we believe we will be able to efficiently generate proof-of-concept data. If any of our product candidates is approved, we then intend to expand to clinical testing and potentially seek regulatory approvals in other neurological and psychiatric disease indications based on genetic and mechanistic overlap with the primary indication. However, even if our product candidates are able to gain regulatory approval in one indication, there is no guarantee that we will be able to gain regulatory approval in another indication or expand to other indications.

In addition, we may focus resources on pursuing indications outside of neurology based on the same strategic approach (*e.g.*, human genetics, mechanistic rationale, the availability of translational tools, clinical development path, commercial opportunity) we utilize in determining on which of our discovery programs to focus. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Additionally, we may reprioritize product candidate development plans and activities at any time and delay or terminate development of any product candidates we identify. Similarly, our potential decisions to delay, terminate, or collaborate with third parties in respect of certain programs may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the biopharmaceutical industry, in particular for neurological and psychiatric diseases, our business, financial condition, and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

Risks Related to Research and Development and the Biopharmaceutical Industry

Risks Related to Preclinical and Clinical Development

The development and commercialization of drug products is subject to extensive regulation, and the regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time-consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates on a timely basis if at all, our business will be substantially harmed.

The clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, import, marketing, distribution, adverse event reporting, including the submission of safety and other post-marketing information and reports, and other possible activities relating to our product candidates are subject to extensive regulation. In the United States, obtaining marketing approval for a new drug requires the submission of a New Drug Application, or NDA, to the FDA, and we are not permitted to market any product candidate in the United States until we obtain approval from the FDA of the NDA for that product candidate. An NDA must be supported by extensive clinical and preclinical data, as well as extensive information regarding pharmacology, chemistry, manufacturing, and controls. Outside the United States, many comparable foreign regulatory authorities employ similar approval processes.

We have not previously submitted an NDA to the FDA or similar marketing authorization application to comparable foreign authorities, for any product candidate, and we cannot be certain that any of our product candidates will receive regulatory approval. Obtaining approval of an NDA can be a lengthy, expensive, and uncertain process, and as a company we have no experience with the preparation of an NDA submission or any other marketing authorization application.

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

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that 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 or comparable foreign 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 or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, or regulatory authorities may not accept a submission due to, among other reasons, the content or formatting of the submission;
- the FDA or comparable foreign regulatory authorities may fail to approve our manufacturing processes or facilities or those of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process, and determining when or whether regulatory approval will be obtained for any of our product candidates. For example, regulatory authorities in various jurisdictions have in the past had, and may in the future have, differing requirements for, interpretations of and opinions on our preclinical and clinical data. As a result, we may be required to conduct additional preclinical studies, alter our proposed clinical trial designs, or conduct additional clinical trials to satisfy the regulatory authorities in each of the jurisdictions in which we hope to conduct clinical trials and develop and market our products, if approved. Further, even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA or any comparable foreign regulatory authority.

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.

Preclinical and clinical drug development involves a lengthy, complex and expensive process, with an uncertain outcome. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA or comparable foreign regulatory authorities.

To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. In particular, pivotal clinical trials typically involve hundreds of patients, have significant costs and take years to complete. A product candidate can fail at any stage of testing, even after observing promising signs of activity in earlier preclinical studies or clinical trials. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed.

There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or emergence of unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence clinical trials are never approved as products and there can be no assurance that any of our future clinical trials will ultimately be successful or support further clinical development of our product candidates. The commencement and rate of completion of preclinical studies and clinical trials for a product candidate may be delayed by many factors, including, for example:

- inability to generate sufficient preclinical or other *in vivo* or *in vitro* data to support the initiation of clinical studies;
- timely completion of preclinical laboratory tests, animal studies and formulation studies in accordance with the FDA's Good Laboratory Practice, or GLP, requirements and other applicable regulations;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site before each trial may be initiated;
- delays in reaching a consensus with regulatory agencies on study design and obtaining regulatory authorization to commence clinical trials; delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in recruiting suitable patients to participate in our clinical trials;
- delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- imposition of a temporary or permanent clinical hold by regulatory authorities;
- developments on trials conducted by competitors for related technology that raises FDA or foreign regulatory authority concerns about risk to patients of the technology broadly, or if the FDA or a foreign regulatory authority finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays in recruiting, screening and enrolling patients and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;

- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties or us to adhere to clinical trial protocols; failure to perform in accordance with the FDA's or any other regulatory authority's Good Clinical Practice, or GCP, requirements, or applicable regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits, or occurrence of adverse events in trial of the same class of agents conducted by other companies;
- changes to the clinical trial protocols;
- clinical sites deviating from trial protocol or dropping out of a trial;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- the cost of clinical trials of our product candidates being greater than we anticipated;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;
- transfer of manufacturing processes to larger-scale facilities operated by a contract manufacturing organization, or CMO, and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and
- third parties being unwilling or unable to satisfy their contractual obligations to us.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing preclinical studies and clinical trials.

Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities' legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and ethics committees or IRBs at the medical institutions where the clinical trials are conducted. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, we may need to amend clinical trial protocols that could require us to resubmit our clinical trial protocols to IRBs or ethics committees for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Some of our trials are, have been, and may in the future be open-label studies, where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes 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. For example, prior MDD studies have exhibited a high placebo effect. 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. Therefore, it is possible that positive results observed in open-label trials will not be replicated in later placebo-controlled trials. Additionally, the trial design differences and placebo effects that may be possible in clinical research for the indications we are studying may make it difficult to extrapolate the results of earlier clinical trials to later clinical trials or to interpret the clinical data in any of our trials.

Further, conducting clinical trials in foreign countries, as we have done and may continue to do, for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

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

Delays in the completion of any preclinical studies or clinical trials of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate product revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Any delays to our preclinical studies or clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. In addition, many compounds that have 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. Additionally, the composition of our product candidates or learnings in preclinical studies or clinical trials may result in contraindications for any product candidates for which we may obtain regulatory approval.

If unacceptable side effects arise in the development of our product candidates, we, foreign regulatory authorities, or the FDA, the IRBs or DSMBs at the institutions in which our trials are conducted could suspend or terminate our preclinical studies or clinical trials or foreign regulatory authorities or the FDA could order us to cease preclinical studies or clinical trials or deny approval of our product candidates for any or all targeted indications.

Treatment-emergent side effects that are deemed to be drug-related could also affect subject recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Undesirable side effects in one of our clinical trials for our product candidates in one indication could adversely affect enrollment in clinical trials, regulatory approval and commercialization of our product candidates in other indications. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. Any of these occurrences may harm 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, or those of any future collaborator, 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. Clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our product candidates receive marketing approval and we or others identify undesirable side effects caused by such product candidates (or any other similar products) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such product candidates;

- regulatory authorities may require the addition of labeling statements, such as a Boxed Warning or contraindications;
- we may be required to change the way such product candidates are distributed or administered, or change the labeling of the product candidates;
- the FDA may require a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools, and regulatory authorities in other jurisdictions may require comparable risk mitigation plans;
- we may be subject to regulatory investigations and government enforcement actions;
- the FDA or a comparable foreign regulatory authority may require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety and efficacy of the product;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- our reputation may suffer.

For example, we are developing PRAX-114, an extrasynaptic-preferring GABAA receptor positive allosteric modulator, or PAM, for the treatment of patients suffering from MDD. There have been documented cases of approved GABAA receptor modulators leading to addiction and having the potential for abuse. We have not observed this in our clinical trials of PRAX-114; however, in any such instance, we would be subject to the risks outlined above, which would impact our ability to achieve or maintain market acceptance.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and could substantially increase the costs of commercializing our product candidates, if approved, and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

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

We have, and may in the future, experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their 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 and nature of the patient population required for analysis of the trial's primary endpoints;
- in the case clinical trials focused on rare disease, the small size of the patient population and the potential of a patient being undiagnosed or misdiagnosed;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- 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;
- the impacts of the COVID-19 pandemic on clinical trial sites, personnel and patient travel (see —Business interruptions resulting from COVID-19 or a similar pandemic, epidemic or outbreak of an infectious disease in the United States or worldwide may adversely affect our business);
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our clinical trials will 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 expect

to 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.

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 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 the value of our company to decline and limit our ability to obtain additional financing if needed.

We are also required to register certain clinical trials and post the results of completed clinical trials on a government-sponsored database, such as www.ClinicalTrials.gov in the United States, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

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

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse changes between interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is typically selected from a more extensive amount of available information. Others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the interim, preliminary or topline data that we report differ from later, final or actual results, or if others, including the FDA and comparable foreign regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

The markets for our product candidates may be smaller than we expect.

Our estimates of the potential market opportunities in each of our franchises include several key assumptions based on our industry knowledge, industry publications and third-party research reports and other data sources and estimates. There can be no assurance that any of these assumptions are, or will remain, accurate. If the actual markets identified in each of our franchises, or for any other product candidate we may develop in the future, is smaller than we expect, our revenues, if any, may be limited and it may be more difficult for us to achieve or maintain profitability.

We may not be successful in our efforts to identify or discover additional product candidates in the future.

Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development or commercialization for a number of reasons, including:

- our inability to design such product candidates with the pharmacological or pharmacokinetic properties that we desire; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be medicines that will receive marketing approval and achieve market acceptance.

Research programs to identify new product candidates require substantial technical, financial and human resources. If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

We have begun conducting clinical trials for our product candidates in the United States, and may in the future conduct clinical trials in Europe and other jurisdictions, and the FDA, the European Medicines Agency, or EMA, and applicable foreign regulatory authorities may not accept data from trials conducted outside those respective jurisdictions.

We previously conducted preclinical studies and clinical trials in Australia and New Zealand. The acceptance of study data from preclinical studies and clinical trials conducted outside the United States may be subject to certain conditions for acceptance. For example, in cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and the trials were performed by clinical investigators of recognized competence; and the data are considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. For trials that are conducted only at sites outside of the United States and not subject to an Investigational New Drug Application, or IND, the FDA requires the clinical trial to have been conducted in accordance with GCP and the FDA must be able to validate the data from the clinical trial through an on-site inspection if it deems such inspection necessary. For such trials not subject to an IND, the FDA generally does not provide advance comment on the clinical protocols for the trials, and therefore there is an additional potential risk that the FDA could determine that the trial design or protocol for a non-United States clinical trial was inadequate, which could require us to conduct additional clinical trials. Many foreign regulatory bodies, such as the EMA, have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, EMA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

We have obtained orphan drug designation for PRAX-562 and PRAX-222 and may plan to seek orphan drug designation for additional product candidates, but we may be unable to obtain or maintain such a designation or the benefits associated with orphan drug status, including marketing exclusivity, which may cause our revenue, if any, to be reduced.

In the United States, under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug. Orphan drug designation must be requested and granted by the FDA before a new NDA is submitted. After the FDA grants orphan drug designation, it will disclose publicly the generic identity of the drug and its potential orphan use. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The FDA has granted orphan drug designation to PRAX-562 for the treatment of SCN2A and SCN8A developmental and epileptic encephalopathies, or SCN2A-DEE and SCN8A-DEE, respectively, and to PRAX-222 for the treatment of SCN2A-DEE.

In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers. In addition, if a product candidate that has orphan designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a biologics license application, to market the same product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. The applicable exclusivity period is ten years

in Europe, but such exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable that market exclusivity is no longer justified.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA or comparable foreign regulatory authority can subsequently approve the same drug for the same condition if such regulatory authority concludes that the later drug is clinically superior because it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or comparable foreign regulatory authority later determines that the initial request for designation was materially defective. In addition, orphan drug exclusivity does not prevent the FDA from approving competing drugs for the same or similar indication containing a different active ingredient. In addition, if a subsequent drug is approved for marketing for the same or a similar indication as any of our product candidates that receive marketing approval, we may face increased competition and lose market share regardless of orphan drug exclusivity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We have received rare pediatric disease designation for PRAX-562 and PRAX-222. However, a marketing application for these product candidates, if approved, may not meet the eligibility criteria for a rare pediatric disease priority review voucher.

In 2012, U.S. Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a “rare pediatric disease” that meets certain criteria may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the United States. within one year following the date of approval.

We received rare pediatric disease designation for PRAX-562 for the treatment of SCN2A-DEE and SCN8A-DEE, and for PRAX-222 for the treatment of SCN2A-DEE. Designation of a drug product as a product for a rare pediatric disease does not guarantee that a NDA for such drug product will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. Under the Federal Food, Drug, and Cosmetic Act, or FDCA, we will need to request a rare pediatric disease priority review voucher in our original NDA for our product candidates for which we have received rare pediatric disease designation. The FDA may determine that a NDA for any such product candidates, if approved, do not meet the eligibility criteria for a priority review voucher.

The authority for the FDA to award rare pediatric disease priority review vouchers for drug products after September 30, 2024 is currently limited to product candidates that receive rare pediatric disease designation on or prior to September 30, 2024, and the FDA may only award rare pediatric disease priority review vouchers through September 30, 2026. However, it is possible the authority for the FDA to award rare pediatric disease priority review vouchers will be further extended by Congress.

Risks Related to Regulatory Approval

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, but 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 approval of a product candidate, comparable regulatory authorities in other jurisdictions, including Australia and Europe, must also approve the manufacturing, marketing and sale of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from 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 also 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 governmental approval.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any partner we work with fail to comply with the regulatory requirements in international markets or fail to 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.

Our product candidates may be regulated as controlled substances, the making, use, sale, importation, exportation, and distribution of which are subject to significant regulation by the U.S. Drug Enforcement Administration, or DEA, and other regulatory agencies.

Our product candidates may be classified as controlled substances, which are subject to state, federal, and foreign laws and regulations regarding their manufacture, use, sale, importation, exportation, and distribution. Among other things, controlled substances are regulated under the federal Controlled Substances Act of 1970, and regulations of the DEA.

The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Prior to commercialization, centrally acting drugs, such as those we are developing, are generally subject to review and potential scheduling by the DEA. It is possible that PRAX-114 or our other product candidates may be regulated by the DEA as controlled substances, which would subject PRAX-114 or such product candidates to additional restrictions regarding their manufacture, shipment, storage, sale and use, depending on the scheduling of the active ingredients, and may limit the commercial potential of any of our product candidates, if approved.

Various states also independently regulate controlled substances. Though state controlled substances laws often mirror federal law, because the states are separate jurisdictions, they may separately schedule drugs as well. While some states automatically schedule a drug when the DEA does so, in other states there must be rule making or a legislative action. State scheduling may delay commercial sale of any controlled substance drug product for which we obtain federal regulatory approval and adverse scheduling could impair the commercial attractiveness of such product. We or our collaborators must also obtain separate state registrations in order to be able to obtain, handle and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions from the states in addition to those from the DEA or otherwise arising under federal law.

For any of our product candidates classified as controlled substances, we and our suppliers, manufacturers, contractors, customers and distributors are required to obtain and maintain applicable registrations from state, federal and foreign law enforcement and regulatory agencies and comply with state, federal and foreign laws and regulations regarding the manufacture, use, sale, importation, exportation and distribution of controlled substances. There is a risk that DEA regulations may limit the supply of the compounds used in clinical trials for our product candidates, and, in the future, the ability to produce and distribute our products in the volume needed to meet commercial demand. Regulations associated with controlled substances govern manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, recordkeeping, reporting, handling, shipment and disposal. These regulations increase the personnel needs and the expense associated with development and commercialization of product candidates including controlled substances. The DEA, and some states, conduct periodic inspections of registered establishments that handle controlled substances. Failure to obtain and maintain required registrations or comply with any applicable regulations could delay or preclude us from developing and commercializing our product candidates containing controlled substances and subject us to enforcement action. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate proceedings to revoke those registrations. In some circumstances, violations could lead to criminal proceedings. Because of their restrictive nature, these regulations could limit commercialization of any of our product candidates that are classified as controlled substances.

We could be subject to product liability lawsuits based on the use of our product candidates in clinical testing or, if obtained, following our products' marketing approval and commercialization. Product liability lawsuits brought against us or any of our future collaborators could divert our resources and attention, require us to cease clinical testing, cause us to incur substantial liabilities or limit commercialization of our product candidates.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of biopharmaceutical products. Currently, we have no products that have been approved for commercial sale; however, the use of our product candidates by us and any collaborators in

clinical trials may expose us to liability claims. We will face an even greater risk if product candidates are approved by regulatory authorities and introduced commercially. Product liability claims may be brought against us or our partners if any product candidate we develop allegedly causes injury or is found to be otherwise unsuitable for human use during product testing, manufacturing, marketing or sale. Any such product liability claim may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. Such claims could be made by participants enrolled in our clinical trials, patients, health care providers, biopharmaceutical companies, our collaborators or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources.

Regardless of the merits or eventual outcome, product liability claims may result in:

- decreased demand for any of our future approved products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- significant litigation costs;
- substantial monetary awards to, or costly settlements with, patients or other claimants;
- product recalls or a change in the indications for which any approved drug products may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

Although the clinical trial process is designed to identify and assess potential side effects, clinical development does not always fully characterize the safety and efficacy profile of a new medicine, and it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If our product candidates were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity associated with illness or other adverse effects resulting from physicians' or patients' use or misuse of our products or any similar products distributed by other companies.

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

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.

The development and commercialization of new drug products is highly competitive. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from biopharmaceutical companies worldwide. 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.

Specifically, we face competition with GABAA receptor modulator programs in development targeting MDD, including that of SAGE Therapeutics, as well as other programs in clinical development targeting other mechanisms of action and approved therapies such as selective serotonin reuptake inhibitors, or SSRIs; T-type calcium channel

inhibitor programs in development targeting ET, including that of Jazz Pharmaceuticals and Neurocrine Biosciences, as well as other programs in clinical development targeting other mechanisms of action, and approved therapies, such as propranolol, and off-label therapies, such as primidone; and sodium channel blocker or similar programs in development for DEEs, including those of SK-Pharma, Xenon Pharmaceuticals, Neurocrine Biosciences and Stoke Therapeutics, as well as other programs in clinical development targeting other mechanisms of action, and approved therapies including other existing ion channel blockers.

If any of these competitors or competitors for our other product candidates receive FDA approval before we do, our product candidates would not be the first treatment on the market, and our market share may be limited. In addition to competition from other companies targeting our target indications, any products we may develop may also face competition from other types of therapies.

Many of our current or potential competitors, either alone or with their strategic partners, have:

- greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products;
- more extensive experience in preclinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing, marketing and selling drug products;
- products that have been approved or are in late stages of development; and
- collaborative arrangements in our target markets with leading companies and research institutions.

Mergers and acquisitions in the biopharmaceutical industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of our targeted disease indications or similar indications, which could give such products significant regulatory and market timing advantages over our product candidates. Our competitors also may obtain FDA or other comparable foreign regulatory approval for their products more rapidly than we may obtain approval for ours and may obtain orphan product exclusivity from the FDA for indications that we are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

Risks Related to the Commercialization of our Product Candidates

Risks Related to Post-Marketing Regulatory Requirements

Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Even if the FDA or a comparable foreign regulatory authority approves any of our product candidates, we will be subject to ongoing regulatory requirements in the applicable jurisdictions 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. In addition, we will be subject to continued compliance with cGMP or similar regulatory requirements outside the United States and GCP requirements for any clinical trials that we conduct post-approval.

Manufacturers and their facilities are required to comply with extensive regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP or other similar regulations.

As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP or similar regulatory requirements and adherence to commitments made in any 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. In the United States, the FDA may also require a 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. Similar requirements may apply in foreign jurisdictions. In addition, if the FDA or a comparable foreign 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.

In the United States and elsewhere, the FDA and foreign regulatory authorities may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events 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 or other restrictions; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS or similar program. Other potential consequences include, among other things:

- restrictions on the manufacturing of our products, the approved manufacturers or the manufacturing process;
- withdrawal of the product from the market or voluntary product recalls;
- requirements to conduct post-marketing studies or clinical trials;
- fines, restitution or disgorgement of profits or revenues;
- warning or untitled letters from the FDA or comparable notice of violations from foreign regulatory authorities;
- suspensions of any of our ongoing clinical trials;
- refusal by the FDA or foreign regulatory authorities to approve pending applications or supplements to approved applications filed by us or suspension or withdrawal of marketing approvals;
- product seizure or detention or refusal to permit the import or export of products; and
- consent decrees, injunctions or the imposition of civil or criminal penalties.

Violations of the FDCA relating to the promotion of prescription drugs may also lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws. Accordingly, to the extent we receive marketing approval for one or more of our product candidates, we and our third-party partners will continue to expend time, money and effort in all areas of regulatory compliance, including promotional and labeling compliance, manufacturing, production, product surveillance and quality control. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products, if approved. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

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

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found or alleged to have improperly promoted off-label uses, we may become subject to significant liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about drug products. These regulations include standards and restrictions for direct-to-consumer advertising, industry-sponsored scientific and educational activities, promotional activities involving the internet and off-label promotion. For example, any regulatory approval that the FDA grants is limited to those indications and patient populations for which a drug is deemed to be safe and effective by the FDA.

While physicians in the United States may choose, and are generally permitted, to prescribe products for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, our ability to promote any of our products candidates, if approved, will be narrowly limited to those indications and populations that are specifically approved by the FDA or such other regulatory agencies, and if we are found to have promoted such off-label uses, we may become subject to significant liability. For example, the federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The government has also required companies to enter into consent decrees or imposed permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Risks Related to Sales, Marketing and Competition

Our commercial success depends upon attaining significant market acceptance of our drug product candidates, if approved, among physicians, patients, third-party payors and other members of the medical community.

Even if any of the product candidates we develop receives marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, such as Medicare and Medicaid programs and managed care organizations in the United States, and others in the medical community. In addition, the availability of coverage by third-party payors may be affected by existing and future health care reform measures designed to reduce the cost of health care. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable.

The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our products, if approved, for sale at competitive prices;
- relative convenience and ease of administration compared to alternative treatments;
- perceptions by the medical community, physicians, and patients, regarding the safety and effectiveness of our products and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the size of the market for such product candidate, based on the size of the patient subsets that we are targeting, in the territories for which we gain regulatory approval;
- the recommendations with respect to our product candidates in guidelines published by various scientific organizations applicable to us and our product candidates;
- the strength of sales, marketing and distribution support;
- the timing of any such marketing approval in relation to other product approvals;
- any restrictions on concomitant use of other medications;
- support from patient advocacy groups;
- the ability to obtain sufficient third-party coverage and adequate reimbursement; and
- the prevalence and severity of any side effects.

If government and other third-party payors do not provide coverage and adequate reimbursement levels for any products we commercialize, market acceptance and commercial success would be reduced.

The successful commercialization of our product candidates in the United States will depend in part on the extent to which third-party payors, including governmental authorities and private health insurers, provide coverage and adequate reimbursement levels, as well as implement pricing policies favorable for our product candidates. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States and in other countries, 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. The availability of coverage and adequacy of reimbursement for our products by third-party payors, including government health care programs (*e.g.*, Medicare, Medicaid, TRICARE), managed care providers, private health insurers, health maintenance organizations and other organizations is essential for most patients to be able to afford medical services and biopharmaceutical products such as our product candidates. Third-party payors decide which medications they will pay for and establish reimbursement levels.

In the United States, the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS, determines whether and to what extent new products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Factors payors consider in determining 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.

Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for our products and related treatments will be available from third-party payors. Moreover, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

In the United States, no uniform policy for coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for our products can differ significantly from payor to payor. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. 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. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates.

A decision by a third-party payor not to cover or not to separately reimburse for our medical products or therapies using our products could reduce physician utilization of our products once approved. Assuming there is coverage for our product candidates, or therapies using our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States will be available for our current or future product candidates, or for any procedures using such product candidates, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future.

Further, increasing efforts by 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. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may

also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may nonetheless not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. We expect to experience pricing pressures from third-party payors in connection with the potential sale of any of our product candidates.

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

In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, in the European Union, member states can restrict the range of medicinal products for which their national health insurance systems provide reimbursement and they can control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Approaches between member states are diverging. For example, in France, effective market access will be supported by agreements with hospitals and products may be reimbursed by the Social Security Fund. The price of reimbursed medicines is negotiated with the Economic Committee for Health Products, or CEPS. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Even if we obtain approval of any of our product candidates in the United States or Europe, we may never obtain approval or commercialize such products in other countries, which would limit our ability to realize their full market potential.

In order to market any products in the United States or Europe, we must establish and comply with numerous and varying regulatory requirements regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals outside of where our clinical trials currently have been conducted could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

We currently have no marketing and sales organization and have no experience as a company in commercializing products, and we may have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may not be able to generate product revenue.

We have no internal sales, marketing or distribution capabilities, nor have we commercialized a product. If any of our product candidates ultimately receives regulatory approval, we expect to establish a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time consuming. We have no prior experience as a company in the marketing, sale and distribution of biopharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may also choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems.

We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing our products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

Risks Related to Ongoing Regulatory and Legal Compliance

Risks Related to Healthcare and Related Laws

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.

Although we do not currently have any products on the market, upon commercialization of our product candidates, if approved, we will be subject to additional health care statutory and regulatory requirements and oversight by federal and state governments in the United States as well as foreign governments in the jurisdictions in which we conduct our business. Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare providers, third-party payors, customers and others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business or financial arrangements.

The applicable federal, state and foreign healthcare laws and regulations 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 and entities 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 reward, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. The term remuneration has been interpreted broadly to include anything of value. Further, courts have found that if “one purpose” of remuneration is to induce referrals, the federal Anti-Kickback statute is violated. The Anti-Kickback Statute has been interpreted to apply to arrangements between biopharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers, among others, on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;
- the federal civil and criminal false claims laws, including the FCA, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false, fictitious or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs; knowingly making, using or causing to be made or used, a false record or statement material to a false, fictitious or fraudulent claim or an obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. In addition, a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the FCA. 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. The FCA also permits a private individual acting as a “whistleblower” to bring qui tam actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery or settlement;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, 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, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false fictitious or fraudulent statement or entry 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 HIPAA fraud provisions without actual knowledge of the statute or specific intent to violate it;

- the federal Physician Payments Sunshine Act and its implementing regulations, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to direct or indirect payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician providers including physician providers including physician assistants and nurse practitioners, and teaching hospitals, as well as ownership and investment interests held by the physicians and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous U.S. state, local and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers, and may be broader in scope than their federal equivalents; state and foreign laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and other relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing; state and local laws that require the registration of biopharmaceutical sales representatives.

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. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

It is possible that governmental and enforcement authorities will conclude that our business practices, including our arrangements with physicians and other healthcare providers, some of whom may receive stock options as compensation for services provided, may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to significant sanctions, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, reputational harm, exclusion from participation in federal and state funded healthcare programs, contractual damages and the curtailment or restricting of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws.

Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to similar penalties. Any action for violation of these laws, even if successfully defended, could cause us to incur significant legal expenses and divert management's attention from the operation of the business. In addition, the approval and commercialization of any product candidate we develop outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws. All of these could harm our ability to operate our business and our financial results.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

We may be subject to, or may in the future become subject to, U.S. federal and state, and foreign laws and regulations imposing obligations on how we collect, use, disclose, store and process personal information. Our actual or perceived failure to comply with such obligations could result in liability or reputational harm and could harm our business. Ensuring compliance with such laws could also impair our efforts to maintain and expand our customer base, and thereby decrease our revenue.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials in the United States and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

In Europe, the General Data Protection Regulation, or GDPR, took effect in May 2018. The GDPR imposes stringent requirements on entities that process personal data of individuals in the European Economic Area, or EEA. These requirements include, for example, establishing a legal basis for processing, providing notice to data subjects about how personal data is collected and processed, developing procedures to vindicate expanded data subject rights, implementing appropriate technical and organizational measures to safeguard personal data, introducing the obligation to notify data protection regulators or supervisory authorities (and in certain cases, affected individuals) of significant data breaches, imposing limitations on retention of personal data, maintaining a record of data processing and complying with the principal of accountability and the obligation to demonstrate compliance through policies, procedures, training and audit. In addition, the GDPR establishes obligations for entities that process "special categories" of personal data, such as health data. Nearly all clinical trials involve the processing of these "special categories" of personal data, and processing of personal data collected during the course of clinical trials is therefore subject to heightened protections under the GDPR. Violations of the GDPR can lead to potential fines of up to €20 million or 4% of the annual global revenues of the noncompliant undertaking, whichever is greater. In addition to the foregoing, a breach of the GDPR could result in regulatory investigations, reputational damage, orders to cease / change our processing of our data, enforcement notices, and/ or assessment notices (for a compulsory audit). We may also face civil claims including representative actions and other class action type litigation (where individuals have suffered harm), potentially amounting to significant compensation or damages liabilities, as well as associated costs, diversion of internal resources, and reputational harm.

Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States, and the efficacy and longevity of current transfer mechanisms between the European Union and the United States remains uncertain. For example, in 2016, the European Union and United States agreed to a transfer framework for data transferred from the European Union to the United States called the Privacy Shield, but in July 2020 the Court of Justice of the EU, or the CJEU, limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on use of the standard contractual clauses, or SCCs. While the CJEU upheld the adequacy of the SCCs, it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. Use of the SCCs must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals and additional measures and/or contractual provisions may need to be put in place, however, the nature of these additional measures is currently uncertain. The CJEU went on to state that if a competent supervisory authority believes that the SCCs cannot be complied with in the destination country and the required level of protection

cannot be secured by other means, such supervisory authority is under an obligation to suspend or prohibit that transfer. The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements must be migrated to the revised clauses by December 27, 2022. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. The revised SCCs apply only to the transfer of personal data outside of the EEA and not the United Kingdom; the UK's Information Commissioner's Office launched a public consultation on its draft revised data transfers mechanisms in August 2021. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Further, since January 2021, we may also be subject to the UK GDPR, which, together with the UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, meaning the potential of parallel fines of up to the greater of £17.5 million or 4% of global turnover. The European Commission has adopted an adequacy decision in favor of the United Kingdom, enabling data transfers from EU member states to the United Kingdom without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews/ extends that decision and remains under review by the Commission during this period. In September 2021, the UK government launched a consultation on its proposals for wide-ranging reform of UK data protection laws following Brexit. There is a risk that any material changes which are made to the UK data protection regime could result in the European Commission reviewing the UK adequacy decision, and the United Kingdom losing its adequacy decision if the European Commission deems the UK to no longer provide adequate protection for personal data. The relationship between the United Kingdom and the European Union in relation to certain aspects of data protection law remains uncertain, and it is unclear how UK data protection laws and regulations will develop in the medium to longer term.

In the United States, HIPAA establishes a set of national privacy and security standards for the protection of individually identifiable health information, including protected health information, or PHI, by health plans, certain health care clearinghouses and health care providers that submit certain covered transactions electronically, or covered entities, and their "business associates," which are persons or entities that perform certain services for, or on behalf of, a covered entity that involve creating, receiving, maintaining or transmitting PHI, as well as their covered subcontractors. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA, we may receive individually identifiable health information from these entities. Failure to receive this information properly could subject us to HIPAA's criminal penalties, which may include fines up to $250,000 per violation and/or imprisonment. Further, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information. In addition, responding to government investigations regarding alleged violations of these and other laws and regulations, even if ultimately concluded with no findings of violations or no penalties imposed, can consume company resources and impact our business and, if public, harm our reputation.

Various states, such as California and Massachusetts, have also implemented similar privacy laws and regulations, such as the California Confidentiality of Medical Information Act, or the CMIA, that impose restrictive requirements regulating the use and disclosure of health information and other personally identifiable information. In addition to imposing fines and penalties, some of these state laws afford private rights of action to individuals who believe their personal information has been misused. California's patient privacy laws, for example, provide for penalties of up to $250,000 and permit injured parties to sue for damages. In addition to the CMIA, California also recently enacted the California Consumer Privacy Act of 2018, or CCPA, which came into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and in other states. Further, the California Privacy Rights Act, or CPRA, recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of

sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. In the event that we are subject to or affected by the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Furthermore, the Federal Trade Commission, or the FTC, and many state Attorneys General continue to enforce federal and state consumer protection laws against companies for online collection, use, dissemination and security practices that appear to be unfair or deceptive. For example, according to the FTC, failing to take appropriate steps to keep consumers' personal information secure can constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act. 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.

The interplay of federal and state laws may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and potentially exposing us to additional expense, adverse publicity and liability. Further, as regulatory focus on privacy issues continues to increase and laws and regulations concerning the protection of personal information expand and become more complex, these potential risks to our business could intensify. The legislative and regulatory landscape for privacy and data security continues to evolve, and there has been an increasing focus on privacy and data security issues which may affect our business. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with current and future laws and regulations could result in government enforcement actions (including the imposition of significant penalties), criminal and/or civil liability for us and our officers and directors, private litigation and/or adverse publicity that negatively affects our business.

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

In the United States and in some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative initiatives and regulatory changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare. For example, in March 2010, the ACA was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. biopharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, expands the types of entities eligible for the 340B drug discount program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations; established annual fees and taxes on manufacturers of certain branded prescription drugs; and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, or BBA, effective as of January 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Since its enactment, there have been numerous judicial, administrative, executive and legislative challenges to certain aspects of the ACA. On June 17, 2021 the U.S. Supreme Court dismissed the recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, on August 2, 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional

Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's AMP, for single source and innovator multiple source drugs, beginning January 1, 2024. Payment methodologies may also 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. Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their products. Such scrutiny has resulted in 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 in the United States, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biologic product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions on coverage or access could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates that we successfully commercialize or put pressure on our product pricing.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or in any other jurisdictions. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

In the United States, inadequate funding for the FDA, the SEC, and 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.

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 the SEC and 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. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs and or modifications to approved drugs or to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities. According to the guidance, the FDA may request such remote interactive evaluations where the FDA determines that remote evaluation would be appropriate based on mission needs and travel limitations. In May 2021, the FDA outlined a detailed plan to move toward a more consistent state of inspectional operations, and in July 2021, the FDA resumed standard inspectional operations of

domestic facilities and was continuing to maintain this level of operation as of September 2021. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to hinder or prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to International Regulations

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

We ultimately 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 EU, the pricing of drugs 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 health care 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 physicians is governed by the national laws of EU member states, and in respect of the United Kingdom (which is longer a member of the European Union), the U.K. Bribery Act of 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU member states must be publicly disclosed. Moreover, agreements with physicians must often be subject to a prior notification and/or 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, the requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. In some countries, we may be required to conduct a clinical study or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical 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.

Legal, political and economic uncertainty surrounding the exit of the United Kingdom from the European Union may be a source of instability in international markets, create significant currency fluctuations, adversely affect our operations in the United Kingdom and pose additional risks to our business, revenue, financial condition and results of operations.

On June 23, 2016, the United Kingdom held a referendum in which a majority of the eligible members of the electorate voted to leave the European Union, commonly referred to as Brexit. Pursuant to Article 50 of the Treaty on EU, the United Kingdom ceased being an EU member state on January 31, 2020. Under the terms of its departure, the United Kingdom entered a transition period, or the Transition Period, during which it continued to follow all EU rules, which ended on December 31, 2020. On December 30, 2020, the United Kingdom and

European Union signed the Trade and Cooperation Agreement, or TCA, which includes an agreement on free trade between the two parties and has been provisionally applicable since January 1,2021. Since January 1, 2021, the United Kingdom. has operated under a separate regulatory regime to the European Union. EU laws regarding medicinal products only apply in respect of the United Kingdom to Northern Ireland (as set out in the Protocol on Ireland/Northern Ireland). The EU laws that have been transposed into U.K. law through secondary legislation remain applicable. While the United Kingdom has indicated a general intention that new laws regarding the development, manufacture and commercialization of medicinal products in the United Kingdom will align closely with EU law, there are limited detailed proposals for future regulation of medicinal products. The TCA includes specific provisions concerning medicinal products, which include the mutual recognition of Good Manufacturing Practice, or GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued (such mutual recognition can be rejected by either party in certain circumstances), but does not foresee wholesale mutual recognition of U.K. and EU pharmaceutical regulations. Therefore, there remains political and economic uncertainty regarding to what extent the regulation of medicinal products will differ between the United Kingdom and the EU in the future. Any divergences will increase the cost and complexity of running our business, including with respect to the conduct of clinical trials. Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our drug candidates is derived from EU directives and regulations, Brexit could materially impact the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our drug candidates in the United Kingdom or the European Union. Great Britain is no longer covered by the European Union's procedures for the grant of marketing authorizations (Northern Ireland is covered by the centralized authorization procedure and can be covered under the decentralized or mutual recognition procedures). A separate marketing authorization will be required to market drugs in Great Britain. It is also currently unclear whether the U.K. regulator, the Medicines and Healthcare Products regulatory Agency, is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, could prevent us and our collaborators or delay us and our collaborators from commercializing our drug candidates in the United Kingdom and/or the EEA and restrict our ability to generate revenue and achieve and sustain profitability.

The uncertainty concerning the United Kingdom's legal, political and economic relationship with the European Union after Brexit may be a source of instability in the international markets, create significant currency fluctuations and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise) beyond the date of Brexit.

These developments, or the perception that any of them could occur, may have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and limit the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the U.K. financial and banking markets, as well as on the regulatory process in Europe. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility.

Such a withdrawal from the European Union is unprecedented, and it is unclear how the United Kingdom's access to the European single market for goods, capital, services and labor within the European Union, or single market, and the wider commercial, legal and regulatory environment, will impact our current and future operations (including business activities conducted by third parties and contract manufacturers on our behalf) and clinical activities in the United Kingdom.

Additional laws and regulations governing international operations could negatively impact or restrict our operations.

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

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

enforcement actions. Recently the SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents or contractors, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information products classified for national security purposes, as well as certain products, technology and technical data relatingto those products. If we continue and expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products, if approved, in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees and our business, prospects, operating results and financial condition. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

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

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

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

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

Risks Related to Our Intellectual Property

Risks Related to Licensed Intellectual Property

Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.

Our business will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, their respective components, synthetic intermediates, formulations, combination therapies and methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities and whether a court would issue an injunctive remedy. If we are unable to secure and maintain patent protection for any product or technology we develop, or if the scope of the patent protection secured is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to commercialize any product candidates we may develop may be adversely affected.

The patenting 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, obtain, or maintain 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 may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors or licensees.

The strength of patents in the biotechnology and biopharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our technology, including our product candidates, or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

We cannot be certain that we were the first to file any patent application related to our technology, including our product candidates, and, if we were not, we may be precluded from obtaining patent protection for our technology, including our product candidates.

We cannot be certain that we are the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. Furthermore, for United States applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States Patent and Trademark Office, or USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Similarly, for United States applications in which at least one claim is not entitled to a priority date before March 16, 2013, derivation proceedings can be instituted to determine whether the subject matter of a patent claim was derived from a prior inventor’s disclosure.

We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent or patent application 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. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, would adequately protect our product candidates, or would be found by a court to be infringed by a competitor’s technology or product. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. The possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights, or will design around the claims of patents that may issue that cover our products.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. Under the enacted Leahy-Smith America Invents Act, or America Invents Act, enacted in 2013, the United States moved from a “first to invent” to a “first-to-file” system. Under a “first-to-file” system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the “first-to-file” provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use compounds that are similar to the compositions of our product candidates but that are not covered by the claims of our patents or those of our licensors;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents or become hostile to us or the patents or patent applications on which they are named as inventors;
- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;
- we have engaged in scientific collaborations in the past, and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business.

Risks Related to License and Collaboration Agreements

We have entered into, and may enter into, license or other collaboration agreements that impose certain obligations on us. If we fail to comply with our obligations under such agreements with third parties, we could lose rights that may be important to our business.

In connection with our efforts to expand our pipeline of product candidates, we have entered into and may further enter into certain licenses or other collaboration agreements in the future pertaining to the in-license of rights to additional candidates. Such agreements may impose various diligence, milestone payment, royalty, insurance or other obligations on us. If we fail to comply with these obligations, our licensor or collaboration partners 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.

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

- the scope of rights granted under the license agreement and other interpretation-related issues;

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

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

In addition, we may have limited control over the maintenance and prosecution of these in-licensed patents and patent applications, 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 any future 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 the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

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

In addition to patent protection, we rely heavily upon know-how and trade secret protection, as well as non-disclosure agreements and invention assignment agreements with our employees, consultants and third parties, to protect our confidential and proprietary information, especially where we do not believe patent protection is appropriate or obtainable. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not, for example, in the case of misappropriation of a trade secret by an employee or third-party with authorized access, provide adequate protection for our proprietary information. Our security measures may not prevent an employee or consultant from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. If any of our confidential or proprietary information, such as our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed.

In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third-party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology.

Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development

or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. We have also adopted policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets.

Risks Related to Potential Third-Party Claims

Third-party claims of intellectual property infringement may prevent or delay our product discovery and development efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and biopharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, *inter partes* review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and biopharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

We also may be subject to other third party claims relating to alleged infringement of intellectual property or other proprietary rights, including breach of nondisclosure, nonuse, noncompetition and non-solicitation provisions, intellectual property assignment and ownership, and misuse or misappropriation of intellectual property, trade secrets and other confidential information, among others. If a court of competent jurisdiction finds us liable for any such claims, we may be prohibited from using certain intellectual property, trade secrets and confidential information, effectively blocking our ability to seek patent protection for our inventions and halting the progress of our clinical development and commercialization efforts. For example, on May 20, 2020, we received a cease and desist letter from Sage Therapeutics, Inc., or Sage, in which Sage alleges a claim that we improperly accessed and benefited from Sage confidential information in connection with the in-license of our PRAX-114 development program as a result of our employment or engagement of former Sage employees and consultants. We believe that there is no merit to these claims and intend to defend our position. However, an adverse result could harm our business and result of operations.

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

- infringement and other intellectual property claims 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, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third-party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third-party licenses its product rights to us, which it is not required to do;
- 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 for our products and any license that is available may be non-exclusive, which could result in our competitors gaining access to the same intellectual property; and
- redesigning our product candidates or processes so they do not infringe, which may not be possible or 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. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure.

Our collaborators may assert ownership or commercial rights to inventions they develop from research we support or that we develop or otherwise arising from the collaboration.

We collaborate with several institutions, universities, medical centers, physicians and researchers in scientific matters and expect to continue to enter into additional collaboration agreements. In certain cases, we do not have written agreements with these collaborators, or the written agreements we have do not cover intellectual property rights. Also, we rely on numerous third parties to provide us with materials that we use to conduct our research activities and develop our product candidates. If we cannot successfully negotiate sufficient ownership and commercial rights to any inventions that result from our use of a third-party collaborator's materials, or if disputes arise with respect to the intellectual property developed with the use of a collaborator's samples, or data developed in a collaborator's study, in cases where written agreements either do or do not exist, we may be limited in our ability to capitalize on the market potential of these inventions or developments.

Third parties may assert that we are employing their proprietary technology without authorization.

There may be third-party patents of which we are currently unaware with claims to compositions of matter, materials, formulations, methods of manufacture or methods for treatment that encompass the composition, use or manufacture of our product candidates. There may be currently pending patent applications of which we are currently unaware which may later result in issued patents that our product candidates or their use or manufacture may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third- party patent were held by a court of competent jurisdiction to cover our product candidates, intermediates used in the manufacture of our product candidates or our materials generally, aspects of our formulations or methods of use, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, 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. 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 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.

Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.

As is common in the biotechnology and biopharmaceutical industries, we employ individuals who were previously employed at universities or other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties.

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 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. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development 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 substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

We may not be successful in obtaining or maintaining necessary rights to develop any future product candidates on acceptable terms.

Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights.

Our product candidates may also require specific formulations to work effectively and efficiently and these rights may be held by others. We may develop products containing our compounds and pre-existing biopharmaceutical compounds. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

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

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

Competitors may infringe our patents or the patents of our current or future 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 one or more of our patents is not valid or is 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 or for other reasons. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

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

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned by or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference or derivation proceeding declared by the USPTO to determine priority of invention in the United States. If we or one of our licensors is a party to an interference or derivation proceeding involving a U.S. patent application on inventions owned by or in-licensed to us, we may incur substantial costs, divert management's time and expend other resources, even if we are successful.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the 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 or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Litigation or interference 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 in 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, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Risks Related to Patent Laws and Protection

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.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other 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, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In certain circumstances, even inadvertent noncompliance events may permanently and irrevocably jeopardize patent rights. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

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

If we or one of our licensors initiate legal proceedings against a third-party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate, 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 numerous 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 (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our 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 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 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.

Likewise, our current licensed or owned patents are expected to expire between 2029 and 2041, without taking into account any possible patent term adjustments or extensions. Our earliest patents may expire before, or soon after, our first product achieves marketing approval in the United States or foreign jurisdictions. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects. Our current licensed or owned pending patent applications covering our proprietary technologies or our product candidates that if issued as patents are expected to expire from 2029 through 2041, without taking into account any possible patent term adjustments or extensions. However, we cannot be assured that the USPTO or relevant foreign patent offices will grant any of these patent applications.

Changes in 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 products.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 16, 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. On March 16, 2013, under the America Invents Act, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO on or after March 16, 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, inter-parties review and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biopharmaceuticals are particularly uncertain. 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.

This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.

We have limited intellectual property rights outside 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 can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims 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, and may require a compulsory license to, patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally.

The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

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

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions such as patent term adjustments and/or extensions, may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. 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 ours.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. 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 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 request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

If 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 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. 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.

Risks Related to Our Dependence on Third Parties

Risks Related to Third Parties Generally

We rely on third parties to assist in conducting our preclinical studies and 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 laboratories, CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our preclinical studies and clinical trials and expect to rely on these third parties to conduct preclinical studies and clinical trials of any other product candidate that we develop. Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. Moreover, delays may occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

Although our reliance on these third parties for preclinical and clinical development activities limits our control over these activities, we remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. Moreover, human clinical research must 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. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and IRBs. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the regulatory authorities 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, a regulatory authority will determine that any of our clinical trials comply with GCPs.

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. These outside contractors may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. 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.

If our relationships with any third parties conducting our studies are terminated, we may be unable to enter into arrangements with alternative third parties on commercially reasonable terms, or at all. Switching or adding third parties to conduct our studies involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired preclinical and clinical development timelines. Although we carefully manage our relationships with third parties conducting our studies, we cannot assure that we will not

encounter similar challenges or delays in the future or that these delays or challenges will not have a material and adverse effect on our business, financial condition and results of operations.

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.

Risks Related to Third-Party Manufacturers

We contract with third parties for the manufacture of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization. We rely, and expect to continue to rely, on third-party manufacturers for the production of our product candidates for preclinical studies and clinical trials under the guidance of members of our organization. If we were to experience an unexpected loss of supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials. For example, the extent to which the COVID-19 pandemic impacts our ability to procure sufficient supplies for the development of our products and product candidates will depend on the severity and duration of the spread of the virus, and the actions undertaken to contain COVID-19 or treat its effects.

We expect to continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture our product candidates according to our schedule, or at all, including if our third-party contractors 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 agreements between us and them;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of the third party to manufacture our product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or study drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time and at expected cost due to inflationary impacts, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP or similar regulations for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP or similar regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain marketing approval for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority 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 marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

If any third-party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates, and/or increase the product yield of its manufacturing, then our costs to manufacture the product 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 that we may develop, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of the product. The transition to larger scale production could prove difficult. In addition, if our third party manufacturers are not able to optimize their manufacturing processes to increase the product yield for our product candidates, or if they are unable to produce increased amounts of our product candidates while maintaining the quality of the product, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operation.

Risks Related to Third-Party Suppliers

We depend on third-party suppliers for key raw materials used in our manufacturing processes, some of which are our sole source of supply, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials could harm our business.

We rely on our CMOs to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical trials. We do not have, nor do we expect to enter into, any agreements for the commercial production of these raw materials, and we do not expect to have any control over the process or timing of our CMOs' acquisition of raw materials needed to produce our product candidates. Any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing clinical trial due to a manufacturer's need to replace a third-party supplier of raw materials could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates. Additionally, if our future manufacturers or we are unable to purchase these raw materials to commercially produce any of our product candidates that gains regulatory approvals, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

Furthermore, for those third-party suppliers who may be our sole source of supply of certain materials, we may not have arrangements in place for a redundant or second-source supply of any such materials in the event any of our current suppliers cease their operations for any reason. Establishing additional or replacement suppliers for the raw materials used in our product candidates, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified and may require additional regulatory inspection or approval, which could result in further delay.

We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.

We may seek third-party collaborators for the research, development and commercialization of certain of the product candidates we may develop. For example, we have a collaboration with Ionis Pharmaceuticals, Inc. to further our development of product candidates and to enhance our research efforts directed to developing a product candidate for the treatment of epilepsy. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies and academic institutions, such as The Florey Institute of Neuroscience. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with

commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs, or any product candidates we may develop, pose the following risks to us:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not properly obtain, maintain, enforce or defend intellectual property or proprietary rights relating to our product candidates or research programs, or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property covering our product candidates or research programs that results from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates or research programs;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- collaborators may control certain interactions with regulatory authorities, which may impact our ability to obtain and maintain regulatory approval of our products candidates;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or research programs or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborators may decide to not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates 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 or research programs if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may restrict us from researching, developing or commercializing certain products or technologies without their involvement;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may grant sublicenses to our technology or product candidates or undergo a change of control and the sublicensees or new owners may decide to take the collaboration in a direction which is not in our best interest;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know-how or intellectual property of the collaborator relating to our products, product candidates or research programs;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders or disrupt our management and business;
- if our collaborators do not satisfy their obligations under our agreements with them, or if they terminate our collaborations with them, we may not be able to develop or commercialize product candidates as planned;

- collaborations may require us to share in development and commercialization costs pursuant to budgets that we do not fully control and our failure to share in such costs could have a detrimental impact on the collaboration or our ability to share in revenue generated under the collaboration;
- collaborations may be terminated in their entirety or with respect to certain product candidates or technologies and, if so terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or technologies; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our development or commercialization program under such collaboration could be delayed, diminished or terminated.

We may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elects not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators could prevent us from receiving future payments under such agreements, which could negatively impact our revenues. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section also apply to the activities of our collaborators and any negative impact on our collaborators may adversely affect us.

We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions or alliances.

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

Risks Related to Employee Matters, Managing Our Business and Operations

Risks Related to Business Operations

Business interruptions resulting from COVID-19 or a similar pandemic, epidemic or outbreak of an infectious disease in the United States or worldwide may adversely affect our business.

In December 2019, a novel strain of coronavirus named SARS-CoV-2 was identified in Wuhan, China. This virus continues to spread globally, including in the United States and the disease it causes, COVID-19, has been declared a pandemic by the World Health Organization. The COVID-19 pandemic has impacted the global economy and may impact our operations, including the potential interruption of our clinical trial activities, regulatory reviews and our supply chain.

The COVID-19 pandemic has and may in the future delay enrollment in our clinical trials due to prioritization of hospital resources or patients being either unwilling to enroll in our trials or unable to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services, which would delay our ability to conduct clinical trials or release clinical trial results and could delay our ability to obtain regulatory approval and commercialize our product candidates. For example, we had previously observed delays in our trial enrollment in Australia for our PRAX-944 Phase 2a trial due to stringent COVID-19 lockdown restrictions. While these lockdowns did not lead to a material impact on this trial from the delay in enrollment, we cannot predict the scope and severity of potential shutdowns or disruptions of businesses due to COVID-19 in the future.

We continue to closely monitor the COVID-19 pandemic as we evolve our business continuity plans, clinical development plans and response strategy. The extent to which the COVID-19 pandemic impacts our business will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of the novel coronavirus, the actions to contain the coronavirus or treat its impact and the extent and duration of the pandemic's impact on economic conditions and social activity, including with respect to inflationary pressures and supply chain shortages and disruptions, among others. At present, we are not experiencing significant impact or delays from the COVID-19 pandemic on our business, operations and, if approved, commercialization plans. In addition, we have taken steps to mitigate against COVID-19 pandemic-related delays, and may take additional measures, intended to help minimize the risk of the virus to our employees, including temporarily requiring all employees to work remotely, suspending all non-essential travel worldwide for our employees, and discouraging employee attendance at industry events and in-person work-related meetings, which could negatively affect our business.

While we have taken and are continuing to take steps to mitigate against possible delays, our planned clinical trials may be affected by the COVID-19 pandemic, including (i) delays or difficulties in enrolling and retaining patients in our planned clinical trials, including patients that may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services; (ii) delays or difficulties in clinical site initiation, including difficulties in recruiting and retaining clinical site investigators and clinical site staff; (iii) diversion or prioritization of healthcare resources away from the conduct of clinical trials and towards the COVID-19 pandemic, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, and because, who, as healthcare providers, may have heightened exposure to COVID-19 and adversely impact our clinical trial operations; (iv) interruption of our future clinical supply chain or key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal, state/provincial or municipal governments, employers and others; and (v) limitations in outsourced third-party resources that would otherwise be focused on the conduct of our planned clinical trials, including because of sickness of third-party personnel or their families, or the desire of third-party personnel to avoid contact with large groups of people. A significant outbreak of other infectious diseases in the future also could result in a widespread health crisis that could adversely affect the economies and financial markets worldwide, resulting in an economic downturn that could impact our business, financial condition and results of operations.

Our business is subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Some of our suppliers and collaborative relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements in non-U.S. countries;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country’s or region’s political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;

- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations
- potential liability under the FCPA, U.K. Bribery Act of 2010 or comparable foreign laws;
- business interruptions resulting from geo-political actions, including war and terrorism, natural disasters including earthquakes, typhoons, floods and fires, or health epidemics such as COVID-19; and
- cyberattacks, which are growing in frequency, sophistication and intensity, and are becoming increasingly difficult to detect.

These and other risks associated with our planned international operations may materially adversely affect our ability to attain profitable operations.

Risks Related to Employees

We depend heavily on our executive officers, principal consultants and others, and the loss of their services would materially harm our business.

Our success depends, and will likely continue to depend, upon our ability to hire, retain the services of our current executive officers, principal consultants and others, including Marcio Souza, our President and Chief Executive Officer, Timothy Kelly, our Chief Financial Officer, and Bernard Ravina, our Chief Medical Officer. We have entered into employment agreements with Mr. Souza, Mr. Kelly and Dr. Ravina, but they may terminate their employment with us at any time. The loss of their services might impede the achievement of our research, development and commercialization objectives. We do not maintain “key person” insurance for any of our executives or other employees.

Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced significant demand for, and a high rate of turnover of, management personnel in recent years. Replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully.

Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited.

We only have a limited number of employees to manage and operate our business. If we are unable to hire to retain adequate personnel, then we may not be able to meet our operational goals.

As of February 18, 2022, we had 139 full-time employees. Our focus on the clinical development of our product candidates requires us to optimize cash utilization and to manage and operate our business in a highly efficient manner. We cannot ensure that we will be able to hire and/or retain adequate staffing levels to develop our product candidates or to run our operations and/or to accomplish all of the objectives that we otherwise would seek to accomplish.

Our employees, independent contractors, consultants, collaborators and contract research organizations may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors, consultants, collaborators and contract research organizations may engage in fraudulent conduct or other illegal activity. Misconduct by those parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates:

- regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities;

- manufacturing standards;
- federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities; and
- laws that require the accurate reporting of financial information or data.

Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of product materials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this kind of 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 be in compliance with such laws, standards or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, integrity oversight and reporting obligations, possible exclusion from participation in the United States in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could have a material adverse effect on our ability to operate our business and our results of operations.

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 support our public company operations. To manage these growth activities, we must continue to implement and improve our managerial, operational 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.

Risks Related to Data Privacy

Cyber-attacks or other failures in our telecommunications or information technology systems, or those of our collaborators, contract research organizations, third-party logistics providers, distributors or other contractors or consultants, could result in information theft, data corruption and significant disruption of our business operations.

We, our collaborators, our CROs, third-party logistics providers, distributors and other contractors and consultants utilize information technology, or IT, systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including third parties gaining access to employee accounts using stolen or inferred credentials, computer malware, viruses, spamming, phishing attacks or other means, and deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. Attacks upon information technology systems are also increasing in their levels of persistence and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period.

While we do not believe that we have experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. These threats pose a risk to the security of our, our collaborators', our CROs', third-party logistics providers', distributors' and other contractors' and consultants' systems and networks, and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our collaborators, CROs, third-party logistics providers, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems. Any cyber-attack, data breach or destruction or loss of data could result in a violation of applicable U.S. and international privacy, data protection and other laws, and subject us to litigation and governmental investigations and proceedings by federal, state and local regulatory entities in the United States and by international regulatory entities, resulting in exposure to material civil and/or criminal liability. Further, our general liability insurance and corporate risk program may not cover all potential claims to which we are exposed and may not be adequate to indemnify us for all liability that may be imposed; and could have a material adverse effect on our business and prospects. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials for any of our product candidates could result in delays in our development and regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

We rely on a set of cloud-based software services and access these services via the Internet for the vast majority of our computing, storage, bandwidth and other services. Any disruption of or interference with our use of our cloud-based services would negatively affect our operations and could seriously harm our business.

We use several distributed computing infrastructure platforms for business operations, or what is commonly referred to as "cloud" computing services and we access these services via the Internet. Any transition of the cloud services currently provided by an existing vendor to another cloud provider would be difficult to implement and will cause us to incur significant time and expense. Given this, any significant disruption of or interference with our use of these cloud computing services would negatively impact our operations and our business would be seriously harmed. If our employees or partners are not able to access our cloud computing services or encounter difficulties in doing so, we may experience business disruption. The level of service provided by our cloud computing vendors, including the ability to secure our confidential information and the confidential information of third parties that is shared with us, may also impact the perception of our company and could seriously harm our business and reputation and create liability for us. If a cloud computing service that we use experiences interruptions in service regularly or for a prolonged basis, or other similar issues, our business could be seriously harmed.

In addition, a cloud computing service may take actions beyond our control that could seriously harm our business, including:

- discontinuing or limiting our access to its platform;
- increasing pricing terms;
- terminating or seeking to terminate our contractual relationship altogether; or
- modifying or interpreting its terms of service or other policies in a manner that impacts our ability to run our business and operations.

Our cloud computing services have broad discretion to change and interpret its terms of service and other policies with respect to us, and those actions may be unfavorable to us. Our cloud computing services may also alter how we are able to process data on the platform. If a cloud computing services makes changes or interpretations that are unfavorable to us, our business could be seriously harmed.

Our efforts to protect the information shared with us may be unsuccessful due to the actions of third parties, software bugs or other technical malfunctions, employee error or malfeasance or other factors. In addition, third parties may attempt to fraudulently induce employees or users to disclose information to gain access to our data or third-party data entrusted to us. If any of these events occur, our or third-party information could be accessed or disclosed improperly. Some partners or collaborators may store information that we share with them on their own computing system. If these third parties fail to implement adequate data-security practices or fail to comply with our policies, our data may be improperly accessed or disclosed. And even if these third parties take all of these steps, their networks may still suffer a breach, which could compromise our data.

Any incidents where our information is accessed without authorization, or is improperly used, or incidents that violate our policies, could damage our reputation and our brand and diminish our competitive position. In addition, affected parties or government authorities could initiate legal or regulatory action against us over those incidents, which could cause us to incur significant expense and liability or result in orders or consent decrees forcing us to modify our business practices. Concerns over our privacy practices, whether actual or unfounded, could damage our reputation and brand and deter users, advertisers and partners from using our products and services. Any of these occurrences could seriously harm our business.

Risks Related to Tax Laws

Legislation or other changes in U.S. tax law could adversely affect our business and financial condition.

The legislation, regulations and rules regarding U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department and by state and local tax agencies. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many changes have been made to applicable tax laws and changes are likely to continue to occur in the future. In particular, the U.S. federal government may enact significant changes to the taxation of business entities including, among others, an increase in the corporate income tax rate and the imposition of minimum taxes or surtaxes on certain types of income.

It cannot be predicted whether, when, in what form or with what effective dates any changes in tax laws, regulations or rules, promulgated or issued under existing or new tax laws, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof. If any such changes are enacted or implemented, we care currently unable to predict the ultimate impact on our business or holders of our common stock.

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

Our ability to use our U.S. federal and state net operating losses and tax credits is dependent upon our generation of future taxable income and income tax liabilities, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income or income tax liabilities to use any or all of our net operating losses or tax credits.

Our unused U.S. federal net operating losses generated in tax years beginning before January 1, 2018, and unused state net operating losses subject to expiration, will carry forward to offset future taxable income, if any, until such unused net operating losses expire. Our unused U.S. federal net operating losses generated in tax years beginning after December 31, 2017 will not expire and may be carried forward indefinitely, although, for taxable years beginning after December 31, 2020, the deductibility of such U.S. federal net operating losses is limited to 80% of our taxable income in such taxable year.

In addition, both our current and future net operating losses and tax credits may be subject to limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, if we undergo an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders or groups of stockholders over a rolling three-year period.

Risks Related to Our Common Stock

Risks Related to Investment in Securities

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely to be highly 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 "Risk Factors" section, these factors include:

- the commencement, enrollment, completion or results of our current clinical trials of 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 any 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 the use of our 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 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, including as a result of the COVID-19 pandemic. 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 and a diversion of management's attention and resources.

If securities or industry analysts do not 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. We may never obtain research coverage by industry or financial analysts. If no securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively impacted. In the event securities or industry analysts initiate coverage, 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. 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.

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

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

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. 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.

Our executive officers, directors and their affiliates and our principal stockholders own a significant percentage of our stock and will be able to exert control over matters subject to stockholder approval.

Based on shares outstanding as of December 31, 2021, our executive officers, directors and their affiliates and our principal stockholders beneficially hold, in the aggregate, approximately 62.2% of our outstanding voting stock. These stockholders, acting together, would be able to control all matters requiring stockholder approval. The concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. This concentration of ownership control may adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change in control;
- entrenching our management and the board of directors;
- impeding a merger, consolidation, takeover or other business combination involving us that other stockholders may desire; and/or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

Risks Related to Our Controls and Reporting Requirements

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

As a public company, we will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or 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 on public companies, 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, or 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. 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 substantially increase our legal and financial compliance costs and 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. The increased costs will 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, we expect these rules and regulations to 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.

We are no longer an "emerging growth company" or a "smaller reporting company" and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies no longer apply to us.

We are no longer an emerging growth company. As a result, we are now subject to certain disclosure requirements that are applicable to other public companies that had not been applicable to us as an emerging growth company. These requirements include:

- compliance with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- compliance with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- full disclosure obligations regarding executive compensation; and
- compliance with the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We are also no longer a smaller reporting company and are no longer permitted to rely on exemptions for smaller reporting companies from certain disclosure requirements that are applicable to other public companies that are not smaller reporting companies. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors.

If we fail to 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.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. 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 will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. 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.

Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, 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 or internal 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. 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 or insufficient disclosures due to error or fraud may occur and not be detected.

We have broad discretion over the use of our cash and cash equivalents and may not use them effectively.

Our management has broad discretion to use our cash and cash equivalents to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending our use to fund operations, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

Risks Related to Charter and Bylaws

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue convertible preferred stock on terms determined by the board of directors without stockholder approval and which convertible preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

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 fiduciary duty owed by any of our directors, officers and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our bylaws (in each case, as they may be amended from time to time) or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein; provided, however, that this exclusive forum provision will not apply to any causes of action arising under the Securities Act or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware, or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated bylaws also specify that unless we consent in writing to the selection of an alternate forum, the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. 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. We recognize that the forum selection clause in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, the forum selection clause in our bylaws may limit our stockholders' ability to bring a claim in a 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. The enforceability of similar choice of forum provisions in other companies' governing documents has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our bylaws to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition, or results of operations.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Facilities

We sublease a facility containing 25,445 square feet of office space, which is located at 99 High Street, Boston, Massachusetts 02110. Our sublease expires on January 31, 2026. We believe that our current facility is sufficient to meet our current and near-term needs and that, should it be needed, suitable additional space will be available. Our previous sublease of 6,374 square feet of office space at One Broadway, Cambridge, Massachusetts 02142 expired on December 30, 2021.

Item 3. Legal Proceedings

We are not currently a party to any material legal matters or claims. We may become party to legal matters and claims arising in the ordinary course of business. We cannot predict the outcome of any such legal matters or claims, and despite the potential outcomes, the existence thereof may have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades under the symbol “PRAX” on the Nasdaq Global Select Market.

Holders of Our Common Stock

As of February 18, 2022, there were approximately 4 holders of record of shares of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings to fund the development and expansion of our business, and therefore we do not anticipate paying cash dividends on our common stock in the foreseeable future.

Recent Sales of Unregistered Securities

We did not make any sales of unregistered securities during the three months ended December 31, 2021.

Use of Proceeds from Initial Public Offering

In October 2020, we completed the initial public offering of our common stock, or IPO, pursuant to which we issued and sold 11,500,000 shares of our common stock at a price to the public of $19.00 per share. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-249074), which was declared effective by the Securities and Exchange Commission on October 15, 2020.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

There were no repurchases of shares of common stock made during the three months ended December 31, 2021.

Item 6. Selected Financial Data

Reserved.

Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and financing needs, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system, or CNS, disorders characterized by neuronal excitation-inhibition imbalance. Normal brain function requires a delicate balance of excitation and inhibition in neuronal circuits, which, when dysregulated, can lead to abnormal function and disease. We are applying insights from genetic epilepsies to both rare and more prevalent neurological and psychiatric disorders, using our understanding of shared biological targets and circuits in the brain. We apply a deliberate and pragmatic precision approach, leveraging a suite of translational tools including novel transgenic and predictive translational animal models and electrophysiology markers, to enable an efficient path to proof-of-concept in patients. Through this approach, we have established a broad CNS portfolio with multiple programs, including product candidates across psychiatric disorders, movement disorders, epilepsy and other exploratory CNS indications, with three clinical-stage product candidates. Each of our clinical-stage product candidates is advancing in more than one indication and we anticipate expansion into additional indications. We expect multiple topline readouts from our clinical-stage programs and anticipate the launch of a fourth clinical development program in 2022. In addition, we have established a robust pipeline of preclinical stage programs through internal research and in-licensing.

Our broad portfolio of CNS programs is currently structured by therapeutic focus in three primary franchises – Psychiatry, Movement Disorders and Epilepsy. In addition, we are pursuing development in other exploratory CNS indications such as rare adult cephalgias. Within our Psychiatry franchise, our most advanced clinical candidate, PRAX-114, is being developed for the treatment of a broad range of patients suffering from major depressive disorder, or MDD, and post-traumatic stress disorder, or PTSD. We expect to report topline results from the Aria Study, a Phase 2/3, placebo-controlled study evaluating PRAX-114 for monotherapy treatment of MDD, in the second quarter of 2022. We also expect to report topline results from the Acapella Study, a Phase 2, placebo-controlled, dose-ranging study evaluating PRAX-114 for treatment of MDD, in mid-2022. In addition, we have initiated a Phase 2, placebo-controlled study evaluating PRAX-114 for the treatment of PTSD and expect to report topline results in the second half of 2022.

Within our Movement Disorders franchise, our second clinical candidate, PRAX-944, is being developed for the treatment of Essential Tremor, or ET, and Parkinson's Disease, or PD. We anticipate reporting topline results from the second cohort of our ongoing Phase 2a trial evaluating PRAX-944 for the treatment of ET in the second quarter of 2022, including both open-label and placebo-controlled, randomized withdrawal period results. We have initiated a Phase 2b placebo-controlled, dose-range finding trial, the Essential1 Study, to evaluate the tolerability, safety and efficacy of PRAX-944 in adults with ET and we expect to report topline results in the second half of 2022. We also expect to initiate a Phase 2, placebo-controlled, crossover study to evaluate the safety, pharmacokinetics, or PK, and efficacy of daytime dosing of PRAX-114 for the treatment of ET in the first quarter of 2022 and expect to report topline results in the second half of 2022. We expect to initiate a Phase 2, placebo-controlled trial to evaluate the safety, PK and efficacy of PRAX-944 as a non-dopaminergic treatment for the motor symptoms of PD in the second quarter of 2022.

Within our Epilepsy franchise, we expect to initiate a Phase 2 study with our third clinical-stage candidate, PRAX-562, in the second quarter of 2022 in patients with rare pediatric Developmental and Epileptic Encephalopathies. Our most advanced preclinical stage product candidate within our Epilepsy franchise, PRAX-222, is an antisense oligonucleotide, or ASO, designed to decrease the expression levels of the protein encoded by the gene SCN2A in patients with gain-of-function SCN2A mutations. We expect to initiate a seamless study of PRAX-222 in the second quarter of 2022, which would be our fourth program to reach clinical stage. We also expect to initiate a Phase 2 proof-of-concept clinical trial evaluating PRAX-562 in patients with rare adult

cephalgias in the first quarter of 2022. In addition, our preclinical pipeline consists of a discovery program in development for KCNT1 related epilepsy, PRAX-628, a product candidate nominated in the fourth quarter of 2021 for focal epilepsy, three ASOs targeting SCN2A in patients with loss-of-function mutations, PCDH19 and SYNGAP1, respectively, and three additional discovery programs for undisclosed targets in psychiatry, movement disorders and epilepsy.

We were incorporated in 2015 and commenced operations in 2016. Since inception, we have devoted substantially all of our resources to developing our preclinical and clinical product candidates, building our intellectual property, or IP, portfolio, business planning, raising capital and providing general and administrative support for these operations. We employ a “virtual” research and development model, relying heavily upon external consultants, collaborators and contract research organizations, or CROs, to conduct our preclinical and clinical activities. Since inception, we have financed our operations primarily with proceeds from the sale and issuance of equity securities.

On May 18, 2021, we completed a follow-on public offering in which we issued and sold 5,750,000 shares of our common stock at a public offering price of $18.25 per share, including 750,000 shares of common stock issued and sold pursuant to the underwriters' exercise, in full, of their option to purchase additional shares of common stock, for aggregate gross proceeds of $104.9 million. We received approximately $98.4 million in net proceeds after deducting discounts, commissions and offering expenses payable by us.

On November 3, 2021, we entered into an Open Market Sale Agreement, or the sales agreement, with Jefferies LLC, or Jefferies, to provide for the offering, issuance and sale of up to an aggregate amount of $125.0 million of common stock from time to time in at-the-market offerings for which Jefferies acts as sales agent. As of December 31, 2021, we issued and sold 391,997 shares under the sales agreement for aggregate gross proceeds of $7.6 million. We received approximately $7.0 million of net proceeds after deducting commissions and offering expenses payable by us.

We are a development stage company and we have not generated any revenue from product sales, and do not expect to do so for several years, if at all. All of our product candidates are still in preclinical and clinical development. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates, if approved. We have incurred recurring operating losses since inception, including net losses of $167.1 million and $61.8 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $316.6 million. We expect to incur significant expenses and operating losses for the foreseeable future as we expand our research and development activities. In addition, our losses from operations may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- advance our lead product candidates, PRAX-114 and PRAX-944, to late stage clinical trials;
- advance our PRAX-562 product candidate to Phase 2 clinical trials;
- advance our PRAX-222 product candidate to clinical trials;
- advance our preclinical candidates to clinical trials;
- further invest in our pipeline;
- further invest in our manufacturing capabilities;
- seek regulatory approval for our product candidates;
- maintain, expand, protect and defend our IP portfolio;
- acquire or in-license technology;
- secure facilities to support continued growth in our research, development and commercialization efforts;
- take temporary precautionary measures to help minimize the risk of COVID-19 to our employees; and
- increase our headcount to support our development efforts and to expand our clinical development team.

In addition, as we progress toward marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2021, we had cash, cash equivalents, and marketable securities of $275.9 million. We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditures into the second quarter of 2023. 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. See “—Liquidity and Capital Resources.”

COVID-19 Business Update

In light of the ongoing COVID-19 pandemic, we continue to experience some disruptions and increased risk in our operations and those third parties upon whom we rely. These include disruptions and risks related to the conduct of our clinical trials and preclinical studies as policies at various clinical sites and federal, state, local and foreign laws, rules and regulations continue to evolve, including quarantines, travel restrictions and redirection of healthcare resources toward pandemic response efforts. The COVID-19 pandemic has impacted the enrollment of some of our ongoing clinical trials, including slower patient enrollment and treatment in some of our clinical studies, the impact of which has varied by clinical study and program, but none of which have significantly impacted our overall clinical trial timelines. While we have experienced limited financial impacts to date, given the global economic slowdown, the overall disruption of global healthcare systems and the other risks and uncertainties associated with the pandemic such as increased inflation, our business, financial condition and results of operations could be materially adversely affected. We continue to closely monitor the COVID-19 pandemic as we evolve our business continuity plans, clinical development plans and response strategy.

Financial Operations Overview

Revenue

We have not generated any revenue since inception and do not expect to generate any revenue from the sale of products for several years, if at all. If our development efforts for our current or future product candidates are successful and result in marketing approval or collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from collaboration or license agreements that we may enter into with third parties.

Operating Expenses

Research and Development Expenses

The nature of our business and primary focus of our activities generate a significant amount of research and development costs. Research and development expenses represent costs incurred by us for the following:

- costs to develop our portfolio;
- discovery efforts leading to development candidates;
- clinical development costs for our product candidates; and

- costs to develop our manufacturing technology and infrastructure.

The costs above comprise the following categories:

- personnel-related expenses, including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with third parties, such as consultants, investigative sites and CROs, that conduct our preclinical and clinical studies and in-licensing arrangements;
- costs incurred to maintain compliance with regulatory requirements;
- costs incurred with third-party contract development and manufacturing organizations to acquire, develop and manufacture materials for preclinical and clinical studies; and
- depreciation, amortization and other direct and allocated expenses, including rent, insurance and other operating costs, incurred as a result of our research and development activities.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our consolidated balance sheets as prepaid expenses or accrued expenses. Non-refundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

A significant portion of our research and development costs have been external costs. We track direct external research and development expenses to specific franchises and product candidates upon commencement. Due to the number of ongoing studies and our ability to use resources across several projects, indirect or shared operating costs incurred for our research and development franchises, such as personnel, facility costs and certain consulting costs, are not recorded or maintained on a franchise-specific basis.

The following table reflects our research and development expenses, including direct expenses summarized by major franchise and other exploratory CNS indications and indirect or shared operating costs recognized as research and development expenses during each period presented (in thousands):

	Year Ended December 31,	
	2021	**2020**
Psychiatry	$ 29,218	$ 13,077
Epilepsy	23,122	9,953
Movement disorders	18,460	4,158
Other exploratory CNS indications	9,509	700
Personnel-related (including stock-based compensation)	31,090	13,483
Other indirect research and development expenses	8,858	3,605
Total research and development expenses	$ 120,257	$ 44,976

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase in the foreseeable future as we advance our product candidates through the development phase, and as we continue to discover and develop additional product candidates, build manufacturing capabilities and expand into additional therapeutic areas.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. We 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:

- our ability to add and retain key research and development personnel;
- the timing and progress of preclinical and clinical development activities;
- the number and scope of our preclinical and clinical product candidates we decide to pursue;
- our ability to successfully complete clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the U.S. Food and Drug Administration, or the FDA, or any comparable foreign regulatory authority;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize, our product candidates;
- our successful enrollment in and completion of clinical trials;
- the costs associated with the development of any additional product candidates we identify in-house or acquire through collaborations;
- our ability to discover, develop and utilize biomarkers to demonstrate target engagement, pathway engagement and the impact on disease progression of our product candidates;
- our ability to establish and maintain agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- the terms and timing of any collaboration, license or other arrangement, including the terms and timing of any milestone payments thereunder;
- our ability to obtain and maintain patent, trade secret and other IP protection and regulatory exclusivity for our product candidates, if approved;
- our receipt of marketing approvals from applicable regulatory authorities;
- our ability to commercialize products, if approved, whether alone or in collaboration with others; and
- the continued acceptable safety profiles of any product candidates following approval.

A change in any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time to complete our clinical development activities. We may never obtain regulatory approval for any of our product candidates. The drug commercialization of any of our product candidates, if ever, will take several years and require significant development costs.

General and Administrative Expense

General and administrative expenses consist primarily of personnel-related costs, including salaries, benefits and stock-based compensation, for personnel in our executive, finance, legal, commercial and administrative functions. General and administrative expenses also include legal fees relating to corporate matters; professional fees for accounting, auditing, tax and administrative consulting services; insurance costs; administrative travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for office rent and other operating costs. These costs relate to the operation of the business, unrelated to the research and development function, or any individual franchise or product candidate. Costs to secure and defend our IP are expensed as incurred and are classified as general and administrative expenses.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support the expected growth in our research and development activities and the potential commercialization of our product candidates. We also expect to incur additional IP-related expenses as we file patent applications to protect innovations arising from our research and development activities.

Other Income

Other Income, Net

Other income, net consists of interest income from our cash, cash equivalents and marketable securities and amortization of investment premiums and discounts.

Income Taxes

Since our inception, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or for our earned research and development tax credits due to our uncertainty of realizing a benefit from those items. As of December 31, 2021 and 2020, we had U.S. federal and state net operating loss carryforwards which may be available to offset future taxable income and which begin to expire in 2035. As of December 31, 2021 and 2020, we also had federal and state research and development tax credit carryforwards which may be available to offset future income tax liabilities and which begin to expire in 2031.

Income taxes are determined at the applicable tax rates adjusted for non-deductible expenses, research and development tax credits and other permanent differences. Our income tax provision may be significantly affected by changes to our estimates. There was no income tax benefit (provision) recognized for the year ended December 31, 2021. The income tax benefit recognized for the year ended December 31, 2020 was not material.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our consolidated statements of operations for each period presented (in thousands):

	Year Ended December 31,		Change
	2021	2020	
Operating expenses:			
Research and development	$ 120,257	$ 44,976	$ 75,281
General and administrative	47,075	16,992	30,083
Total operating expenses	167,332	61,968	105,364
Loss from operations	(167,332)	(61,968)	(105,364)
Other income:			
Other income, net	271	140	131
Total other income	271	140	131
Loss before income taxes	(167,061)	(61,828)	(105,233)
Benefit from income taxes	—	8	(8)
Net loss	$ (167,061)	$ (61,820)	$ (105,241)

Research and Development Expense

The following table summarizes our research and development expenses for each period presented, along with the changes in those items (in thousands):

	Year Ended December 31,		Change
	2021	2020	
Psychiatry	$ 29,218	$ 13,077	$ 16,141
Epilepsy	23,122	9,953	13,169
Movement disorders	18,460	4,158	14,302
Other exploratory CNS indications	9,509	700	8,809
Personnel-related (including stock-based compensation)	31,090	13,483	17,607
Other indirect research and development expenses	8,858	3,605	5,253
Total research and development expenses	$ 120,257	$ 44,976	$ 75,281

The $75.3 million increase in research and development expenses was primarily attributable to the following:

- $17.6 million increase in personnel-related costs due to increased headcount, driven primarily by an increase of $8.0 million in stock-based compensation expense;
- $16.1 million increase in expense related to our psychiatry franchise, driven primarily by an increase in clinical-related and toxicology spend for our PRAX-114 Phase 2/3 Aria and Acapella clinical trials;
- $13.2 million increase in expense related to our epilepsy franchise, driven primarily by an increase in clinical-related and toxicology spend to support the initiation of our PRAX-562 Phase 2 developmental epileptic encephalopathies clinical trial and an increase in preclinical activities for our earlier stage assets;
- $14.3 million increase in expense related to our movement disorders franchise, driven primarily by an increase in toxicology and clinical-related spend for our PRAX-944 Phase 2 Essential1 clinical trial;
- $8.8 million increase in other exploratory CNS indications, driven primarily by an increase in clinical-related expenses for our PRAX-562 Phase 2 trial in Short-lasting Unilateral Neuralgiform headache attacks, Short-lasting Unilateral Neuralgiform headache with Autonomic symptoms and Trigeminal Neuralgia, as well as increased preclinical activities for our earlier stage assets; and
- $5.3 million increase in other indirect research and development expenses, driven primarily by an increase in general clinical related spend, as well as increases in facility and other allocated overhead costs and technology spend and related consulting costs to support our clinical and quality operations.

General and Administrative Expense

The $30.1 million increase in general and administrative expenses was primarily attributable to the following:

- $14.6 million increase in personnel-related costs, driven primarily by increased headcount, including an increase of $9.5 million in stock-based compensation expense;
- $9.9 million increase in professional fees, driven primarily by $5.1 million of increased commercial-related spend to support market assessments of our clinical-stage programs, a $2.2 million increase in audit and legal fees and a $1.7 million increase in general and administrative infrastructure-related costs; and
- $5.6 million increase in other general and administrative expenses, driven primarily by a $3.5 million increase in insurance and related costs due to our first full year as a public company, a $0.8 million increase in technology spend and a $0.7 million increase in donations and sponsorships.

Other Income

Other income for the years ended December 31, 2021 and 2020 was comprised of interest income on our cash, cash equivalents and marketable securities and investment premium and discount amortization.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant losses in each period. We have not yet commercialized any of our product candidates, which are in various phases of preclinical and clinical development, and we do not expect to generate revenue from sales of any products for several years, if at all.

To date, we have financed our operations primarily with proceeds from the sale and issuance of equity securities. From inception through December 31, 2021, we have raised $516.4 million in aggregate cash proceeds from such transactions, net of issuance costs. As of December 31, 2021, we had cash, cash equivalents and marketable securities of $275.9 million.

Cash Flows

The following table provides information regarding our cash flows for each period presented (in thousands):

	Year Ended December 31,	
	2021	2020
Net cash (used in) provided by:		
Operating activities	$ (124,554)	$ (52,623)
Investing activities	(140,520)	—
Financing activities	107,586	304,416
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (157,488)	$ 251,793

Operating Activities

Our cash flows from operating activities are greatly influenced by our use of cash for operating expenses and working capital requirements to support the business. We have historically experienced negative cash flows from operating activities as we have invested in developing our portfolio, drug discovery efforts and related infrastructure. The cash used in operating activities resulted primarily from our net losses adjusted for non-cash charges and changes in operating assets and liabilities, which are primarily the result of increased expenses and timing of vendor payments.

During the year ended December 31, 2021, net cash used in operating activities of $124.6 million was primarily due to our $167.1 million net loss, partially offset by $26.4 million of non-cash charges primarily related to stock-based compensation, amortization of premiums and discounts on marketable securities and non-cash operating lease expense, and $16.1 million in changes in operating assets and liabilities primarily related to increases in accounts payable and accrued expenses.

During the year ended December 31, 2020, net cash used in operating activities of $52.6 million was primarily due to our $61.8 million net loss, partially offset by $6.0 million of non-cash charges primarily related to stock-based compensation and $3.2 million in changes in operating assets and liabilities primarily related to an increase in accrued expenses.

Investing Activities

During the year ended December 31, 2021, net cash used in investing activities of $140.5 million primarily related to the purchase of marketable securities, partially offset by the maturity of marketable securities. There were no cash flows from investing activities during the year ended December 31, 2020.

Financing Activities

During the year ended December 31, 2021, net cash provided by financing activities of $107.6 million consisted of net proceeds from our follow-on public offering and at-the-market offerings of $105.7 million and net proceeds from the exercise of stock options of $2.4 million partially offset by the payment of issuance costs for our initial public offering, or IPO.

During the year ended December 31, 2020, net cash provided by financing activities of $304.4 million primarily consisted of net proceeds from our IPO and from the issuance of our Series C and Series C-1 redeemable convertible preferred stock, partially offset by our repurchase of Series C redeemable convertible preferred stock.

Plan of Operation and Future Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing research and development activities, particularly as we advance the preclinical activities and clinical trials of our product candidates. In addition, we expect to incur additional costs associated with operating as a public company and as we transition from being an emerging growth company and a smaller reporting company. As a result, we expect to incur substantial operating losses and negative operating cash flows for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- advance the clinical development of our clinical-stage product candidates within our psychiatry, movement disorders and epilepsy franchises, respectively;
- advance the development of any additional product candidates;
- conduct research and continue preclinical development of potential product candidates;
- make strategic investments in manufacturing capabilities;
- maintain our IP portfolio and opportunistically acquire complementary IP;
- seek to obtain regulatory approvals for our product candidates;
- potentially establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts and to support our operations as a public company; and
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges.

We are unable to estimate the exact amount of our working capital requirements, but based on our current operating plan, we expect that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2023. However, we have based this estimate on assumptions that may prove to be wrong and we could exhaust our capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with product development and potential collaborations with third parties for the development of our product candidates, we may incorrectly estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our funding requirements and timing and amount of our operating expenditures will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of preclinical studies and clinical trials for our franchises and product candidates;
- the number and characteristics of product candidates and technologies that we develop or may in-license;
- 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 costs necessary to obtain regulatory approvals, if any, for products in the United States and other jurisdictions, and the costs of post-marketing studies that could be required by regulatory authorities in jurisdictions where approval is obtained;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our IP rights and defending any IP-related claims;
- the continuation of our existing licensing arrangements and entry into new collaborations and licensing arrangements;
- the costs we incur in maintaining business operations;
- the costs associated with being a public company;
- the revenue, if any, received from commercial sales of any product candidates for which we receive marketing approval;
- the effect of competing technological and market developments;
- the impact of any business interruptions to our operations or to those of our manufacturers, suppliers or other vendors resulting from the COVID-19 pandemic or similar public health crisis; and
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates, although we currently have no commitments or agreements to complete any such acquisitions or investments in businesses.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Adequate additional funds may not be available to us on acceptable terms, or at all. We do not currently have any committed external source of funds. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of holders of our common stock. Additional debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially result in dilution to the holders of our common stock.

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

Contractual Obligations and Commitments

We have entered into certain agreements under which we have incurred or may in the future incur obligations and commitments that could have a material impact on our capital resources.

We sublease building space in Boston, Massachusetts. Our sublease will expire on January 31, 2026. As of December 31, 2021, our operating lease commitments for the remainder of the lease term were $5.2 million.

In addition, we have entered into collaboration and license agreements with Purdue Neuroscience Company, or Purdue, RogCon Inc., or RogCon, and Ionis Pharmaceuticals, Inc., or Ionis, under which we could be obligated to pay certain fees, milestone payments and cost reimbursements.

Under our license agreement with Purdue, we are obligated to make future milestone payments of up to $33.0 million based on the achievement of specified development and sales milestones. Furthermore, we are obligated to pay Purdue royalties of a low-single-digit percentage of annual net sales of licensed products. Either party may terminate the license agreement for convenience or in the event of a material breach by the other party and failure to cure such breach within a certain period of time. If the agreement is voluntarily terminated by Purdue, our license rights will survive such termination and such rights will become fully paid, perpetual and irrevocable. See “Business—License Agreements—License Agreement with Purdue.”

Under our license agreement with RogCon, we are obligated to reimburse RogCon for its out-of-pocket costs incurred for activities performed under the license agreement. Additionally, we may be obligated to pay RogCon a milestone payment of $3.0 million and profit share payments. The $3.0 million milestone payment is due when the first profit share payment has become due and payable and certain contingent payments have become due and payable to Ionis under our collaboration agreement with Ionis. The profit share payments are based on a low-double-digit percentage of net profits, depending on sales volume. Either party may terminate the license agreement for material breach or insolvency of the other party. Additionally, we may terminate for convenience with prior notice to RogCon. See “Business—License Agreements—License Agreement with RogCon.”

Under our collaboration agreement with Ionis, we are obligated to reimburse any out-of-pocket costs incurred by Ionis related to research activities, identification of a development candidate and conducting an investigational new drug application, or IND, enabling toxicology study. Ionis granted us an exclusive option to obtain the rights and license to further develop and commercialize a development candidate in the field of epilepsy and neurodevelopmental disorders, other than Dravet Syndrome, following the results of the IND-enabling toxicology study. We exercised this exclusive option in January 2022 and paid a $2.0 million license fee. We may be required

to make additional payments to Ionis including development milestone payments, additional milestone payments and sales royalties or sublicense fees. Either party may terminate the collaboration agreement upon material breach or insolvency of the other party. Ionis may terminate if we fail to achieve a performance milestone. See “Business—License Agreements—Ionis Collaboration Agreement.”

We have also entered into multiple agreements with third parties under which we may be obligated to make future development, regulatory and commercial milestone payments and royalty payments on future sales of specified product candidates. Payments under these agreements generally become due and payable upon achievement of such milestones and sales. When the achievement of these milestones or sales have not occurred, such contingencies are not recorded in our financial statements.

We have agreements with certain vendors for various services, including services related to clinical operations and support, for which we are not contractually able to terminate for convenience and avoid any and all future obligations to the vendors. Under such agreements, we are contractually obligated to make certain payments to vendors to reimburse them for their unrecoverable outlays incurred prior to cancellation. The exact amounts of such obligations are dependent on the timing of termination and the exact terms of the relevant agreement and cannot be reasonably estimated.

In addition, we enter into indemnification agreements and agreements containing indemnification provisions in the ordinary course of business. Pursuant to these agreements, we agree to indemnify, hold harmless and reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally our business collaborators, in connection with any U.S. patent or any copyright or other IP infringement claim by any third party with respect to our product candidates. The term of these indemnification agreements is generally perpetual upon execution of the agreement. The maximum potential amount of future payments we could be required to make under these indemnification agreements cannot be reasonably estimated.

Critical Accounting Policies and Significant Judgments and Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of these 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 expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies used in the preparation of our consolidated financial statements require the most significant judgments and estimates.

Research and Development Expenses and Related Accruals and Prepaids

Research and development expenses include costs directly attributable to the conduct of research and development activities, including personnel-related expenses such as salaries, benefits and stock-based compensation expense; materials; supplies; manufacturing and external costs related to outside vendors engaged to conduct both preclinical studies and clinical trials; and the allocable portions of facility costs, such as rent, utilities, depreciation and general support services. All costs associated with research and development activities are expensed as incurred.

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued and prepaid research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates in determining our accrued and prepaid research and development expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us

at that time. When evaluating the adequacy of the accrued liabilities and prepaid expenses, we analyze progress of the studies or trials related to these services, including the phase or completion of events, invoices received and contracted costs. Examples of estimated accrued and prepaid research and development expenses include fees paid to:

- CROs in connection with performing research services and preclinical and clinical studies;
- investigative sites or other providers in connection with preclinical and clinical studies;
- vendors in connection with preclinical and clinical development activities; and
- vendors related to product manufacturing, development and distribution of preclinical and clinical supplies.

The financial terms of our agreements with CROs are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of milestones. In expensing service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the expense accordingly. Significant judgments and estimates are made in determining the accrued and prepaid research and development expenses at the end of any reporting period. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period.

Recently Issued Accounting Pronouncements

For a discussion of recent account of recent accounting standards, see Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Fluctuation Risk

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our cash, cash equivalents and marketable securities are or may be in the form of money market funds or marketable debt securities and are or may be invested in U.S. Treasury and U.S. government agency obligations. However, because of the short-term nature and low risk profile of the instruments in our portfolio, an immediate change in market interest rates of 100 basis points would not have a material impact on the fair market value of our investment portfolio or on our financial position or results of operations.

Foreign Currency Fluctuation Risk

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation Fluctuation Risk

Inflation generally affects us by increasing our costs of labor and materials. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2021 and 2020.

Item 8. Financial Statements and Supplementary Data

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15, Exhibits and Financial Statement Schedules, of this Annual Report on Form 10-K.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Praxis Precision Medicines, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Praxis Precision Medicines, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework)**,** and our report dated February 28, 2022 expressed an unqualified opinion thereon.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

PRAX-114 Accrued and Prepaid Research and Development Costs

Description of the Matter

The Company's accrued costs for research and development expenses totaled $17.8 million at December 31, 2021, including accruals related to the Company's PRAX-114 Aria and Acapella clinical trials. In addition, the Company's prepaid expenses and other current assets were $11.5 million, which included amounts that were paid in advance of services incurred pursuant to PRAX-114 Aria and Acapella clinical trials. As discussed in Note 2 to the consolidated financial statements, the Company analyzes the progress of the clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued and prepaid balances at the end of any reporting period for the Company's PRAX-114 Aria and Acapella clinical trials. The Company is required to estimate such accruals and prepaids using judgment based on certain information, including actual costs incurred or level of effort expended, as provided by its vendors. Payments for such activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheet within accrued or prepaid expenses and other current assets.

Auditing the Company's accrued and prepaid research and development costs for PRAX-114 Aria and Acapella clinical trials was complex, as accounting for the costs associated with these clinical trials required subjective estimates of the level of services performed and the associated costs incurred by service providers. Furthermore, due to the duration of the Company's PRAX-114 Aria and Acapella clinical trials, and the timing of information received from third parties, the actual amounts incurred are not typically known at the time the consolidated financial statements are issued.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design, and tested the operating effectiveness of internal controls over accrued and prepaid research and development costs, including assessing management's controls over the significant judgments and estimates regarding costs incurred or level of effort expended by service providers.

To evaluate the accrued and prepaid research and development costs for PRAX-114 Aria and Acapella clinical trials, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used in the estimates and evaluating the significant judgments and estimates made by management to estimate the recorded accruals and prepayments. To test the significant judgments and estimates, we corroborated the progress of research and development activities through discussion with the Company's research and development personnel that oversee the research and development projects and inspected the Company's contracts with third parties and any pending change orders to assess the impact on amounts recorded. In addition, we reviewed estimates of costs incurred to date provided to the Company from third parties. We also analyzed fluctuations in accruals by vendor and by trial throughout the period subject to audit, evaluated the costs incurred per trial, site and/or patient for reasonableness and tested subsequent invoices received from third parties.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2019.
Boston, Massachusetts
February 28, 2022

PRAXIS PRECISION MEDICINES, INC.

CONSOLIDATED BALANCE SHEETS

(Amounts in thousands, except share and per share data)

	December 31,	
	2021	**2020**
Assets		
Current assets:		
Cash and cash equivalents	$ 138,704	$ 296,608
Marketable securities	137,207	—
Prepaid expenses and other current assets	11,498	5,718
Total current assets	287,409	302,326
Property and equipment, net	1,213	82
Operating lease right-of-use assets	3,653	754
Other non-current assets	472	15
Total assets	$ 292,747	$ 303,177
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 10,780	$ 4,088
Accrued expenses	26,844	10,869
Operating lease liabilities	810	763
Total current liabilities	38,434	15,720
Long-term liabilities:		
Non-current portion of operating lease liabilities	3,501	—
Total liabilities	41,935	15,720
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized and no shares issued or outstanding as of December 31, 2021 and December 31, 2020	—	—
Common stock, $0.0001 par value; 150,000,000 shares authorized; 45,300,514 shares issued and outstanding as of December 31, 2021, and 38,268,543 shares issued and outstanding as of December 31, 2020	5	4
Additional paid-in capital	567,598	437,007
Accumulated other comprehensive loss	(176)	—
Accumulated deficit	(316,615)	(149,554)
Total stockholders' equity	250,812	287,457
Total liabilities and stockholders' equity	$ 292,747	$ 303,177

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

PRAXIS PRECISION MEDICINES, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

(Amounts in thousands, except share and per share data)

	Year Ended December 31,	
	2021	**2020**
Operating expenses:		
Research and development	$ 120,257	$ 44,976
General and administrative	47,075	16,992
Total operating expenses	167,332	61,968
Loss from operations	(167,332)	(61,968)
Other income:		
Other income, net	271	140
Total other income	271	140
Loss before income taxes	(167,061)	(61,828)
Benefit from income taxes	—	8
Net loss	$ (167,061)	$ (61,820)
Accretion and cumulative dividends on redeemable convertible preferred stock	—	(8,996)
Gain on repurchase of redeemable convertible preferred stock	—	493
Net loss attributable to common stockholders	$ (167,061)	$ (70,323)
Net loss per share attributable to common stockholders, basic and diluted	$ (3.94)	$ (7.86)
Weighted average common shares outstanding, basic and diluted	42,454,055	8,950,152

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

PRAXIS PRECISION MEDICINES, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(Amounts in thousands, except share and per share data)

	Year Ended December 31,	
	2021	**2020**
Net loss	$ (167,061)	$ (61,820)
Net unrealized losses on marketable securities, net of tax	(176)	—
Comprehensive loss	$ (167,237)	$ (61,820)

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

PRAXIS PRECISION MEDICINES, INC.

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

(Amounts in thousands, except share data)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2020	38,268,543	$ 4	$ 437,007	$ (149,554)	$ —	$ 287,457
Stock-based compensation expense	—	—	4,666	—	—	4,666
Issuance of common stock upon exercise of stock options	352,506	—	851	—	—	851
Change in unrealized loss on marketable securities, net of tax	—	—	—	—	(86)	(86)
Net loss	—	—	—	(27,373)	—	(27,373)
Balance at March 31, 2021	38,621,049	$ 4	$ 442,524	$ (176,927)	$ (86)	$ 265,515
Stock-based compensation expense	—	—	5,400	—	—	5,400
Issuance of common stock from follow-on public offering, net of offering costs of $229	5,750,000	1	98,412	—	—	98,413
Issuance of common stock upon exercise of stock options	322,113	—	809	—	—	809
Change in unrealized loss on marketable securities, net of tax	—	—	—	—	36	36
Net loss	—	—	—	(36,401)	—	(36,401)
Balance at June 30, 2021	44,693,162	$ 5	$ 547,145	$ (213,328)	$ (50)	$ 333,772
Stock-based compensation expense	—	—	6,521	—	—	6,521
Issuance of common stock upon exercise of stock options	90,909	—	309	—	—	309
Change in unrealized loss on marketable securities, net of tax	—	—	—	—	25	25
Net loss	—	—	—	(44,705)	—	(44,705)
Balance at September 30, 2021	44,784,071	$ 5	$ 553,975	$ (258,033)	$ (25)	$ 295,922
Stock-based compensation expense	—	—	6,106	—	—	6,106
Issuance of common stock from at-the-market public offerings, net of offering costs of $598	391,997	—	7,039	—	—	7,039
Issuance of common stock upon exercise of stock options	124,446	—	478	—	—	478
Change in unrealized loss on marketable securities, net of tax	—	—	—	—	(151)	(151)
Net loss	—	—	—	(58,582)	—	(58,582)
Balance at December 31, 2021	45,300,514	$ 5	$ 567,598	$ (316,615)	$ (176)	$ 250,812

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

PRAXIS PRECISION MEDICINES, INC.

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

(Amounts in thousands, except share data)

	Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Series B-1 Redeemable Convertible Preferred Stock		Series C Redeemable Convertible Preferred Stock		Series C-1 Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2019	8,075,799	$ 9,932	14,913,704	$ 49,969	2,666,666	$ 10,431	9,805,827	$ 50,789	—	$ —	1,621,880	$ 1	$ —	$ (81,009)	$ —	$ (81,008)
Repurchase of Series C redeemable convertible preferred stock	—	—	—	—	—	—	(5,825,243)	(30,493)	—	—	—	—	—	493	—	493
Series C redeemable convertible preferred stock issuance costs	—	—	—	—	—	—	—	(37)	—	—	—	$ —	—	—	—	—
Vesting of restricted common stock awards	—	—	—	—	—	—	—	—	—	—	13,143	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	147	—	—	147
Accretion of redeemable convertible preferred stock to redemption value	—	160	—	890	—	199	—	815	—	—	—	—	(147)	(1,917)	—	(2,064)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(8,330)	—	(8,330)
Balance at March 31, 2020	8,075,799	$ 10,092	14,913,704	$ 50,859	2,666,666	$ 10,630	3,980,584	$ 21,074	—	$ —	1,635,023	$ 1	$ —	$ (90,763)	$ —	$ (90,762)
Issuance of Series C redeemable convertible preferred stock, net of issuance costs of $4	—	—	—	—	—	—	4,563,108	23,496	—	—	—	—	—	—	—	—
Vesting of restricted common stock awards	—	—	—	—	—	—	—	—	—	—	13,142	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	285	—	—	285
Accretion of redeemable convertible preferred stock to redemption value	—	162	—	890	—	198	—	789	—	—	—	—	(285)	(1,754)	—	(2,039)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(11,568)	—	(11,568)
Balance at June 30, 2020	8,075,799	$ 10,254	14,913,704	$ 51,749	2,666,666	$ 10,828	8,543,692	$ 45,359	—	$ —	1,648,165	$ 1	$ —	$ (104,085)	$ —	$ (104,084)
Issuance of Series C-1 redeemable convertible preferred stock, net of issuance costs of $154	—	—	—	—	—	—	—	—	19,444,453	110,096	—	—	—	—	—	—
Vesting of restricted common stock awards	—	—	—	—	—	—	—	—	—	—	13,142	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	953	—	—	953
Issuance of common stock upon exercise of stock options	—	—	—	—	—	—	—	—	—	—	11,628	—	27	—	—	27
Accretion of redeemable convertible preferred stock to redemption value	—	162	—	899	—	201	—	885	—	1,796	—	—	(980)	(2,963)	—	(3,943)
Net Loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(16,216)	—	(16,216)
Balance at September 30, 2020	8,075,799	$ 10,416	14,913,704	$ 52,648	2,666,666	$ 11,029	8,543,692	$ 46,244	19,444,453	$ 111,892	1,672,935	$ 1	$ —	$ (123,264)	$ —	$ (123,263)
Issuance of common stock upon initial public offering, net of issuance costs of $2,864											11,500,000	1	200,310	—	—	200,311
Vesting of restricted common stock awards	—	—	—	—	—	—	—	—	—	—	8,763	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	3,826	—	—	3,826
Issuance of common stock upon exercise of stock options	—	—	—	—	—	—	—	—	—	—	18,868	—	61	—	—	61
Accretion of redeemable convertible preferred stock to redemption value	—	35	—	196	—	44	—	193	—	482	—	—	(366)	(584)	—	(950)
Conversion of redeemable convertible preferred stock to common stock	(8,075,799)	(10,451)	(14,913,704)	(52,844)	(2,666,666)	(11,073)	(8,543,692)	(46,437)	(19,444,453)	(112,374)	25,067,977	2	233,176	—	—	233,178
Net Loss	—	—	—	—	—	—	—	—	—	—	—	—	—	(25,706)	—	(25,706)
Balance at December 31, 2020	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	38,268,543	$ 4	$ 437,007	$ (149,554)	$ —	$ 287,457

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

PRAXIS PRECISION MEDICINES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(Amounts in thousands)

	Year Ended December 31,	
	2021	**2020**
Cash flows from operating activities:		
Net loss	$ (167,061)	$ (61,820)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	182	50
Stock-based compensation expense	22,693	5,211
Non-cash operating lease expense	1,412	696
Amortization of premiums and discounts on marketable securities, net	2,087	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(5,780)	(4,437)
Accounts payable	7,267	960
Accrued expenses	15,450	7,408
Operating lease liabilities	(763)	(696)
Other	(41)	5
Net cash used in operating activities	(124,554)	(52,623)
Cash flows from investing activities:		
Purchases of property and equipment	(1,050)	—
Purchases of marketable securities	(164,170)	—
Maturities of marketable securities	24,700	—
Net cash used in investing activities	(140,520)	—
Cash flows from financing activities:		
Proceeds from at-the-market offerings, net of issuance costs	7,301	—
Proceeds from follow-on public offering, net of issuance costs	98,413	—
Proceeds from initial public offering of common stock, net of issuance costs	—	200,886
Payment of issuance costs for initial public offering	(575)	—
Proceeds from exercise of options to purchase common stock	2,447	88
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	133,442
Repurchase of Series C redeemable convertible preferred stock	—	(30,000)
Net cash provided by financing activities	107,586	304,416
Increase (decrease) in cash, cash equivalents and restricted cash	(157,488)	251,793
Cash, cash equivalents and restricted cash, beginning of period	297,208	45,415
Cash, cash equivalents and restricted cash, end of period	$ 139,720	$ 297,208
Reconciliation of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	138,704	296,608
Restricted cash	1,016	600
Total cash, cash equivalents and restricted cash	$ 139,720	$ 297,208
Supplemental disclosures of non-cash activities:		
Operating lease right-of-use assets obtained in exchange for operating lease liabilities	$ 4,086	$ —
Offering costs included in accounts payable and accrued expenses	$ 262	$ 575
Purchases of property and equipment included in accounts payable and accrued expenses	$ 267	$ 4
Accretion of redeemable convertible preferred stock to redemption value	$ —	$ 8,996

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

1. Nature of the Business

Praxis Precision Medicines, Inc. (“Praxis” or the “Company”) is a clinical-stage biopharmaceutical company translating genetic insights into the development of therapies for central nervous system, or CNS, disorders characterized by neuronal excitation-inhibition imbalance. Normal brain function requires a delicate balance of excitation and inhibition in neuronal circuits, which, when dysregulated, can lead to abnormal function and disease. The Company is applying insights from genetic epilepsies to both rare and more prevalent neurological and psychiatric disorders, using its understanding of shared biological targets and circuits in the brain. The Company applies a deliberate and pragmatic precision approach, leveraging a suite of translational tools including novel transgenic and predictive translational animal models and electrophysiology markers, to enable an efficient path to proof-of-concept in patients. Through this approach, the Company has established a broad CNS portfolio with multiple programs, including product candidates across psychiatric disorders, movement disorders, epilepsy and other exploratory CNS indications, with three clinical-stage product candidates. Each of the Company's clinical-stage product candidates is advancing in more than one indication and the Company anticipates expansion into additional indications. The Company expects multiple topline readouts from its clinical-stage programs and anticipates the launch of a fourth clinical development program in 2022. In addition, the Company has established a robust pipeline of preclinical stage programs through internal research and in-licensing.

The Company's broad portfolio of CNS programs is currently structured by therapeutic focus in three primary franchises – Psychiatry, Movement Disorders and Epilepsy. In addition, the Company is pursuing development in other exploratory CNS indications such as rare adult cephalgias. Within the Psychiatry franchise, the Company's most advanced clinical candidate, PRAX-114, is being developed for the treatment of a broad range of patients suffering from major depressive disorder and post-traumatic stress disorder, or PTSD. In addition, the Company has initiated a Phase 2, placebo-controlled study evaluating PRAX-114 for the treatment of PTSD. Within the Movement Disorders franchise, the Company's second clinical candidate, PRAX-944, is being developed for the treatment of Essential Tremor, or ET, and Parkinson's Disease, or PD. The Company has initiated a Phase 2b placebo-controlled dose-range finding trial, the Essential1 Study, to evaluate the tolerability, safety and efficacy of PRAX-944 in adults with ET. The Company also expects to initiate a Phase 2, placebo-controlled, crossover study to evaluate the safety, pharmacokinetics, or PK, and efficacy of daytime dosing of PRAX-114 for the treatment of ET in the first quarter of 2022. The Company expects to initiate a Phase 2, placebo-controlled trial to evaluate the safety, PK and efficacy of PRAX-944 as a non-dopaminergic treatment for the motor symptoms of PD in the second quarter of 2022. Within the Epilepsy franchise, the Company expects to initiate a Phase 2 study with its third clinical-stage candidate, PRAX-562, in the second quarter of 2022 in patients with rare pediatric Developmental and Epileptic Encephalopathies. The Company's most advanced preclinical stage product candidate within its Epilepsy franchise, PRAX-222, is an antisense oligonucleotide, or ASO, designed to decrease the expression levels of the protein encoded by the gene SCN2A in patients with gain-of-function SCN2A mutations. The Company expects to initiate a seamless study of PRAX-222 in the second quarter of 2022, which would be its fourth program to reach clinical stage. The Company also expects to initiate a Phase 2 proof-of-concept clinical trial evaluating PRAX-562 in patients with rare adult cephalgias in the first quarter of 2022. In addition, the Company's preclinical pipeline consists of a discovery program in development for KCNT1 related epilepsy, PRAX-628, a product candidate nominated in the fourth quarter of 2021 for focal epilepsy, three ASOs targeting SCN2A in patients with loss-of-function mutations, PCDH19 and SYNGAP1, respectively, and three additional discovery programs for undisclosed targets in psychiatry, movement disorders and epilepsy.

Praxis was incorporated in 2015 and commenced operations in 2016. The Company has funded its operations primarily with proceeds from the issuance of redeemable convertible preferred stock, and from the sale of common stock through an initial public offering ("IPO"), a follow-on public offering and at-the-market offerings under its shelf registration statement. From inception through December 31, 2021, the Company raised $516.4 million in aggregate cash proceeds from these transactions, net of issuance costs.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including but not limited to, risks associated with completing preclinical studies and clinical trials, receiving regulatory approvals for product candidates, development by competitors of new biopharmaceutical products, dependence on key personnel, protection of proprietary technology, compliance with government regulations and

the ability to secure additional capital to fund operations. Programs currently under development will require significant additional research and development efforts, including 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 product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales.

Liquidity

In accordance with the Financial Accounting Standards Board ("FASB") Accounting Standards Update ("ASU") 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued.

The Company has incurred recurring losses since its inception, including a net loss of $167.1 million for the year ended December 31, 2021. In addition, as of December 31, 2021, the Company had an accumulated deficit of $316.6 million. The Company expects to continue to generate operating losses for the foreseeable future.

The Company expects that its cash, cash equivalents and marketable securities as of December 31, 2021 of $275.9 million will be sufficient to fund the operating expenditures and capital expenditure requirements necessary to advance its research efforts and clinical trials for at least one year from the date of issuance of these consolidated financial statements. The future viability of the Company is dependent on its ability to raise additional capital to finance its operations. The Company's inability to raise capital as and when needed could have a negative impact on its financial condition and ability to pursue its business strategies. There can be no assurance that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all.

2. Summary of Significant Accounting Policies

Basis of Presentation

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 ASUs of the FASB.

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries, Praxis Security Corporation and Praxis Precision Medicines Australia Pty Ltd. All intercompany transactions have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, accrued and prepaid research and development expenses, stock-based compensation expense and the recoverability of the Company's net deferred tax assets and related valuation allowance. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ materially from those estimates.

Segments

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of assessing performance and allocating resources. The majority of the Company's long-lived assets are held in the United States.

Cash, Cash Equivalents and Restricted Cash

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in interest-bearing money market funds. Cash equivalents are carried at cost, which approximates their fair market value.

Restricted cash comprises letters of credit for the benefit of the landlord in connection with the Company's lease facilities. Restricted cash is classified as either current or non-current based on the terms of the underlying lease arrangement.

The following table presents cash and cash equivalents and restricted cash as reported on the consolidated balance sheets that equal the total amounts on the consolidated statements of cash flows (in thousands):

	December 31,	
	2021	2020
Cash and cash equivalents	$ 138,704	$ 296,608
Restricted cash	1,016	600
Total cash, cash equivalents and restricted cash as shown on the consolidated statements of cash flows	$ 139,720	$ 297,208

Marketable Securities

The Company invests its excess cash in money market funds and debt instruments of the U.S. Treasury, financial institutions, corporations and U.S. government agencies with strong credit ratings and an investment grade rating at or above A-1 or P-1 by two of the three nationally recognized statistical rating organizations. The Company does not believe that it is exposed to more than a nominal amount of credit risk in its marketable securities. The Company has established guidelines relative to diversification and maturities that maintain safety and liquidity, and periodically reviews and modifies these guidelines to maximize trends in yields and interest rates without compromising safety and liquidity. The Company classifies its investments in debt instruments as available-for-sale. Available-for-sale investments are reported at fair value at each balance sheet date, and include any unrealized holding gains and losses in accumulated other comprehensive loss, a component of stockholders' equity. Realized gains and losses are included in the Company's consolidated statements of operations. All of the Company's available-for-sale securities are available for use in its current operations. As a result, the Company has categorized all of these securities as current assets even though the stated maturity of some individual securities may be one year or more beyond the balance sheet date.

The Company evaluates securities for impairment at the end of each reporting period. Impairment is evaluated considering numerous factors, and their relative significance varies depending on the situation. Factors considered include whether a decline in fair value below the amortized cost basis is due to credit-related factors or non-credit-related factors, the financial condition and near-term prospects of the Company, and the Company's intent and ability to hold the investment to allow for an anticipated recovery in fair value. A credit-related impairment is recognized as an allowance on the balance sheet with a corresponding adjustment to earnings. Any impairment that is not credit-related is recognized in other comprehensive loss, net of applicable taxes unless deemed other than temporary.

Concentrations of Credit Risk and Significant Suppliers and License Agreements

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents, restricted cash and marketable securities. The Company's investment portfolio comprises money market funds, marketable debt securities, including debt securities issued by U.S. government agencies and

corporations, and commercial paper. The Company investments are limited to investment-grade securities with strong credit ratings with the objective of maintaining safety and liquidity. The Company also maintains deposits in accredited financial institutions in excess of federally insured limits. Bank accounts in the United States are insured by the Federal Deposit Insurance Corporation (the "FDIC") up to $250,000. As of December 31, 2021 and 2020, the Company's primary operating accounts significantly exceeded the FDIC limits. The Company deposits its cash in financial institutions that it believes have high credit quality, and has not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party manufacturers to supply materials for research and development activities of its programs, including preclinical and clinical testing. In particular, the Company relies, and expects to continue to rely, on a small number of third-party manufacturers to produce and process its current and potential product candidates and to manufacture supply of its current and potential product candidates for preclinical and clinical activities. These programs could be adversely affected by a significant interruption in the supply of the necessary materials. The Company is also dependent on third parties who provide license rights used in the development of certain programs. The Company could experience delays in the development of its programs if any of these license agreements are terminated, if the Company fails to meet the obligations required under its arrangements, or if the Company is unable to successfully secure new strategic alliances or licensing agreements.

Off-Balance Sheet Risk

As of December 31, 2021 and 2020, the Company had no off-balance sheet risk such as foreign exchange contracts, option contracts or other hedging arrangements.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. The fair values of the Company's financial assets and liabilities reflects the Company's estimate of 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.

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

An entity may choose to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings.

Items measured at fair value on a recurring basis include cash equivalents and marketable securities (Note 4 and Note 5). The carrying amounts reflected in the consolidated balance sheets for cash, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities.

Property and Equipment

Property and equipment are recorded at cost. Depreciation is calculated using the straight-line method over the following estimated useful lives of the assets:

	Estimated Useful Life
Office furniture and equipment	5 years
Laboratory equipment	3 years
Computer equipment	3 years

Upon disposal, retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in the results of operations. Expenditures for repairs and maintenance that do not improve or extend the lives of the respective assets are charged to expense as incurred.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. 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. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. The Company did not record any impairment losses on long-lived assets in either year ended December 31, 2021 or December 31, 2020.

Leases

The Company accounts for leases in accordance with ASC 842. The Company determines if an arrangement is a lease at contract inception. Operating lease right-of-use assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent its obligation to make lease payments arising from the lease. Operating right-of-use assets and liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. When determining the lease term, the Company includes options to extend or terminate the lease when it is reasonably certain that the option will be exercised.

The Company uses the implicit rate when readily determinable and uses its incremental borrowing rate when the implicit rate is not readily determinable, based upon the information available at the commencement date in determining the present value of the lease payments. The incremental borrowing rate is determined using a secured borrowing rate for the same currency and term as the associated lease.

The lease payments used to determine operating lease right-of-use assets may include lease incentives and stated rent increases. The Company's lease agreements may include both lease and non-lease components, which the Company accounts for as a single lease component when the payments are fixed, for all classes of underlying assets. Variable payments included in the lease agreement are expensed as incurred.

The Company's operating leases are reflected in operating lease right-of-use assets and in current operating lease liabilities and long-term operating lease liabilities in its consolidated balance sheets. The Company's operating lease right-of-use asset as of December 31, 2021 and 2020 did not include any lease incentives. Lease expense for future lease payments is recognized on a straight-line basis over the lease term.

Redeemable Convertible Preferred Stock

Prior to the automatic conversion of all outstanding shares of the Redeemable Convertible Preferred Stock upon the closing of the IPO, the Company recorded all Redeemable Convertible Preferred Stock upon issuance at its respective fair value or original issuance price, less issuance costs and any associated discounts. The Company classified its Redeemable Convertible Preferred Stock outside of stockholders' (deficit) equity as the redemption of such shares was outside the Company's control. The Company adjusted the carrying values of the Redeemable Convertible Preferred Stock to redemption value when the redemption value exceeded the carrying value. Upon the closing of the IPO, all of the outstanding shares of Redeemable Convertible Preferred Stock automatically converted into 25,067,977 shares of common stock.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries, stock-based compensation and benefits, facilities costs, depreciation, third-party license fees, and external costs of outside vendors engaged to conduct preclinical development activities and clinical trials as well as to manufacture research and development materials. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are recognized as an expense as the goods are delivered or the related services are performed or until it is no longer expected that the goods will be delivered or the services rendered. Costs incurred to obtain licenses are recognized as research and development expense as incurred if the technology licensed has no alternative future uses.

The Company has entered into various research and development related contracts with parties both inside and outside of the United States. These agreements are cancellable, and related fees are recorded as research and development expenses as incurred. The Company records accrued liabilities and prepaid expenses for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities and prepaid expenses, the Company analyzes progress of the studies or clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued and prepaid balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical estimates have not been materially different from the actual costs.

Patent-Related Costs

Patent-related costs incurred in connection with 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 accompanying consolidated statement of operations.

Stock-Based Compensation

The Company accounts for all stock-based awards granted to employees and non-employees as stock-based compensation expense at fair value in accordance with FASB ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). For stock-based awards issued to employees, non-employees and members of the Company's board of directors (the "Board") for their services on the Board, the Company measures the estimated fair value of the stock-based award on the date of the grant. The Company recognizes compensation expense for those awards granted to employees and members of the Board over the requisite service period, which is generally the vesting period of the respective award. For non-employee awards, compensation expense is recognized as the services are provided, which is generally ratably over the vesting period. The Company determines the fair value of restricted stock awards in reference to the fair value of its common stock less any applicable purchase price. The Company issues stock-based awards with service-based vesting conditions and records the expense for these awards on a straight-line basis over the vesting period. To date, the Company has not issued any stock-based awards with performance or market-based vesting conditions. The Company accounts for forfeitures as they occur.

The Company classifies stock-based compensation expense in its consolidated statement of operations in the same manner in which the award recipient's salary or service payments are classified.

The fair value of each stock option award is estimated on the date of grant using the Black-Scholes option pricing model, which requires inputs of subjective assumptions, including: (i) the expected volatility of the

Company's stock; (ii) the expected term of the award; (iii) the risk-free interest rate; (iv) expected dividends; and (v) the fair value of common stock. Due to the lack of Company-specific historical and implied volatility data, the Company determines the volatility for awards granted based on an analysis of reported data for a group of guideline publicly-traded companies that issued options with substantially similar terms. For this analysis, the Company selects companies with comparable characteristics including enterprise value, risk profiles, and with historical share price information sufficient to meet the expected life of the stock-based awards. The Company determines expected volatility using a weighted average of the historical volatilities of the guideline group of companies. The Company expects to continue to apply this process until such time as it has adequate historical data regarding the volatility of its own traded stock price. As permitted under ASC 718, the Company has elected to use the contractual term as the expected term for certain non-employee awards, on an award-by-award basis. For all other awards, the expected term of the Company's stock options has been determined utilizing the "simplified" method whereby the expected term equals the average of the vesting term and the original contractual term of the option, on a weighted basis based on the vesting of each tranche. The Company utilizes this method as it has insufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. 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 instruments with a term commensurate with the expected term assumption. The expected dividend yield is assumed to be zero as the Company has never paid dividends, and does not have current plans to pay any dividends on its common stock. Subsequent to the IPO, the fair value of the common stock underlying the Company's stock-based awards is the closing price of the Company's common stock on the date of grant. Historically, for periods prior to the IPO, the fair value of the shares of common stock underlying the Company's stock-based compensation awards was determined on each grant date by its Board based on valuation estimates from management considering its most recently available independent third-party valuation of the Company's common stock. The Board also assessed and considered, with input from management, 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 grant date.

The grant date fair value of RSUs is estimated based on the fair value of the Company's underlying common stock on the date of grant.

Foreign Currency

The functional currency of the Company's wholly owned foreign subsidiary in Australia is the U.S. dollar. Monetary assets and liabilities resulting from transactions denominated in currencies other than the functional currency are remeasured into the functional currency at exchange rates prevailing at the balance sheet date. Non-monetary assets and liabilities denominated in foreign currencies are measured using historical exchange rates prevailing at the date of the transaction and are not subsequently remeasured. Exchange gains or losses arising from foreign currency transactions are included in the determination of net loss. There were no material foreign currency gains or losses for the years ended December 31, 2021 and 2020.

Income Taxes

Deferred tax assets and liabilities are determined on the basis of the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent that it believes based upon the weight of available evidence 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.

The Company accounts for uncertain tax positions recognized in the consolidated financial statements by prescribing a more-likely-than-not threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. 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.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' equity (deficit) that are excluded from net loss. For the year ended December 31, 2021, comprehensive loss consists of net loss and changes in

unrealized gains and losses on marketable securities. Comprehensive loss was equal to net loss for the year ended December 31, 2020.

Net Loss per Share

The Company follows the two-class method to compute net loss per share attributable to common stockholders as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income (losses) for the period to be allocated between common and participating securities based upon their respective rights to share in the earnings as if all income (losses) for the period had been distributed. During periods of loss, there is no allocation required under the two-class method since the participating securities do not have a contractual obligation to fund the losses of the Company.

Net loss attributable to common stockholders is equal to the net loss for the period, as adjusted for: (i) cumulative dividends accrued for redeemable convertible preferred stock, whether or not declared, (ii) increases in carrying value recorded for redeemable convertible preferred stock, including accretion of redeemable convertible preferred stock to redemption value for amounts other than cumulative dividends and (iii) gains on the redemptions of redeemable convertible preferred stock.

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, which excludes shares of restricted common stock that are not vested. Diluted net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, after giving consideration to the dilutive effect of potentially dilutive common shares. For purposes of this calculation, outstanding options to purchase shares of common stock, unvested shares of restricted common stock and shares of redeemable convertible preferred stock are considered potentially dilutive common shares. The Company has generated a net loss in all periods presented so the basic and diluted net loss per share attributable to common stockholders are the same as the inclusion of the potentially dilutive securities would be anti-dilutive.

Recent Accounting Pronouncements

Recently Adopted Accounting Pronouncements

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740)—Simplifying the Accounting for Income Taxes* ("ASU 2019-12"). The ASU simplifies the accounting for income taxes by eliminating certain exceptions to the guidance in ASC 740, Income Taxes, related to the approach for allocating income tax expense or benefit for the year to continuing operations, discontinued operations, other comprehensive income, and other charges or credits recorded directly to shareholders' equity; the methodology for calculating income taxes in an interim period; and the recognition of deferred tax liabilities for outside basis differences. On January 1, 2021, the Company early adopted ASU 2019-12 on a prospective basis, with no material impact on its consolidated financial statements and related disclosures.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326)—Measurement of Credit Losses on Financial Instruments,* which has been subsequently amended by ASU No. 2018-19, ASU No. 2019-04, ASU No. 2019-05, ASU No. 2019-10, ASU No. 2019-11 and ASU No. 2020-03 ("ASU 2016-13"). The provisions of ASU 2016-13 modify the impairment model to utilize an expected loss methodology in place of the currently used incurred loss methodology and require a consideration of a broader range of reasonable and supportable information to inform credit loss estimates. On October 1, 2021, the Company early adopted ASU 2016-13 and its related amendments using a modified retrospective approach. Given the composition of the Company's investment portfolio, there was no material impact on the Company's consolidated financial statements and related disclosures.

Recently Issued Accounting Pronouncements

None.

3. Restricted Cash

As of December 31, 2021 and 2020 the Company had restricted cash of $1.0 million and $0.6 million, respectively, held as letters of credit for the benefit of its current and former landlords. The Company's Boston, Massachusetts sublease expires on January 31, 2026, and the related letter of credit of $0.4 million was classified within other non-current assets on the consolidated balance sheet as of December 31, 2021. The Company's Cambridge, Massachusetts sublease expired on December 30, 2021,and the related letter of credit of $0.6 million was classified within prepaid expenses and other current assets on the consolidated balance sheet as of December 31, 2021 and 2020.

4. Marketable Securities

The following is a summary of the Company's investment portfolio at December 31, 2021 (in thousands). The Company did not have any marketable securities as of December 31, 2020.

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Available-for-sale securities:				
Corporate debt securities	$ 52,214	$ —	$ (31)	$ 52,183
Commercial paper	34,993	—	—	34,993
Debt securities issued by U.S. government agencies	12,111	—	(8)	12,103
Other debt securities	6,398	1	—	6,399
Total securities with a maturity of one year or less	$ 105,716	$ 1	$ (39)	$ 105,678
Corporate debt securities	31,667	—	(138)	31,529
Total securities with a maturity of one to two years	$ 31,667	$ —	$ (138)	$ 31,529
Total available-for-sale securities	$ 137,383	$ 1	$ (177)	$ 137,207

As of December 31, 2021, the Company had 14 securities with a total fair market value of $95.8 million in an unrealized loss position. The Company believes that any unrealized losses associated with the decline in value of its securities is temporary and is primarily related to the change in market interest rates since purchase, and believes that it is more likely than not that it will be able to hold its debt securities to maturity. Therefore, the Company anticipates a full recovery of the amortized cost basis of its debt securities at maturity and an allowance for credit losses was not recognized.

Securities are evaluated for impairment at the end of each reporting period. The Company did not record any impairment related to its available-for-sale securities during the year ended December 31, 2021.

5. Fair Value of Financial Assets

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values (in thousands):

	As of December 31, 2021			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 131,372	$ —	$ —	$ 131,372
Marketable securities:				
Corporate debt securities	—	83,712	—	83,712
Commercial paper	—	34,993	—	34,993
Debt securities issued by U.S. government agencies	12,103	—	—	12,103
Other debt securities	—	6,399	—	6,399
	$ 143,475	$ 125,104	$ —	$ 268,579

	As of December 31, 2020			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash equivalents:				
Money market funds	$ 290,931	$ —	$ —	$ 290,931
	$ 290,931	$ —	$ —	$ 290,931

The Company estimates the fair value of its marketable securities classified as Level 2 by taking into consideration valuations obtained from third-party pricing sources. These pricing sources utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include market pricing based on real-time trade data for the same or similar securities, issuer credit spreads, benchmark yields, and other observable inputs. The Company validates the prices provided by its third-party pricing sources by understanding the models used, obtaining market values from other pricing sources and analyzing pricing data in certain instances.

6. Property and Equipment, Net

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

	December 31,	
	2021	2020
Computer equipment	$ 579	$ 9
Office furniture and equipment	545	113
Laboratory equipment	242	48
Total property and equipment	1,366	170
Less: Accumulated depreciation	(153)	(88)
Property and equipment, net	$ 1,213	$ 82

Depreciation expense was not significant for the years ended December 31, 2021 and 2020.

7. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2021	2020
Accrued external research and development expenses	$ 17,763	$ 4,206
Accrued personnel-related expenses	7,180	5,516
Accrued professional services	1,539	133
Accrued other	362	1,014
Total accrued expenses	$ 26,844	$ 10,869

8. Commitments and Contingencies

Leases

In May 2021, the Company entered into a sublease agreement for office space located in Boston, Massachusetts, which became the Company's corporate headquarters beginning on October 1, 2021. The sublease expires on January 31, 2026, with no option to renew or terminate early. The base rent increases by approximately 2% annually. The Company issued a letter of credit to the landlord related to the security deposit, secured by restricted cash (Note 3). This lease qualifies as an operating lease. At inception, the Company recorded an operating lease right-of-use asset and operating lease liability of $4.1 million.

In October 2018, the Company entered into a sublease agreement for office space located in Cambridge, Massachusetts which expired on December 30, 2021, with no option to renew or terminate early. The base rent increased by approximately 1% annually. The Company issued a letter of credit to the landlord related to the security deposit, secured by restricted cash (Note 3). This lease qualified as an operating lease.

The following table summarizes the presentation of the operating lease in the Company’s consolidated balance sheets (in thousands):

	As of December 31,	
	2021	2020
Assets:		
Operating lease right-of-use assets	$ 3,653	$ 754
Liabilities:		
Current operating lease liabilities	$ 810	$ 763
Non-current portion of operating lease liabilities	3,501	—
Total lease liabilities	$ 4,311	$ 763

The following table summarizes total lease costs recognized in the Company’s consolidated statements of operations (in thousands):

	For the year ended	
	2021	2020
Operating lease cost	$ 1,412	$ 782
Variable lease costs	34	14
Total lease costs	$ 1,446	$ 796

Variable lease costs were primarily related to operating expenses, taxes and insurance associated with the operating leases, which were assessed based on the Company’s proportionate share of such costs for the leased premises. As these costs are generally variable in nature, they were not included in the measurement of the

operating lease right-of-use asset and related lease liability. Total lease costs are included as operating expenses in the Company's consolidated statements of operations and comprehensive loss.

Future lease payments under non-cancelable lease agreements as of December 31, 2021 were as follows (in thousands):

Year Ended December 31,	Future Lease Payments
2022	$ 1,160
2023	1,270
2024	1,296
2025	1,321
2026	110
Total future lease payments	$ 5,157
Less: interest	(846)
Present value of operating lease liabilities	$ 4,311

The weighted average remaining lease term and weighted average incremental borrowing rate of the Company's operating lease were as follows:

	As of December 31,	
	2021	2020
Weighted average remaining lease term (in years)	4.1	1.0
Weighted average incremental borrowing rate	9.0 %	8.0 %

Legal Proceedings

The Company, from time to time, may be party to litigation arising in the ordinary course of business. The Company was not subject to any legal proceedings during the years ended December 31, 2021 and 2020, and no material legal proceedings are currently pending or threatened.

Purchase Orders

The Company has agreements with third parties for various services, including services related to research, preclinical and clinical operations and support, for which the Company is not contractually able to terminate for convenience to avoid future obligations to the vendors. Certain agreements provide for termination rights subject to termination fees or wind down costs. Under such agreements, the Company is contractually obligated to make certain payments to vendors, primarily to reimburse them for their unrecoverable outlays incurred prior to cancellation. The actual amounts the Company could pay in the future to the vendors under such agreements may differ from the purchase order amounts due to cancellation provisions.

Indemnification Agreements

The Company enters into indemnification agreements and agreements containing indemnification provisions in the ordinary course of business. Pursuant to these agreements, the Company agrees to indemnify, hold harmless, and to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third party with respect to the Company's products. The term of these indemnification agreements is generally perpetual upon execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements.

Agreements

The Company has entered into multiple agreements with third parties under which it may be obligated to make future development, regulatory and commercial milestone payments and royalty payments on future sales of

specified product candidates. Payments under these agreements generally become due and payable upon achievement of such milestones and sales. When the achievement of these milestones or sales have not occurred, such contingencies are not recorded in the Company's financial statements.

9. Redeemable Convertible Preferred Stock

On October, 20 2020, upon the closing of the IPO, all 53,644,314 outstanding shares of the Redeemable Convertible Preferred Stock were converted into 25,067,977 shares of common stock. Pursuant to the terms of the Company's Amended and Restated Certificate of Incorporation, all series of the Redeemable Convertible Preferred Stock outstanding automatically converted into shares of common stock based on each series' respective then-current conversion ratio.

As of December 31, 2021 and 2020, the Company did not have any shares of redeemable convertible preferred stock authorized, issued or outstanding.

On January 20, 2020, the Company granted two investors holding 5,825,243 shares of Series C Preferred Stock that were purchased in December 2019 the option to put their shares back to the Company at the original issuance price. On February 19, 2020 and March 3, 2020, the investors exercised their put option in full via the execution of Stock Redemption and Release Agreements in order to effect the repurchase. Pursuant to the Stock Redemption and Release Agreements, the Company agreed to repurchase a total of 5,825,243 shares of Series C Preferred Stock at the original issuance price of $5.15 per share, for an aggregate cash repurchase price of 30.0 million. Under the terms of the Stock Redemption and Release Agreements, the investors waived their right to cumulative dividends that had accumulated from the original issuance date through the date of repurchase. The 5,825,243 shares of Series C Preferred Stock were retired upon repurchase, and subsequently authorized for reissuance pursuant to a waiver to the Company’s Amended and Restated Certificate of Incorporation entered into by the Company and the holders of the Redeemable Convertible Preferred Stock.

The Company determined that the additional put right that was granted to the investors represented a modification of the affected shares of Series C Preferred Stock, but that it did not result in incremental value to the shareholders. As there was no incremental value associated with the modification, there was no impact to the accounting for the Series C Preferred Stock. The Company also determined that the put right did not require bifurcation, as it does not contain the characteristics of a derivative instrument. Further, the Company determined that the shares of Series C Preferred Stock that were subject to repurchase did not become mandatorily redeemable until the execution of the Stock Redemption and Release Agreements because the parties did not have an unconditional legal obligation to complete the redemptions until the associated agreements were finalized. Such determination was made in consultation with legal counsel. Accordingly, the Company recorded each of the redemptions on the respective date of repurchase and recognized a gain on repurchase equal to the difference between the repurchase price and the carrying value of the Series C Preferred Stock on the respective date of repurchase. The aggregate gain of $0.5 million was recorded upon repurchase as an adjustment to accumulated deficit in the statement of redeemable convertible preferred stock and stockholders’ deficit. The gain relates exclusively to the dividends accrued on the repurchased shares, which were waived by the investors as part of the Stock Redemption and Release Agreements.

On April 15, 2020 and May 8, 2020, the Company completed additional closings for the sale and issuance of its Series C Preferred Stock for a total of 4,563,108 shares at $5.15 per share for aggregate cash proceeds of $23.5 million, less an immaterial amount of issuance costs.

On July 24, 2020, the Company entered into the Series C-1 Preferred Stock Purchase Agreement, which authorized the sale and issuance of up to 19,444,453 shares of its Series C-1 Preferred Stock at a purchase price of $5.67 per share. During the year ended December 31, 2020, the Company issued all 19,444,453 shares of Series C-1 Preferred Stock for gross cash proceeds of $110.3 million, and incurred issuance costs of approximately $0.2 million. Although there were multiple closings of the Series C-1 Preferred Stock, there was no obligation under the initial closing for investors to purchase, or for the Company to sell to such investors, additional shares of Series C-1 Preferred Stock. The issuance of the Series C-1 Preferred Stock resulted in changes to certain rights, preferences and privileges of the Series A Preferred Stock, the Series B Preferred Stock, the Series B-1 Preferred

Stock and the Series C Preferred Stock. The Company concluded that such changes were not significant and resulted in a modification, rather than an extinguishment, of the previously outstanding Redeemable Convertible Preferred Stock. The changes to the terms of the Series A Preferred Stock, the Series B Preferred Stock, the Series B-1 Preferred Stock and the Series C Preferred Stock did not result in incremental value to the shareholders, and therefore there was no impact to the accounting for the previously outstanding Redeemable Convertible Preferred Stock.

Rights, Preferences and Privileges

Prior to the conversion of the Redeemable Convertible Preferred Stock into shares of common stock upon the completion of the IPO on October 20, 2020, the holders of the Redeemable Convertible Preferred Stock had the following rights, preferences and privileges:

Voting Rights

The holders of outstanding shares of the Redeemable Convertible Preferred Stock were entitled to vote, together with the holders of common stock, on all matters submitted to the stockholders for a vote, and were entitled to the number of votes equal to the number of whole shares of common stock into which such holders of the Redeemable Convertible Preferred Stock could convert on the record date for determining stockholders entitled to vote. Except for the actions requiring the approval or consent of the majority of the holders of the Redeemable Convertible Preferred Stock, the holders of the Redeemable Convertible Preferred Stock would vote together with the holders of common stock and vote as a single class. The holders of the Series A Preferred Stock, exclusively and as a separate class, were entitled to elect two directors of the Company. The holders of the Series B Preferred Stock and Series B-1 Preferred Stock, exclusively and together as a separate class, were entitled to elect two directors of the Company. The holders of common stock and of any other class or series of voting stock (including the Redeemable Convertible Preferred Stock), exclusively and voting as a single class, were entitled to elect the balance of total number of directors of the Company.

Dividends

The holders of the Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series C-1 Preferred Stock were entitled to accrue cumulative dividends at an annual rate of $0.08, $0.24, $0.30, $0.412 and $0.4536 per share, respectively, subject to adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Redeemable Convertible Preferred Stock. Dividends accrued from day to day whether or not declared by the Board, and were payable only when, as, and if declared by the Board. No dividends were declared or paid by the Company on the Redeemable Convertible Preferred Stock.

No dividends could be declared, paid or set aside to any other class or series of capital stock (other than dividends on shares of common stock payable in common stock) unless, in addition to obtaining any consents otherwise required in the Company's Amended and Restated Certificate of Incorporation, the holders of the Redeemable Convertible Preferred Stock first received a dividend on each outstanding share in an amount at least equal to the greater of: (i) all accrued and unpaid dividends and (ii) in the case of a dividend being distributed to common stock or any class or series of capital stock that is convertible into common stock, the equivalent dividend on an as-converted basis or (iii) in the case of a dividend being distributed on a series or class not convertible into common stock, an additional dividend equal to a dividend rate calculated based on the respective original issue price of the Preferred Stock. The original issue price per share was equal to $1.00 for the Series A Preferred Stock, $3.00 for the Series B Preferred Stock, $3.75 for the Series B-1 Preferred Stock and $5.15 for the Series C Preferred Stock. The holders of the Series C Preferred Stock, Series B Preferred Stock and Series B-1 Preferred Stock were entitled to receive dividends prior to any dividends on the Series A Preferred Stock.

Liquidation Rights

In the event of any voluntary or involuntary liquidation event, dissolution, winding up of the Company or upon the occurrence of certain events designated by a majority of the holders of the Redeemable Convertible Preferred Stock, and at least two out of three specific holders, to be a deemed liquidation event, each holder of the then outstanding Series C-1 Preferred Stock, Series C Preferred Stock, Series B-1 Preferred Stock and Series B Preferred Stock was entitled to receive, prior and in preference to any distributions to the holders of Series A

Preferred Stock and common stock, an amount equal to the greater of (i) original issuance price (adjusted in the event of any stock dividend, stock split, combination or other similar activity) plus any cumulative accrued dividends, whether or not declared, with any other dividends declared but unpaid thereon, or (ii) the amount such holder would have received if such holder had converted its shares into common stock immediately prior to such liquidation event.

After the payment of all preferential amounts to the holders of the Series C-1 Preferred Stock, Series C Preferred Stock, Series B-1 Preferred Stock and Series B Preferred Stock, each holder of the then outstanding Series A Preferred Stock was entitled to receive, prior and in preference to any distributions to the holders of common stock, an amount equal to the greater of (i) original issuance price (adjusted in the event of any stock dividend, stock split, combination or other similar activity) plus any cumulative accrued dividends, whether or not declared, with any other dividends declared but unpaid thereon, or (ii) the amount such holder would have received if such holder had converted its shares into common stock immediately prior to such liquidation event.

After payments have been made in full to the holders of the Redeemable Convertible Preferred Stock, then, to the extent available, the remaining amounts would be distributed among the holders of the shares of common stock, pro rata based on the number of shares held by each holder.

Conversion

Each share of the Redeemable Convertible Preferred Stock was convertible, at any time, at the option of the holder, and without the payment of additional consideration, into such shares of non-assessable shares of common stock as is determined by dividing the original issue price by the applicable conversion price in effect at the time of conversion. The applicable conversion price for the Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series C-1 Preferred Stock was initially equal to $2.14, $6.42, $8.03, $11.02 and $12.13, respectively, as adjusted for the Company's reverse stock split. Each share of the Redeemable Convertible Preferred Stock would automatically convert into common stock at the applicable conversion ratio then in effect for each series of the Redeemable Convertible Preferred Stock upon either (i) the closing of the sale of shares of common stock at a price of at least $10.30 per share in a firm-commitment underwritten public offering pursuant to an effective registration statement resulting in at least $75.0 million of gross proceeds and the listing of the Company’s common stock on the New York Stock Exchange, The Nasdaq Global Select Market, or The Nasdaq Global Market or (ii) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of a majority of the outstanding Redeemable Convertible Preferred Stock, voting together as a single class and at least two of three specific holders. Upon conversion pursuant to the completion of the IPO, the applicable conversion price for the Series A Preferred Stock, Series B Preferred Stock, Series B-1 Preferred Stock, Series C Preferred Stock and Series C-1 Preferred Stock was equal to $2.14, $6.42, $8.03, $11.02 and $12.13, respectively, as adjusted for the Company’s reverse stock split. Accordingly, each share of the Redeemable Convertible Preferred Stock converted into approximately 0.4673 shares of common stock.

Redemption

Each series of the Redeemable Convertible Preferred Stock was redeemable at a price equal to the applicable original issuance price per share (adjusted in the event of any stock dividend, stock split, combination or other similar activity), plus any cumulative accrued dividends, whether or not declared together with any other dividends declared but unpaid, in three annual installments commencing not more than 60 days on or after July 24, 2025 at the written election of at least a majority of the holders of the Redeemable Convertible Preferred Stock voting together as a single class and at least two out of three specific parties.

10. Common Stock and Preferred Stock

Common Stock

On October 8, 2020, the Board and the Company’s stockholders approved a one-for-2.14 reverse stock split of its issued and outstanding shares of common stock. Accordingly, all shares of common stock, per share amounts, aggregate par value and additional paid-in capital amounts for all periods presented in the accompanying consolidated financial statements and related notes have been retroactively adjusted, where applicable, to reflect the reverse stock split.

On October 20, 2020, the Company completed its IPO in which the Company issued and sold 11,500,000 shares of its common stock at a public offering price of $19.00 per share, including 1,500,000 shares of common stock issued and sold pursuant to the underwriters' exercise of their option to purchase additional shares of common stock. The Company raised approximately $200.3 million in net proceeds after deducting underwriting discounts and commissions and offering expenses payable by the Company. Upon the closing of the IPO, all 53,644,314 outstanding shares of the Company's Redeemable Convertible Preferred Stock automatically converted into 25,067,977 shares of common stock pursuant to the terms of the Company's Amended and Restated Certificate of Incorporation filed on October 20, 2020 at the then-current conversion ratio for each series, as adjusted for the Company's reverse stock split.

On May 18, 2021, the Company completed a follow-on public offering in which the Company issued and sold 5,750,000 shares of its common stock at a public offering price of $18.25 per share, including 750,000 shares of common stock issued and sold pursuant to the underwriters' exercise, in full, of their option to purchase additional shares of common stock, for aggregate gross proceeds of $104.9 million. The Company received approximately $98.4 million in net proceeds after deducting discounts, commissions and offering expenses payable by the Company.

On November 3, 2021, the Company filed an automatic shelf registration with the Securities and Exchange Commission , which was automatically declared effective on November 3, 2021 in relation to the registration of common stock, preferred stock, debt securities, warrants and units or any combination thereof. The Company also simultaneously entered into an Open Market Sales Agreement ("the sales agreement"), with Jefferies LLC ("Jefferies"), to provide for the offering, issuance and sale of up to an aggregate amount of $125.0 million of common stock from time to time in at-the-market offerings under the shelf registration and subject to the limitations thereof. Jefferies is entitled to compensation at a commission rate of 3% of the gross sales price of common stock sold under the sales agreement. As of December 31, 2021, the Company had issued 391,997 shares under the sales agreement for aggregate gross proceeds of $7.6 million. The Company received approximately $7.0 million of net proceeds after deducting discounts, commissions and offering expenses payable by the Company.

As of December 31, 2021 and 2020, the authorized capital stock of the Company included 150,000,000 shares of common stock, $0.0001 par value, pursuant to the Amended and Restated Certificate of Incorporation effective upon the completion of the IPO. Holders of such shares of common stock have the exclusive right to vote for the election of the Company's directors and are entitled to one vote per share. In the event of the voluntary or involuntary liquidation, dissolution or winding up of the Company, the holders of common stock are entitled to a pro rata distribution of the Company's net assets. Dividends may be declared and paid to such holders only when, as, and if declared by the Board or an authorized committee thereof.

As of December 31, 2021, the Company did not hold any treasury shares.

Shares Reserved for Future Issuance

The Company had reserved the following shares of common stock for future issuance:

	December 31,	
	2021	**2020**
Shares reserved for exercise of outstanding stock options	6,468,501	5,944,546
Shares reserved for future awards under the 2020 Stock Option and Incentive Plan	2,667,780	3,036,776
Shares reserved for future awards under the 2020 Employee Stock Purchase Plan	654,204	327,102
Shares reserved for vesting of restricted stock units	440,079	—
Total shares of authorized common stock reserved for future issuance	10,230,564	9,308,424

Preferred Stock

As of December 31, 2021 and 2020, the Company was authorized to issue 10,000,000 shares of undesignated preferred stock, $0.0001 par value, in one or more series, and is authorized to fix the powers, designations, preferences and relative participating option or other rights thereof, including dividend rights, conversion rights, voting rights, redemption rights, liquidation preferences and the number of shares constituting any series, without any further vote or action by the Company's shareholders. As of December 31, 2021 and 2020, the Company had no shares of undesignated preferred stock issued or outstanding.

11. Stock-Based Compensation

On September 9, 2020, the Board approved the 2020 Stock Option and Incentive Plan (the "2020 Plan"), which was subsequently approved by its stockholders and became effective upon the Company's IPO on October 15, 2020. The 2020 Plan replaced the 2017 Stock Incentive Plan (the "2017 Plan") and no additional awards will be granted under the 2017 Plan following the closing of the IPO. The 2017 Plan will continue to govern outstanding equity awards granted thereunder.

The 2020 Plan allows the Company to grant stock options, restricted stock, restricted stock units and other stock-based awards to officers, employees, directors and consultants. The total number of shares of common stock authorized for issuance under the 2020 Plan as of December 31, 2021 and 2020 was 5,184,455 shares and 3,271,028 shares, respectively.

Stock options issued under the 2020 Plan and 2017 Plan expire ten years from the date of grant. Shares that expire, are terminated, surrendered or canceled under the 2020 Plan and 2017 Plan without having been fully exercised will be available for future awards. In addition, shares of common stock that are tendered to the Company by a participant to exercise an award are added to the number of shares of common stock available for future awards. Upon stock option exercise, the Company issues new shares and delivers them to the participant.

2020 Employee Stock Purchase Plan

On September 9, 2020, the Board approved the 2020 Employee Stock Purchase Plan (the "2020 ESPP"), which was subsequently approved by its stockholders and became effective on October 15, 2020. The first offering under the 2020 ESPP opened on November 15, 2021. During the years ended December 31, 2021 and 2020, there were no shares issued under the 2020 ESPP. The total shares authorized for issuance under the 2020 ESPP as of December 31, 2021 and 2020 was 654,204 shares and 327,102 shares, respectively.

Restricted Common Stock

Prior to the adoption of the 2017 Plan, the Company granted restricted common stock in 2016 with time-based vesting conditions to certain employees and non-employee founders of the Company pursuant to individual award agreements. All granted restricted common stock had vested as of December 31, 2020. The total fair value of restricted common stock that vested during the year ended December 31, 2020 was $0.5 million. The Company did not grant any restricted common stock during the years ended December 31, 2021 and 2020.

Restricted Stock Units

The following table summarizes the Company’s restricted stock unit activity:

	Shares	Weighted Average Grant Date Fair Value
Unvested as of December 31, 2020	—	$ —
Issued	496,113	41.57
Vested	—	—
Forfeited	(56,034)	39.25
Unvested as of December 31, 2021	440,079	$ 41.86

As of December 31, 2021, total unrecognized compensation cost related to unvested restricted stock units was $14.5 million, which is expected to be recognized over a weighted-average period of 3.23 years.

Stock Options

The following table summarizes the Company's stock option activity:

	Number of Shares	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			(In years)	(In thousands)
Outstanding as of December 31, 2020	5,944,546	$ 7.47		
Granted	2,018,903	38.60		
Exercised	(889,974)	2.75		$ 19,735
Cancelled or Forfeited	(604,974)	17.27		
Outstanding as of December 31, 2021	6,468,501	$ 16.92	8.62	$ 57,146
Exercisable as of December 31, 2021	2,001,767	$ 8.77	8.08	$ 24,971
Vested and expected to vest as of December 31, 2021	6,468,501	$ 16.92	8.62	$ 57,146

The aggregate intrinsic value of stock options exercised for the year ended December 31, 2020 was $0.7 million. The aggregate intrinsic value of stock options outstanding, exercisable, and vested and expected to vest is calculated as the difference between the exercise price of the underlying stock options and the estimated fair value of the Company's common stock for those stock options that had exercise prices lower than the estimated fair value of the Company's common stock at December 31, 2021. The aggregate intrinsic value of stock options exercised is calculated as the difference between the exercise price of the underlying stock options and the estimated fair value of the Company's common stock on the date of exercise for those stock options that had exercise prices lower than the fair value of the Company's common stock on the exercise date.

Valuation of Stock Options

The weighted-average assumptions that the Company used in the Black-Scholes option pricing model to determine the grant-date fair value of stock options granted to employees, members of the Board and non-employees and share purchases under the ESPP on the date of grant were as follows:

	Year Ended December 31,	
	2021	2020
Options:		
Risk-free interest rate	0.86 %	0.47 %
Expected term (in years)	6.08	6.20
Expected volatility	85.52 %	85.94 %
Expected dividend yield	— %	— %
Weighted average grant-date fair value per share	$ 27.58	$ 6.51

As of December 31, 2021, total unrecognized compensation cost related to unvested stock options was $57.0 million, which is expected to be recognized over a weighted-average period of 2.72 years.

In December 2020, the Company recognized approximately $2.1 million of stock-based compensation expense, recorded within general and administrative expense, related to the modification of option awards granted to former employee in conjunction with their termination of employment.

Stock-Based Compensation

Stock--based compensation expense was allocated as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	$ 9,350	$ 1,357
General and administrative	13,343	3,854
Total stock-based compensation expense	$ 22,693	$ 5,211

12. Significant Agreements

Purdue License Agreement

On December 31, 2017, the Company entered into a License Agreement with Purdue (the "Purdue License Agreement"), pursuant to which Purdue granted the Company exclusive rights under certain Purdue know-how to research, develop and commercialize pharmaceutical products concerning a GABAA positive allosteric modulator. The Company is obligated to make future milestone payments based on the achievement of specified development and sales milestones up to $33.0 million. Furthermore, the Company is required to pay Purdue royalties of a low-single-digit percentage of annual net sales of licensed products.

The Purdue License Agreement will remain in effect until the expiration of the Company's royalty obligation for all licensed products. Either the Company or Purdue may terminate the agreement in the event of a material breach by the other party and fails to cure such breach within a certain period of time. Either party may voluntarily terminate the agreement with prior notice. If the agreement is voluntarily terminated by Purdue, the Company's license rights will survive such termination and such rights will become fully paid, perpetual and irrevocable.

As of December 31, 2021, none of the developmental or sales milestones under the Purdue License Agreement were achieved.

RogCon and Ionis Agreements

During 2018, the Company began negotiating a license agreement with RogCon Inc. ("RogCon") for intellectual property related to treating SCN2A mutations in epilepsy, which is recognized as the second most common genetic cause of epilepsy. RogCon had an existing collaboration with Ionis Pharmaceuticals, Inc. ("Ionis") and as a result the Company needed to negotiate an agreement with Ionis in order to complete the license agreement with RogCon. On December 21, 2018, the Company entered into an agreement with RogCon to advance RogCon a deposit of up to $1.0 million on the pending license agreement while the agreement with Ionis was being negotiated. The deposit was fully refundable to the Company. On September 11, 2019, the Company entered into both a Cooperation and License Agreement (the "License Agreement") with RogCon, and a Research, Collaboration, Option and License Agreement (the "Collaboration Agreement") with Ionis. The agreements were entered into contemporaneously to enable the parties to advance their collective efforts related to SCN2A. Upon execution of the License Agreement, the $1.0 million outstanding balance of the deposit was applied toward the purchase price of the License Agreement.

RogCon Agreement

Under the License Agreement, RogCon granted to the Company an exclusive, worldwide license under RogCon's intellectual property to research, develop and commercialize products for the treatment of all forms of epilepsy and/or neurodevelopmental disorders in each case caused by any mutation of the SCN2A gene. Under the License Agreement, the Company will conduct, at its own cost and expense, the research and development activities assigned to it under the research plan. In addition, the Company is responsible for reimbursing RogCon for any costs associated with research and development activities RogCon performs at the request of the Company. As part of the agreement, the Company agreed to provide up-front consideration of $2.1 million, consisting of the $1.0 million deposit, $0.7 million in cash reimbursements for certain historical costs previously incurred by RogCon, and $0.4 million for the retirement of existing loan balances as of September 11, 2019.

The Company concluded that the License Agreement represented the acquisition of in-process research and development assets with no alternative future use. Therefore, the aggregate acquisition cost of $2.2 million, consisting of the $2.1 million of up-front consideration and $0.1 million of acquisition costs, was expensed as research and development on September 11, 2019.

Subsequent to September 11, 2019, the Company will reimburse RogCon for its out-of-pocket costs incurred for activities performed under the License Agreement. The Company expenses these costs as incurred as research and development. The Company expensed $0.1 million and $0.2 million for the reimbursement of RogCon's out-of-pocket costs in the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021 and 2020, the Company had accrued expenses of $0.3 million due to RogCon under the License Agreement.

Additionally, the Company may pay RogCon a milestone payment of $3.0 million and profit share payments. The $3.0 million milestone payment will become due when the first profit share payment has become due and certain contingent payments have become payable to Ionis under the Collaboration Agreement, which are subject to the Company exercising its option to obtain license rights to a development candidate, as well as other contingent events. The profit share payments will be based on a low-double-digit percentage of net profits, depending on sales volume.

The License Agreement, unless earlier terminated, will continue until the latest of: (i) expiration of all patent rights within RogCon patents, (ii) the Company and its affiliates certify they have abandoned the research, development and commercialization of product with no intention to re-establish such activities, and (iii) no third party is obligated to pay the Company or its affiliates any amounts that comprise net sublicense revenue. Either party may terminate the License Agreement for material breach or insolvency of the other party. Additionally, the Company may terminate for convenience with prior written notice to RogCon. Upon termination by either party, all rights and licenses granted by RogCon to the Company will revert back to RogCon.

Ionis Collaboration Agreement

Under the Collaboration Agreement, both parties will participate in research activities related to the downregulation of SCN2A gene products associated with the treatment of any and all forms of epilepsy and/or neurodevelopmental disorders in each case caused by any mutation of the SCN2A gene, other than one severe type of epilepsy. Ionis will also be responsible for identifying a development candidate and conducting an IND-enabling toxicology study. The Company will reimburse Ionis for any out-of-pocket costs incurred related to the research activities, identification of a development candidate and conducting an IND-enabling toxicology study. Additionally, the Company agreed to reimburse $0.3 million of costs incurred by Ionis for the performance of research activities prior to the execution of the Collaboration Agreement, which the Company recognized as research and development expense. The reimbursement of out-of-pocket costs is recognized as research and development expense as incurred. The Company expensed a total of $1.9 million and $1.7 million, as research and development expense under the Collaboration Agreement for the years ended December 31, 2021 and 2020, respectively.

Ionis granted the Company an exclusive option to obtain the rights and license to further develop and commercialize a development candidate in the field of epilepsy and neurodevelopmental disorders, other than Dravet Syndrome, following the results of the IND-enabling toxicology study. The Company exercised this exclusive option in January 2022 and paid a $2.0 million license fee.The Company concluded that there was no accounting recognition for the exclusive option until such option was exercised because it was a unilateral right of the Company that was priced at an amount that approximated fair value. The Company recognized the license fee in January 2022. After option exercise, the Company is responsible for clinical development and commercialization of the development candidate.

Ionis may be entitled to development milestone payments, additional milestone payments, and sales royalties or sublicense fees.

The Collaboration Agreement will continue until the expiration of all payment obligations to Ionis, unless earlier terminated. Either party may terminate the Collaboration Agreement upon material breach or insolvency of the other party. Ionis may terminate if the Company fails to achieve a performance milestone. The Company may terminate

for convenience with prior written notice to Ionis. Upon termination by the Company for convenience, the Company will stop selling all products, subject to certain wind-down provisions, and all products will revert back to Ionis.

13. Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows (in thousands, except share and per share data):

	Years Ended December 31,	
	2021	2020
Numerator:		
Net loss	$ (167,061)	$ (61,820)
Accretion and cumulative dividends on redeemable convertible preferred stock	—	(8,996)
Gain on repurchase of redeemable convertible preferred stock	—	493
Net loss attributable to common stockholders	$ (167,061)	$ (70,323)
Denominator:		
Weighted average common shares outstanding, basic and diluted	42,454,055	8,950,152
Net loss per share attributable to common stockholders, basic and diluted	$ (3.94)	$ (7.86)

The following potential common shares, presented based on amounts outstanding at each period end, were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have been anti-dilutive:

	Year Ended December 31,	
	2021	2020
Outstanding stock options	6,468,501	5,944,546
Unvested restricted stock units	440,079	—
Potential shares issuable under the ESPP	33,425	—
	6,942,005	5,944,546

14. Income Taxes

The Company maintains a full valuation allowance on its U.S. net deferred tax assets due to the uncertainty of future taxable income. The Company did not recognize an income tax benefit in the years ended December 31, 2021 or 2020 related to its U.S. operations due to the uncertainty regarding future taxable income. In the years ended December 31, 2021 and 2020, the difference between the statutory tax rate in the U.S. and the Company's effective tax rate was due primarily to the valuation allowance recorded to offset any potential tax benefit. The income tax benefit (provision) recognized for the years ended December 31, 2021 and 2020 was not material.

The reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows:

	Year Ended December 31,	
	2021	2020
Federal statutory income tax rate	21.0 %	21.0 %
State taxes, net of federal benefit	4.8 %	5.6 %
Federal and state research and development credits	3.8 %	2.9 %
Non-deductible items	(0.5)%	(1.8)%
Change in valuation allowance	(29.4)%	(27.9)%
Other	0.3 %	0.2 %
Effective income tax rate	— %	— %

Net deferred tax assets consisted of the following (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 56,482	$ 26,441
Amortization	14,295	5,774
Research and development credits	9,296	3,053
Stock-based compensation	3,759	170
Accrued expenses	1,952	1,433
Leases	1,132	207
Total gross deferred tax assets	$ 86,916	$ 37,078
Less: Valuation allowance	(85,957)	(36,873)
Net deferred tax assets	$ 959	$ 205
Deferred tax liabilities:		
Operating lease right-of-use asset	(959)	(205)
Total gross deferred tax liabilities	(959)	(205)
Net deferred tax assets	$ —	$ —

As of December 31, 2021 and 2020, the Company had U.S. federal net operating loss carryforwards which may be able to offset future income tax liabilities of approximately $212.3 million and $97.1 million, respectively. Federal net operating loss carryforwards of $7.7 million will expire at various dates from 2035 through 2037 and approximately $204.6 million may be carried forward indefinitely. As of December 31, 2021 and 2020, the Company also had state net operating loss carryforwards of approximately $187.6 million and $94.5 million, respectively, which may be available to offset future income tax liabilities and expire at various dates from 2036 through 2041.

As of December 31, 2021 and 2020, the Company had federal research and development tax credit carryforwards of approximately $7.3 million and $2.4 million, respectively, available to reduce future tax liabilities which expire at various dates from 2039 through 2041. As of December 31, 2021 and 2020, the Company had state research and development tax credit carryforwards of approximately $2.5 million and $0.9 million, respectively, available to reduce future tax liabilities which expire at various dates from 2031 through 2036. The Company has generated research credits but has not conducted a study to document the qualified activity. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional

adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all of the evidence, both positive and negative, the Company has recorded a valuation allowance against its deferred tax assets at December 31, 2021 and 2020 because management has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets, primarily due to its history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception. As a result, a valuation allowance of $86.0 million and $36.9 million has been established at December 31, 2021 and 2020, respectively. Management reevaluates the positive and negative evidence at each reporting period. The valuation allowance increased by approximately $49.1 million and $17.3 million during the years ended December 31, 2021 and 2020, respectively, due primarily to the generation of net operating losses.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2021 and 2020. The Company's policy is to record interest and penalties related to uncertain tax positions as part of its income tax provision. As of December 31, 2021 and 2020, the Company had no accrued interest or penalties related to uncertain tax positions and no such amounts have been recognized in the Company's consolidated statement of operations for either year ended December 31, 2021 or 2020. The statute of limitations for federal and state tax authorities is open for tax years ended December 31, 2018 through December 31, 2021. Since the Company is in a net loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available.

15. Related Party Transactions

One of the founders of RogCon became the Company's General Counsel in June 2020. During the years ended December 31, 2021 and 2020, the Company reimbursed RogCon for its out-of-pocket costs incurred for activities performed under the License Agreement (Note 12).

A former member of the Board was affiliated with Purdue through September 2020. During the years ended December 31, 2021 and 2020, the Company performed certain research and development activities pursuant to the Purdue License Agreement (Note 12).

During the year ended December 31, 2020, related parties participated in each of the Company's offerings of the Redeemable Convertible Preferred Stock (Note 9).

16. Employee Benefit Plan

The Company has a defined contribution savings plan under Section 401(k) of the Internal Revenue Code for eligible employees. The plan covers substantially all employees who meet a minimum age requirement and allows participants to defer a portion of their annual compensation on a pre-tax basis. Under the plan, the Company is not obligated to match any participant contributions. The Company made contributions of $1.0 million and $0.5 million during the years ended December 31, 2021 and 2020, respectively.

17. Subsequent Events

The Company has completed an evaluation of subsequent events after the consolidated balance sheet date of December 31, 2021 through the date these consolidated financial statements were issued. The Company has concluded that no subsequent events have occurred that require disclosure.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosures

None.

Item 9A. Controls and Procedures

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

We maintain “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as controls and other procedures of an issuer that are designed to ensure that information required to be disclosed by the issuer in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act is accumulated and communicated to the issuer's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

Our management, with the participation of our Chief Executive Officer (our principal executive officer) and Chief Financial Officer (our principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021. Based on the evaluation of our disclosure controls and procedures as of December 31, 2021, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the the three months ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Exchange Act Rules 13a-15(f), to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Management assessed our internal control over financial reporting as of December 31, 2021. Management based its assessment on criteria established in "Internal Control - Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on that assessment, our management concluded that our internal control over financial reporting was effective as of December 31, 2021.

Ernst & Young LLP, an independent registered public accounting firm, audited the effectiveness of our internal control over financial reporting as of December 31, 2021, as stated in their attestation report included in this Annual Report on Form 10-K.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Praxis Precision Medicines, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Praxis Precision Medicines, Inc.'s internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Praxis Precision Medicines, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of Praxis Precision Medicines, Inc. as of December 31, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2021, and the related notes and our report dated February 28, 2022 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's 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 for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP
Boston, Massachusetts
February 28, 2022

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders 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 SEC with respect to our 2022 Annual Meeting of Stockholders 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 SEC with respect to our 2022 Annual Meeting of Stockholders 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 SEC with respect to our 2022 Annual Meeting of Stockholders 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 SEC with respect to our 2022 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a)(1) Financial Statements.

For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page 122 of this Annual Report on Form 10-K, incorporated into this Item by reference.

(a)(2) Financial Statement Schedules.

Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

(a)(3) List of Exhibits

3.1	Amended and Restated Certificate of Incorporation of Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on October 20, 2020)
3.2	Amended and Restated Bylaws of Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on January 7, 2022)
4.1	Specimen Stock Certificate Evidencing the Shares of Common Stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
4.2	Fourth Amended and Restated Investors' Rights Agreement among Praxis Precision Medicines, Inc. and certain of its stockholders, effective as of July 24, 2020, as amended (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-3 (File No. 333-260726) filed on November 3, 2021)
4.3*	Description of Securities of Praxis Precision Medicines, Inc.
10.1	Form of Director Indemnification Agreement, as amended (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.2	Form of Officer Indemnification Agreement (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
10.3#	Praxis Precision Medicines, Inc. 2017 Stock Incentive Plan, as amended, and form of award agreements thereunder (incorporated by reference to Exhibit 10.3 to the Registrant's Annual Report on Form 10-K (File No. 001-39620) filed on March 17, 2021)
10.4#	Praxis Precision Medicines, Inc. 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.5#	Form of Incentive Stock Option Agreement under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.6#	Form of Non-Qualified Stock Option Agreement for Company Employees under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.7#	Form of Non-Qualified Stock Option Agreement for Non-Employee Directors under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.8#	Form of Restricted Stock Award Agreement under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.9#	Form of Restricted Stock Award Agreement for Company Employees under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)

10.10#	Form of Restricted Stock Award Agreement for Non-Employee Directors under the 2020 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.11#	Praxis Precision Medicines, Inc. 2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020)
10.12#*	Amended and Restated Employment Agreement, dated October 20, 2020, by and between Praxis Precision Medicines, Inc. and Marcio Souza
10.13#*	Amended and Restated Employment Agreement, dated October 20, 2020, by and between Praxis Precision Medicines, Inc. and Bernard Ravina
10.14#*	Amended and Restated Employment Agreement, dated October 20, 2020, by and between Praxis Precision Medicines, Inc. and Nicole Sweeny
10.15#	Retention Incentive Award Letter Agreement, dated August 30, 2021, by and between Praxis Precision Medicines, Inc. and Bernard Ravina (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on August 30, 2021)
10.16#*	Non-Employee Director Compensation Policy
10.17†	License Agreement, dated December 31, 2017, by and between Purdue Neuroscience Company and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
10.18†	Cooperation and License Agreement, dated September 11, 2019, by and between RogCon Inc. and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
10.19†	Research Collaboration, Option and License Agreement, dated September 11, 2019, by and between Ionis Pharmaceuticals, Inc. and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.16 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
10.2	Sublease, dated May 27, 2021, by and between CBRE, Inc. and Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on June 2, 2021)
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-249074) filed on September 25, 2020)
23.1*	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
24.1*	Power of Attorney (included on signature page hereto)
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 and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

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* Filed herewith.

** The certifications furnished in Exhibit 32.1 hereto are deemed to accompany this Annual Report on Form 10-K and will not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

#	Indicates a management contract or any compensatory plan, contract or arrangement.
†	Portions of this exhibit (indicated by asterisks) have been omitted in accordance with the rules of the Securities and Exchange Commission.

Item 16. Form 10–K Summary

None.

SIGNATURES

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

PRAXIS PRECISION MEDICINES, INC.

Date: February 28, 2022

By: /s/ Marcio Souza
Marcio Souza
Chief Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Marcio Souza and Alex Nemiroff, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/ Marcio Souza Marcio Souza	Chief Executive Officer and Director (Principal Executive Officer)	February 28, 202
/s/ Timothy Kelly Timothy Kelly	Chief Financial Officer (Principal Financial Officer)	February 28, 202
/s/ Lauren Mastrocola Lauren Mastrocola	Principal Accounting Officer	February 28, 202
/s/ Dean Mitchell Dean Mitchell	Chairman of the Board	February 28, 202
/s/ Merit Cudkowicz, M.D. Merit Cudkowicz, M.D.	Director	February 28, 202
/s/ Gregory Norden Gregory Norden	Director	February 28, 202
/s/ Jeffrey Chodakewitz, M.D. Jeffrey Chodakewitz, M.D.	Director	February 28, 202
/s/ Stefan Vitorovic Stefan Vitorovic	Director	February 28, 202
/s/ William Young William Young	Director	February 28, 202

Exhibit 4.3

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

The common stock, par value $0.0001 per share ("common stock"), of Praxis Precision Medicines, Inc. ("Praxis," "we," or "our") is registered under Section 12 of the Securities Exchange Act of 1934, as amended. The following description sets forth certain general terms and provisions of our common stock. These descriptions are in all respects subject to and qualified in their entirety by, and should be read in conjunction with, the applicable provisions of our amended and restated certificate of incorporation (our "certificate of incorporation") and our amended and restated bylaws (our "bylaws"), each of which is incorporated herein by reference and copies of which are incorporated by reference as exhibits to our most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission, and the applicable provisions of General Corporation Law of the State of Delaware (the "DGCL").

Authorized Capital Stock

We are authorized to issue 150,000,000 shares of common stock and 10,000,000 shares of preferred stock, par value $0.0001 per share ("preferred stock").

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive dividends declared by our board of directors out of funds legally available for that purpose. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share pro rata in the distribution of our assets remaining after payment of all debts and other liabilities.

Preferred Stock

Our board of directors or any authorized committee thereof is authorized, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our Company or other corporate action.

Registration Rights

Pursuant to the terms of our Fourth Amended and Restated Investors' Rights Agreement, dated as of July 24, 2020, as amended, or the Investors' Rights Agreement, certain of our stockholders are entitled to rights with respect to the registration of their shares (which we refer to herein as "registrable securities") under the Securities Act, including demand registration rights and piggyback registration rights.

Form S-1 Registration Rights

Under the terms of the Investors' Rights Agreement, we are required, upon the request of holders holding at least a majority of the registrable securities then outstanding, to file a registration statement on Form S-1 registering the resale of such holders' registrable securities and the registrable securities of such other holders who elect to have their shares registered; provided that the anticipated aggregate offering price, net of related fees and expenses, of the registrable securities registered on such registration statement would equal at least $10 million. We are required to effect only two registrations pursuant to this provision of the Investors' Rights Agreement. If the holders requesting registration intend to distribute their shares by means of an underwriting, the managing underwriter of such offering

will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

Form S-3 Registration Rights

Pursuant to the Investors' Rights Agreement, if we are eligible to file a registration statement on Form S-3, we are required, upon the request of holders holding at least a majority of the registrable securities then outstanding, to file a registration restatement on Form S-3 registering the resale of such holders' registrable securities and the registrable securities of such other holders who elect to have their shares registered; provided that the anticipated aggregate offering price, net of related fees and expenses, of the registrable securities registered on such registration statement would equal at least $3 million. We are required to effect only two registrations in any twelve-month period pursuant to this provision of the Investors' Rights Agreement. If the holders requesting registration intend to distribute their shares by means of an underwriting, the managing underwriter of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

Piggyback Registration Rights

Subject to certain exceptions, if we register any of our securities either for our own account or for the account of security holders other than the holders party to the Investors' Rights Agreements, the holders of shares of registrable securities are entitled to include their shares in the registration. If our proposed registration involves an underwriting, the managing underwriter of such offering will have the right to limit the number of shares to be underwritten for reasons related to the marketing of the shares.

Indemnification

The Investors' Rights Agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights and short-form registration rights granted under the Investors' Rights Agreement will terminate on the earliest to occur of: (i) the fifth anniversary of the completion of our initial public offering and (ii) as to each holder of registrable securities, such time as either Rule 144 as promulgated under the Securities Act or another similar exemption under the Securities Act is available for the sale of all of such holder's shares without limitation during a three-month period without registration or such holder no longer holds any registrable securities.

Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Undesignated Preferred Stock

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control.

Exclusive Jurisdiction for Certain Actions

Our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of or based on a fiduciary duty owed by any current or former director, officer or other employee or stockholder to us or our stockholders, (iii) any action asserting a claim against us or any current or former director, officer or other employee or stockholder arising pursuant to any provision of the DGCL, our certificate of incorporation or our bylaws or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware, or (iv) any action asserting a claim governed by the internal affairs doctrine, in each case subject to said Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein; provided that, the provisions of this sentence do not apply to suits brought to enforce any liability or duty created by the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Unless the Corporation consents in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. Any person or entity purchasing or otherwise acquiring any interest in shares of capital stock of the Corporation shall be deemed to have notice of and consented to these exclusive jurisdiction provisions.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the General Corporation Law of the State of Delaware, which prohibits persons deemed to be “interested stockholders” from engaging in a “business combination” with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an “interested stockholder” is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation’s voting stock. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Certificate of Incorporation and Bylaws

Provisions of our certificate of incorporation and our bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our certificate of incorporation and bylaws:

- permit our board of directors or any authorized committee thereof to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that the authorized number of directors may be changed only by resolution adopted by the board of directors;
- provide that the board of directors or any individual director may only be removed with cause and the affirmative vote of the holders of at least two thirds of the outstanding shares of capital stock then entitled vote at an election of directors;
- provide that all vacancies, including newly created directorships, may, subject to the rights of holders of preferred stock as designated from time to time, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide our board of directors into three classes;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;

- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner and also specify requirements as to the form and content of a stockholder's notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- provide that special meetings of our stockholders may be called only by our board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office; and
- provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims, as described above.

The amendment of any of these provisions included in our certificate of incorporation, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, the removal of directors by our stockholders, the filling of vacancies by our board of directors, and cumulative voting rights, would require the affirmative vote of two thirds of the outstanding shares of capital stock entitled to vote on such amendment and the affirmative vote of two thirds of the outstanding shares of each class entitled to vote on such amendment as a class.

The amendment of any of these provisions included in our bylaws, with the exception of the exclusive forum provision, would require the affirmative vote of two thirds of the outstanding shares of capital stock entitled to vote on such amendment, and the affirmative vote of not less than two thirds of the outstanding shares of each class entitled to vote on such amendment as a class; provided, however, that if our Board of Directors recommends that stockholders approve such amendment, such amendment shall only require the affirmative vote of a majority of the outstanding shares entitled to vote on such amendment, voting together as a single class.

PRAXIS PRECISION MEDICINES, INC.

AMENDED AND RESTATED EMPLOYMENT AGREEMENT
for Marcio Souza

This Amended and Restated Executive Employment Agreement (the "**Agreement**") is made between Praxis Precision Medicines, Inc. (the "**Company**") and Marcio Souza ("**Executive**") (collectively, the "**Parties**") and is effective as of the closing of the Company's first underwritten public offering of its equity securities pursuant to an effective registration statement under the Securities Act of 1933, as amended (the "**Effective Date**"). This Agreement supersedes in all respects all prior agreements between Executive and the Company regarding the subject matter herein, including without limitation, the Employment Agreement between Executive and the Company dated March 6, 2020 (the "**Prior Agreement**").

WHEREAS, the Company desires Executive to continue to provide services to the Company, and wishes to provide Executive with certain compensation and benefits in return for such employment services; and

WHEREAS, Executive wishes to continue to be employed by the Company and to provide personal services to the Company in return for certain compensation and benefits;

NOW, THEREFORE, in consideration of the mutual promises and covenants contained herein and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties hereto agree as follows:

1. Employment by the Company.

1.1 Position and Duties. Executive shall continue to serve as the Company's Chief Executive Officer (the "**Position**"). During the term of Executive's employment with the Company, Executive shall devote one hundred percent of Executive's business time on behalf of the Company and, on a full time basis, use Executive's skills and render services to the best of Executive's abilities on behalf of the Company, and shall comply fully with the policies and procedures of the Company. Executive shall report directly to the Company's **Board of Directors (the "Board")**. Executive shall perform those duties typically associated with the Position and such other duties consistent with the Position as may be assigned by the **Board**, including but not limited to executive responsibility for R&D and G&A. Notwithstanding the foregoing, nothing herein shall preclude Executive from (i) serving, with the prior written consent of the **Board**, as a member of the boards of directors or advisory boards of non-competitive businesses and charitable organizations, (ii) engaging in charitable activities and community affairs, and (iii) managing Executive's personal investments and affairs; *provided*, *however*, that the activities set out in clauses (i), (ii), and (iii) shall be limited by Executive so as not to materially interfere, individually or in the aggregate, with the performance of Executive's duties and responsibilities hereunder and shall not, in the judgment of the **Board** pose a conflict of interest with Executive's duties to the Company or its affiliates.

1.2 Location of Work. Executive shall work **remotely** in Califon, New Jersey, USA. The Company reserves the right to reasonably require Executive to perform Executive's duties at places other than Executive's primary office location from time to time, and to require reasonable business travel. Understanding that the Executive currently lives outside of Massachusetts and is expected to relocate to the Boston metropolitan area within 24 months of the Start Date, the Company will provide Executive with a housing and living allowance not to exceed $60,000 total for the period of twenty-four months from the Start Date. The Company will provide Executive with a maximum relocation expense of $200,000, subject to the Expense Reimbursement Agreement between Executive and Company dated March 18, 2020, and agrees to repay the full amount of any relocation expenses provided by Company in the event that he resigns from employment within two years of the Start Date.

1.3 Policies and Procedures. The employment relationship between the Parties shall be governed by the general employment policies and practices of the Company, except that when the terms of this Agreement differ from or are in conflict with the Company's general employment policies or practices, this Agreement shall control.

2. Compensation.

2.1 Salary. For services to be rendered hereunder, Executive shall receive an initial base salary at the rate of $550,000 per year, subject to standard payroll deductions and withholdings and payable in accordance with the Company's regular payroll schedule (the "**Base Salary**"). Executive's Base Salary will be reviewed annually by the Board or the Compensation Committee of the Board (the "**Compensation Committee**").

2.2 Annual Cash Bonus. Executive will be eligible for an annual cash bonus with a target amount of seventy percent (70%) of Executive's Base Salary (the "**Annual Bonus**"). Whether Executive receives an Annual Bonus for any given year, and the amount of any such Annual Bonus, will be determined by the Board or the Compensation Committee based upon the Company's and Executive's achievement of objectives and milestones to be determined by the Board or the Compensation Committee on an annual basis. Except as otherwise provided herein or in applicable incentive compensation plan that may be in effect from time to time, Executive will not be eligible for, and will not earn, any Annual Bonus if Executive is not employed by the Company on the payment date (regardless of the reason for the separation from employment). Notwithstanding the foregoing, the Company will guarantee Executive the full amount of his Annual Bonus for calendar year 2020, provided that Executive is employed by the Company on the date on which the Annual Bonuses are paid to employees on or about March 31, 2021.

2.3 Equity. The stock options and other stock-based awards held by Executive shall continue to be governed by the terms and conditions of the Company's applicable equity incentive plan(s) and the applicable award agreement(s) governing the terms of such stock options and other stock-based awards (collectively, the "**Equity Documents**"); *provided*, *however*, and notwithstanding anything to the contrary in the Equity Documents, Section 5.3(ii)(b) of this Agreement shall apply in the event of a termination of Executive's employment by the Company without Cause or by Executive for Good Reason, in either case within the Change of Control Period (as such terms are defined below).

3. Standard Company Benefits. Executive shall be entitled to participate in all employee benefit programs for which Executive is eligible under the terms and conditions of the benefit plans that may be in effect from time to time and provided by the Company to its employees. The Company reserves the right to cancel or change the benefit plans or programs it offers to its employees at any time.

4. Additional Benefits. In addition to the standard Company benefits, (i) the Company shall reimburse the Executive for the premiums on a supplemental long- term disability policy owned by him the benefits of which, when combined with the benefits from any Company long-term disability plan or arrangement in which he participates, will replace 65% of his Base Salary; (ii) the Company shall reimburse the Executive for the premiums on a 20-year term life insurance policy that he owns with a death benefit of $3,000,000; and (iii) the Executive shall participate in a Company-sponsored supplemental retirement plan that will provide benefits equal to those provided under the Company's qualified retirement plan that would be accrued but for the limitations on compensation and contributions applicable to qualified retirement plans.

5. Expenses. The Company will reimburse Executive for reasonable travel, entertainment or other expenses incurred by Executive in furtherance or in connection with the performance of Executive's duties hereunder, in accordance with the Company's expense reimbursement policy as in effect from time to time.

6. Termination of Employment; Severance.

6.1 At-Will Employment. Executive's employment relationship is at- will. Either Executive or the Company may terminate the employment relationship at any time, with or without cause subject to the terms of this Agreement.

6.2 Severance Pay and Benefits Upon a Termination Without Cause or Resignation for Good Reason Outside the Change of Control Period.

(i) The Company may terminate Executive's employment with the Company at any time without Cause. Executive may terminate Executive's employment with the Company at any time for any reason, including for Good Reason.

(ii) In the event that Executive's employment with the Company is terminated by the Company without Cause or by Executive for Good Reason, in either case outside of the Change of Control Period, then, provided that Executive remains in compliance with the terms of this Agreement, the Company shall provide Executive with the following severance benefits:

(a) The Company shall pay Executive, as severance, 12 months of Executive's Base Salary in effect as of the date of Executive's employment termination, subject to standard payroll deductions and withholdings (the "**Severance**"). Subject to Section 5.2(iii) below, the Severance will be paid in equal installments on the Company's regular payroll schedule over the 12 month period following Executive's termination of employment.

(b) Provided Executive timely elects continued coverage under COBRA, the Company shall pay the Company's portion of Executive's COBRA premiums, equal to the percentage of health premiums paid by the Company prior to Executive's termination, to continue Executive's coverage (including coverage for eligible dependents, if applicable) ("**COBRA Premiums**") through the period (the "**COBRA Premium Period**") starting on Executive's date of termination and ending on the earliest to occur of: (i) the 12 month anniversary of Executive's date of termination; (ii) the date Executive becomes eligible for group health insurance coverage through a new employer; or (iii) the date Executive ceases to be eligible for COBRA continuation coverage for any reason, including plan termination. In the event Executive becomes covered under another employer's group health plan or otherwise ceases to be eligible for COBRA during the COBRA Premium Period, Executive must immediately notify the Company of such event. Notwithstanding the foregoing, if the Company determines, in its sole discretion, that it cannot pay the COBRA Premiums without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company instead shall pay to Executive, on the first day of each calendar month, a fully taxable cash payment equal to the applicable COBRA premiums for that month (including premiums for Executive and Executive's eligible dependents who have elected and remain enrolled in such COBRA coverage), subject to applicable tax withholdings (such amount, the "**Special Cash Payment**"), for the remainder of the COBRA Premium Period. Executive may, but is not obligated to, use such Special Cash Payments toward the cost of COBRA premiums.

(iii) The amounts payable under this Section 5.2, to the extent taxable, shall be paid or commence to be paid within 60 days after the date of termination; *provided*, *however*, that if the 60-day period begins in one calendar year and ends in a second calendar year, such payments to the extent they qualify as "non-qualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "**Code**"), shall be paid or commence to be paid in the second calendar year by the last day of such 60-day period.

6.3 Severance Pay and Benefits Upon Termination Without Cause or Resignation for Good Reason Within the Change of Control Period.

(i) The provisions of this Section 5.3 shall apply in lieu of, and expressly supersede, the provisions of Section 5.2 regarding severance pay and benefits upon a termination of employment by the Company without Cause or by Executive for Good Reason if such termination of employment occurs on or within 12 months after the occurrence of the first event constituting a Change of Control (such period, the "**Change of Control Period**"). These provisions shall terminate and be of no further force or effect after the Change of Control Period.

(ii) In the event that Executive's employment with the Company is terminated by the Company without Cause or by Executive for Good Reason, in either case during the Change of Control Period, then, provided Executive remains in compliance with the terms of this Agreement, the Company shall provide Executive with the following severance benefits:

(a) The Company shall pay Executive, as severance, a lump sum in cash in an amount equal to 1.5 times the sum of (A) Executive's then current Base Salary (or Executive's Base Salary in effect immediately prior to the Change of Control, if higher) plus (B) Executive's Annual Bonus for the then-current year (or Executive's Annual Bonus in effect immediately prior to the Change of Control, if higher) (the "**Change of Control Severance**").

(b) Notwithstanding anything to the contrary in any applicable option agreement or other stock-based award agreement, all time-based stock options and other stock-based awards subject to time-based vesting held by Executive (the "**Time-Based Equity Awards**") shall immediately accelerate and become fully exercisable or nonforfeitable as of the later of (i) the date of termination or (ii) the effective date of the Separation Agreement (as defined below) (the "**Accelerated Vesting Date**"); *provided* that any termination or forfeiture of the unvested portion of such Time-Based Equity Awards that would otherwise occur on the date of termination in the absence of this Agreement will be delayed until the effective date of the Separation Agreement and will only occur if the vesting pursuant to this subsection does not occur due to the absence of the Separation Agreement becoming fully effective within the time period set forth therein. Notwithstanding the foregoing, no additional vesting of the Time-Based Equity Awards shall occur during the period between Executive's date of termination and the Accelerated Vesting Date.

(c) Provided Executive timely elects continued coverage under COBRA, the Company shall pay the Company's portion of Executive's COBRA premiums, equal to the percentage of health premiums paid by the Company prior to Executive's termination, to continue Executive's coverage (including coverage for eligible dependents, if applicable) ("**COC COBRA Premiums**") through the period (the "**COC COBRA Premium Period**") starting on Executive's date of termination and ending on the earliest to occur of: (i) the 18 month anniversary of Executive's date of termination; (ii) the date Executive becomes eligible for group health insurance coverage through a new employer; or (iii) the date Executive ceases to be eligible for COBRA continuation coverage for any reason, including plan termination. In the event Executive becomes covered under another employer's group health plan or otherwise ceases to be eligible for COBRA during the COC COBRA Premium Period, Executive must immediately notify the Company of such event. Notwithstanding the foregoing, if the Company determines, in its sole discretion, that it cannot pay the COC COBRA Premiums without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company instead shall pay to Executive, on the first day of each calendar month, a fully taxable cash payment equal to the applicable COBRA premiums for that month (including premiums for Executive and Executive's eligible dependents who have elected and remain enrolled in such COBRA coverage), subject to applicable tax withholdings (such amount, the "**COC Special Cash Payment**"), for the remainder of the COC COBRA Premium Period. Executive may, but is not obligated to, use such COC Special Cash Payments toward the cost of COBRA premiums.

(iii) The amounts payable under this Section 5.3, to the extent taxable, shall be paid or commence to be paid within 60 days after the date of termination; *provided*, *however*, that if the 60-day period begins in one calendar year and ends in a second calendar year, such payments to the extent they qualify as "non-qualified deferred compensation" within the meaning of Section 409A of the Code, shall be paid or commence to be paid in the second calendar year by the last day of such 60-day period.

(iv) Additional Limitation.

(a) Anything in this Agreement to the contrary notwithstanding, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 280G of the Code, and the applicable regulations thereunder (the "**Aggregate Payments**"), would be subject to the excise tax imposed by Section 4999 of the Code, then the Aggregate Payments shall be reduced (but not below zero) so that the sum of all of the Aggregate Payments shall be $1.00 less than the amount at which Executive becomes subject to the excise tax imposed by Section 4999 of the Code; *provided* that such reduction shall only occur if it would result in Executive receiving a higher After Tax Amount (as defined below) than Executive would receive if the Aggregate Payments were not subject to such reduction. In such event, the Aggregate Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Aggregate Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (1) cash payments not subject to Section 409A of the Code; (2) cash payments subject to Section 409A of the Code; (3) equity-based payments and acceleration; and (4) non-cash forms of benefits; *provided* that in the case of all the foregoing Aggregate Payments, all amounts or payments that are not subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c).

(b) For purposes of this Section 5.3(iv), the "**After Tax Amount**" means the amount of the Aggregate Payments less all federal, state, and local income, excise and employment taxes imposed on Executive as a result of Executive's receipt of the Aggregate Payments. For purposes of determining the After Tax Amount, Executive shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes.

(c) The determination as to whether a reduction in the Aggregate Payments shall be made pursuant to Section 5.3(iv)(a) shall be made by a nationally recognized accounting firm selected by the Company (the "**Accounting Firm**"), which shall provide detailed supporting calculations both to the Company and Executive within 15 business days of the date of termination, if applicable, or at such earlier time as is reasonably requested by the Company or Executive. Any determination by the Accounting Firm shall be binding upon the Company and Executive.

6.4 Termination for Cause; Resignation without Good Reason; Death or Disability.

(i) The Company may terminate Executive's employment with the Company at any time for Cause. Further, Executive may resign at any time for any reason other than Good Reason. Executive's employment with the Company may also be terminated due to Executive's death or Disability (as defined below).

(ii) If Executive resigns without Good Reason, or the Company terminates Executive's employment for Cause, or upon Executive's death or Disability, then (i) all payments of compensation by the Company to Executive hereunder will terminate immediately (except as to amounts already earned), and (ii) Executive will not be entitled to any severance benefits, including (without limitation) the Severance, COBRA Premiums, the Change of Control Severance or the COC COBRA Premiums.

7. Conditions to Receipt of Severance, COBRA Premiums, Special Cash Payments and Vesting Acceleration. The receipt of the payments and benefits described in Section 5.2 and Section 5.3 will be subject to subject to (i) Executive signing a separation agreement and release in a form and manner satisfactory to the Company, which shall include, without limitation, a general release of claims against the Company and all related persons and entities and, in the Company's sole discretion, a one-year post-employment noncompetition agreement (the "**Separation Agreement"**) and (ii) the Separation Agreement becoming irrevocable, all within 60 days after the date of termination (or such shorter period as set forth in the Separation Agreement), which shall include a seven business day revocation period. No amounts will be paid or provided under Section 5.2 or Section 5.3 until the Separation Agreement becomes effective. Executive shall be deemed to have resigned from all officer and board member positions that the Executive holds with the Company or any of its respective subsidiaries and affiliates upon the termination of Executive's employment for any reason. Executive shall execute any documents in reasonable form as may be requested to confirm or effectuate any such resignations.

8. Section 409A.

8.1 Anything in this Agreement to the contrary notwithstanding, if at the time of Executive's separation from service within the meaning of Section 409A of the Code, the Company determines that Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that Executive becomes entitled to under this Agreement or otherwise on account of Executive's separation from service would be considered deferred compensation otherwise subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after Executive's separation from service, or (B) Executive's death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six- month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule.

8.2 All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year (except for any lifetime or other aggregate limitation applicable to medical expenses). Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

8.3 To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon Executive's termination of employment, then such payments or benefits shall be payable only upon Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

8.4 The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2). The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

8.5 The Company makes no representation or warranty and shall have no liability to Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

9. Definitions.

9.1 **Cause**. For purposes of this Agreement, "**Cause**" for termination will mean: (a) conviction of or please of guilty or *nolo contendere* to any felony or any crime involving dishonesty; (b) participation in any fraud against the Company; (c) material breach of any Company's policy or procedure after written notice from the Company and a reasonable period of not less than twenty-one (21) calendar days in which to cure such breach (if deemed curable); (d) persistent failure or refusal to perform Executive's job duties after written notice from the Company and a reasonable period of not less than twenty-one (21) calendar days in which to cure such performance issues (if deemed curable); (e) intentional damage to any property of the Company; (f) willful misconduct, or other violation of Company policy that causes harm; (g) breach of any written agreement by and between Executive and the Company; and (h) conduct by Executive which in the good faith and reasonable determination of the Company demonstrates gross unfitness to serve.

9.2 Change of Control. For purposes of this Agreement, "**Change of Control**" shall mean: a "Sale Event," as defined in the Company's 2020 Stock Option and Incentive Plan.

9.3 Disability. For purposes of this Agreement, "**Disability**" shall mean Executive's physical or mental condition that renders Executive unable to substantially perform for a period of ninety (90) aggregate days (regardless of whether or not continuous) during any three hundred sixty (360) day period, Executive's regular responsibilities hereunder, with or without a reasonable accommodation.

9.4 Good Reason. For purposes of this Agreement, "**Good Reason**" shall mean: (a) a material reduction in Executive's Base Salary (unless pursuant to a salary reduction applicable generally to the Company's similarly situated employees); or (b) the relocation of Executive's place of work for the Company that is more than 40 miles from Executive's primary place of work, unless mutually agreed upon. Notwithstanding the foregoing, no act or omission described in subclauses (a) or (b) above shall constitute "Good Reason" unless: (1) Executive first gives the Company written notice of such act or omission within forty-five (45) days of the later of the occurrence of such act or omission or Executive's first becoming aware thereof, (2) the Company fails to cure such act or omission within twenty-one (21) days after receiving such written notice from Executive, and (3) Executive resigns from employment (and all other positions, including as a member of the Board) within ten (10) days after the end of the cure period.

10. Other Obligations.

10.1 Restrictive Covenants. In connection with Executive's employment with the Company, Executive will continue to receive access to Company confidential information and trade secrets and develop valuable goodwill with the Company's customers, partners and vendors. To protect the Company's legitimate business interests, Executive executed the Employee Confidentiality, Assignment and Nonsolicitation Agreement on May 14, 2020 (the "**Confidentiality Agreement**"). In connection with Executive's execution of this Amended and Restated Employment Agreement and in further consideration of Executive's employment with the Company, Executive agrees to execute a Non- Competition Agreement (the "Non-Competition Agreement") in a form acceptable to the Company, which Executive will do in or around September 2020. Executive herein acknowledges and agrees that (i) the Confidentiality Agreement shall continue in full force and effect in accordance with its terms, and (ii) Executive will abide by the terms of the Confidentiality Agreement and the Non-Competition Agreement at all times.

10.2 Third-Party Agreements and Information. Executive represents and warrants that Executive's employment by the Company does not conflict with any prior employment or consulting agreement or other agreement with any third party, and that Executive will perform Executive's duties to the Company without violating any such agreement. Executive represents and warrants that Executive will not use or disclose confidential information arising out of prior employment, consulting, or other third party relationships, in connection with Executive's employment by the Company, except as expressly authorized by that third party. During Executive's employment by the Company, Executive will use in the performance of Executive's duties only information which is generally known and used by persons with training and experience comparable to Executive's own, common knowledge in the industry, otherwise legally in the public domain, or obtained or developed by the Company or by Executive in the course of Executive's work for the Company.

11. Outside Activities During Employment.

11.1 Non-Company Business. Except with the prior written consent of the Board, Executive will not during the term of Executive's employment with the Company undertake or engage in any other employment, occupation or business enterprise, other than ones in which Executive is a passive investor. In any event, Executive may engage in civic and not-for-profit activities so long as such activities do not materially interfere with the performance of Executive's duties hereunder.

11.2 No Adverse Interests. Executive agrees not to acquire, assume or participate in, directly or indirectly, any position, investment or interest known to be adverse or antagonistic to the Company, its business or prospects, financial or otherwise.

12. General Provisions.

12.1 Notices. Any notices provided must be in writing and will be deemed effective upon the earlier of personal delivery (including personal delivery by fax) or the next day after sending by overnight carrier, to the Company at its primary office location and to Executive at the address as listed on the Company payroll.

12.2 Severability. Whenever possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be invalid, illegal or unenforceable in any respect under any applicable law or rule in any jurisdiction, such invalidity, illegality or unenforceability will not affect any other provision or any other jurisdiction, but this Agreement will be reformed, construed and enforced in such jurisdiction to the extent possible in keeping with the intent of the parties.

12.3 Waiver. Any waiver of any breach of any provisions of this Agreement must be in writing to be effective, and it shall not thereby be deemed to have waived any preceding or succeeding breach of the same or any other provision of this Agreement.

12.4 Complete Agreement. This Agreement, together with the Confidentiality Agreement, constitutes the entire agreement between Executive and the Company and is the complete, final, and exclusive embodiment of the Parties' agreement and supersedes all prior agreements between the parties concerning such subject matter, including the Prior Agreement. This Agreement is entered into without reliance on any promise or representation, written or oral, other than those expressly contained herein, and it supersedes any other such promises, warranties or representations. It is entered into without reliance on any promise or representation other than those expressly contained herein, and it cannot be modified or amended except in a writing signed by a duly authorized officer of the Company.

12.5 Counterparts. This Agreement may be executed in separate counterparts, any one of which need not contain signatures of more than one party, but all of which taken together will constitute one and the same Agreement.

12.6 Headings. The headings of the paragraphs hereof are inserted for convenience only and shall not be deemed to constitute a part hereof nor to affect the meaning thereof.

12.7 Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of and be enforceable by Executive and the Company, and their respective successors, assigns, heirs, executors and administrators, except that Executive may not assign any of his duties hereunder and he may not assign any of his rights hereunder without the written consent of the Company, which shall not be withheld unreasonably.

12.8 Tax Withholding and Indemnification. All payments and awards contemplated or made pursuant to this Agreement will be subject to withholdings of applicable taxes in compliance with all relevant laws and regulations of all appropriate government authorities. Executive acknowledges and agrees that the Company has neither made any assurances nor any guarantees concerning the tax treatment of any payments or awards contemplated by or made pursuant to this Agreement. Executive has had the opportunity to retain a tax and financial advisor and fully understands the tax and economic consequences of all payments and awards made pursuant to the Agreement.

12.9 Choice of Law. All questions concerning the construction, validity and interpretation of this Agreement will be governed by the laws of the Commonwealth of Massachusetts.

IN WITNESS WHEREOF, the Parties have executed this Agreement on the day and year first above written.

PRAXIS PRECISION MEDICINES, INC.

By: /s/ Dean Mitchell
Name: Dean Mitchell
Title: Chairman of the Board

Date: 9/24/2020

Executive

/s/ Marcio Souza
Name: Marcio Souza

Date: 9/30/2020

PRAXIS PRECISION MEDICINES, INC.

AMENDED AND RESTATED EMPLOYMENT AGREEMENT
for Bernard Ravina

This Amended and Restated Executive Employment Agreement (the "**Agreement**") is made between Praxis Precision Medicines, Inc. (the "**Company**") and Bernard Ravina ("**Executive**") (collectively, the "**Parties**") and is effective as of the closing of the Company's first underwritten public offering of its equity securities pursuant to an effective registration statement under the Securities Act of 1933, as amended (the "**Effective Date**"). This Agreement supersedes in all respects all prior agreements between Executive and the Company regarding the subject matter herein, including without limitation, the Employment Agreement between Executive and the Company dated April 17, 2020 (the "**Prior Agreement**").

WHEREAS, the Company desires Executive to continue to provide services to the Company, and wishes to provide Executive with certain compensation and benefits in return for such employment services; and

WHEREAS, Executive wishes to continue to be employed by the Company and to provide personal services to the Company in return for certain compensation and benefits;

NOW, THEREFORE, in consideration of the mutual promises and covenants contained herein and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties hereto agree as follows:

1. Employment by the Company.

1.1 Position and Duties. Executive shall continue to serve as the Company's Chief Medical Officer (the "**Position**"). During the term of Executive's employment with the Company, Executive shall devote one hundred percent of Executive's business time on behalf of the Company and, on a full time basis, use Executive's skills and render services to the best of Executive's abilities on behalf of the Company, and shall comply fully with the policies and procedures of the Company. Executive shall report directly to the Company's **Chief Executive Officer (the "CEO")**. Executive shall perform those duties typically associated with the Position and such other duties consistent with the Position as may be assigned by the **CEO**, including but not limited to executive responsibility for clinical development and executive leadership. Notwithstanding the foregoing, nothing herein shall preclude Executive from (i)serving, with the prior written consent of the **CEO**, as a member of the boards of directors or advisory boards of non- competitive businesses and charitable organizations, (ii) engaging in charitable activities and community affairs, and (iii) managing Executive's personal investments and affairs; *provided*, *however*, that the activities set out in clauses (i), (ii), and (iii) shall be limited by Executive so as not to materially interfere, individually or in the aggregate, with the performance of Executive's duties and responsibilities hereunder and shall not, in the judgment of the **CEO** pose a conflict of interest with Executive's duties to the Company or its affiliates.

1.2 Location of Work. Executive shall work in Cambridge, Massachusetts, USA. The Company reserves the right to reasonably require Executive to perform Executive's duties at places other than Executive's primary office location from time to time, and to require reasonable business travel.

1.3 Policies and Procedures. The employment relationship between the Parties shall be governed by the general employment policies and practices of the Company, except that when the terms of this Agreement differ from or are in conflict with the Company's general employment policies or practices, this Agreement shall control.

2. Compensation.

2.1 Salary. For services to be rendered hereunder, Executive shall receive an initial base salary at the rate of $425,000 per year, subject to standard payroll deductions and withholdings and payable in accordance with the Company's regular payroll schedule (the "**Base Salary**"). Executive's Base Salary will be reviewed annually by the Board or the Compensation Committee of the Board (the "**Compensation Committee**").

2.2 Annual Cash Bonus. Executive will be eligible for an annual cash bonus with a target amount of forty percent (40%) of Executive's Base Salary (the "**Annual Bonus**"). Whether Executive receives an Annual Bonus for any given year, and the amount of any such Annual Bonus, will be determined by the Board or the Compensation Committee based upon the Company's and Executive's achievement of objectives and milestones to be determined by the Board or the Compensation Committee on an annual basis. Except as otherwise provided herein or in applicable incentive compensation plan that may be in effect from time to time, Executive will not be eligible for, and will not earn, any Annual Bonus if Executive is not employed by the Company on the payment date (regardless of the reason for the separation from employment).

2.3 Equity. The stock options and other stock-based awards held by Executive shall continue to be governed by the terms and conditions of the Company's applicable equity incentive plan(s) and the applicable award agreement(s) governing the terms of such stock options and other stock-based awards (collectively, the "**Equity Documents**"); *provided*, *however*, and notwithstanding anything to the contrary in the Equity Documents, Section 5.3(ii)(b) of this Agreement shall apply in the event of a termination of Executive's employment by the Company without Cause or by Executive for Good Reason, in either case within the Change of Control Period (as such terms are defined below).

3. Standard Company Benefits. Executive shall be entitled to participate in all employee benefit programs for which Executive is eligible under the terms and conditions of the benefit plans that may be in effect from time to time and provided by the Company to its employees. The Company reserves the right to cancel or change the benefit plans or programs it offers to its employees at any time.

4. Expenses. The Company will reimburse Executive for reasonable travel, entertainment or other expenses incurred by Executive in furtherance or in connection with the performance of Executive's duties hereunder, in accordance with the Company's expense reimbursement policy as in effect from time to time.

5. Termination of Employment; Severance.

5.1 At-Will Employment. Executive's employment relationship is at- will. Either Executive or the Company may terminate the employment relationship at any time, with or without cause subject to the terms of this Agreement.

5.2 Severance Pay and Benefits Upon a Termination Without Cause or Resignation for Good Reason Outside the Change of Control Period.

(i) The Company may terminate Executive's employment with the Company at any time without Cause. Executive may terminate Executive's employment with the Company at any time for any reason, including for Good Reason.

(ii) In the event that Executive's employment with the Company is terminated by the Company without Cause or by Executive for Good Reason, in either case outside of the Change of Control Period, then, provided that Executive remains in compliance with the terms of this Agreement, the Company shall provide Executive with the following severance benefits:

(a) The Company shall pay Executive, as severance, 9 months of Executive's Base Salary in effect as of the date of Executive's employment termination, subject to standard payroll deductions and withholdings (the "**Severance**"). Subject to Section 5.2(iii) below, the Severance will be paid in equal installments on the Company's regular payroll schedule over the 9-month period following Executive's termination of employment.

(b) Provided Executive timely elects continued coverage under COBRA, the Company shall pay the Company's portion of Executive's COBRA premiums, equal to the percentage of health premiums paid by the Company prior to Executive's termination, to continue Executive's coverage (including coverage for eligible dependents, if applicable) ("**COBRA Premiums**") through the period (the "**COBRA Premium Period**") starting on Executive's date of termination and ending on the earliest to occur of: (i) the 9 month anniversary of Executive's date of termination; (ii) the date Executive becomes eligible for group health insurance coverage through a new employer; or (iii) the date Executive ceases to be eligible for COBRA continuation coverage for any reason, including plan termination. In the event Executive becomes covered under another employer's group health plan or otherwise ceases to be eligible for COBRA during the COBRA Premium Period, Executive must immediately notify the Company of such event. Notwithstanding the foregoing, if the Company determines, in its sole discretion, that it cannot pay the COBRA Premiums without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company instead shall pay to Executive, on the first day of each calendar month, a fully taxable cash payment equal to the applicable COBRA premiums for that month (including premiums for Executive and Executive's eligible dependents who have elected and remain enrolled in such COBRA coverage), subject to applicable tax withholdings (such amount, the "**Special Cash Payment**"), for the remainder of the COBRA Premium Period. Executive may, but is not obligated to, use such Special Cash Payments toward the cost of COBRA premiums.

(iii) The amounts payable under this Section 5.2, to the extent taxable, shall be paid or commence to be paid within 60 days after the date of termination; *provided*, *however*, that if the 60-day period begins in one calendar year and ends in a second calendar year, such payments to the extent they qualify as "non-qualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "**Code**"), shall be paid or commence to be paid in the second calendar year by the last day of such 60-day period.

5.3 Severance Pay and Benefits Upon Termination Without Cause or Resignation for Good Reason Within the Change of Control Period.

(i) The provisions of this Section 5.3 shall apply in lieu of, and expressly supersede, the provisions of Section 5.2 regarding severance pay and benefits upon a termination of employment by the Company without Cause or by Executive for Good Reason if such termination of employment occurs on or within 12 months after the occurrence of the first event constituting a Change of Control (such period, the "**Change of Control Period**"). These provisions shall terminate and be of no further force or effect after the Change of Control Period

(ii) In the event that Executive's employment with the Company is terminated by the Company without Cause or by Executive for Good Reason, in either case during the Change of Control Period, then, provided Executive remains in compliance with the terms of this Agreement, the Company shall provide Executive with the following severance benefits:

(a) The Company shall pay Executive, as severance, a lump sum in cash in an amount equal to 1 times the sum of (A) Executive's then current Base Salary (or Executive's Base Salary in effect immediately prior to the Change of Control, if higher) plus (B) Executive's Annual Bonus for the then-current year (or Executive's Annual Bonus in effect immediately prior to the Change of Control, if higher) (the "**Change of Control Severance**").

(b) Notwithstanding anything to the contrary in any applicable option agreement or other stock-based award agreement, all time-based stock options and other stock-based awards subject to time-based vesting held by Executive (the "**Time-Based Equity Awards**") shall immediately accelerate and become fully exercisable or nonforfeitable as of the later of (i) the date of termination or (ii) the effective date of the Separation Agreement (as defined below) (the "**Accelerated Vesting Date**"); *provided* that any termination or forfeiture of the unvested portion of such Time-Based Equity Awards that would otherwise occur on the date of termination in the absence of this Agreement will be delayed until the effective date of the Separation Agreement and will only occur if the vesting pursuant to this subsection does not occur due to the absence of the Separation Agreement becoming fully effective within the time period set forth therein. Notwithstanding the foregoing, no additional vesting of the Time-Based Equity Awards shall occur during the period between Executive's date of termination and the Accelerated Vesting Date.

(c) Provided Executive timely elects continued coverage under COBRA, the Company shall pay the Company's portion of Executive's COBRA premiums, equal to the percentage of health premiums paid by the Company prior to Executive's termination, to continue Executive's coverage (including coverage for eligible dependents, if applicable) ("**COC COBRA Premiums**") through the period (the "**COC COBRA Premium Period**") starting on Executive's date of termination and ending on the earliest to occur of: (i) the 12 month anniversary of Executive's date of termination; (ii) the date Executive becomes eligible for group health insurance coverage through a new employer; or (iii) the date Executive ceases to be eligible for COBRA continuation coverage for any reason, including plan termination. In the event Executive becomes covered under another employer's group health plan or otherwise ceases to be eligible for COBRA during the COC COBRA Premium Period, Executive must immediately notify the Company of such event. Notwithstanding the foregoing, if the Company determines, in its sole discretion, that it cannot pay the COC COBRA Premiums without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company instead shall pay to Executive, on the first day of each calendar

month, a fully taxable cash payment equal to the applicable COBRA premiums for that month (including premiums for Executive and Executive's eligible dependents who have elected and remain enrolled in such COBRA coverage), subject to applicable tax withholdings (such amount, the "**COC Special Cash Payment**"), for the remainder of the COC COBRA Premium Period. Executive may, but is not obligated to, use such COC Special Cash Payments toward the cost of COBRA premiums.

(iii) The amounts payable under this Section 5.3, to the extent taxable, shall be paid or commence to be paid within 60 days after the date of termination; *provided*, *however*, that if the 60-day period begins in one calendar year and ends in a second calendar year, such payments to the extent they qualify as "non-qualified deferred compensation" within the meaning of Section 409A of the Code, shall be paid or commence to be paid in the second calendar year by the last day of such 60-day period.

(iv) Additional Limitation.

(a) Anything in this Agreement to the contrary notwithstanding, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 280G of the Code, and the applicable regulations thereunder (the "**Aggregate Payments**"), would be subject to the excise tax imposed by Section 4999 of the Code, then the Aggregate Payments shall be reduced (but not below zero) so that the sum of all of the Aggregate Payments shall be $1.00 less than the amount at which Executive becomes subject to the excise tax imposed by Section 4999 of the Code; *provided* that such reduction shall only occur if it would result in Executive receiving a higher After Tax Amount (as defined below) than Executive would receive if the Aggregate Payments were not subject to such reduction. In such event, the Aggregate Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Aggregate Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (1) cash payments not subject to Section 409A of the Code; (2) cash payments subject to Section 409A of the Code; (3) equity-based payments and acceleration; and (4) non-cash forms of benefits; *provided* that in the case of all the foregoing Aggregate Payments, all amounts or payments that are not subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c).

(b) For purposes of this Section 5.3(iv), the "**After Tax Amount**" means the amount of the Aggregate Payments less all federal, state, and local income, excise and employment taxes imposed on Executive as a result of Executive's receipt of the Aggregate Payments. For purposes of determining the After Tax Amount, Executive shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes.

(c) The determination as to whether a reduction in the Aggregate Payments shall be made pursuant to Section 5.3(iv)(a) shall be made by a nationally recognized accounting firm selected by the Company (the "**Accounting Firm**"), which shall provide detailed supporting calculations both to the Company and Executive within 15 business days of the date of termination, if applicable, or at such earlier time as

is reasonably requested by the Company or Executive. Any determination by the Accounting Firm shall be binding upon the Company and Executive.

5.4 Termination for Cause; Resignation without Good Reason; Death or Disability.

(i) The Company may terminate Executive's employment with the Company at any time for Cause. Further, Executive may resign at any time for any reason other than Good Reason. Executive's employment with the Company may also be terminated due to Executive's death or Disability (as defined below).

(ii) If Executive resigns without Good Reason, or the Company terminates Executive's employment for Cause, or upon Executive's death or Disability, then (i) all payments of compensation by the Company to Executive hereunder will terminate immediately (except as to amounts already earned), and (ii) Executive will not be entitled to any severance benefits, including (without limitation) the Severance, COBRA Premiums, the Change of Control Severance or the COC COBRA Premiums.

6. Conditions to Receipt of Severance, COBRA Premiums, Special Cash Payments and Vesting Acceleration. The receipt of the payments and benefits described in Section 5.2 and Section 5.3 will be subject to subject to (i) Executive signing a separation agreement and release in a form and manner satisfactory to the Company, which shall include, without limitation, a general release of claims against the Company and all related persons and entities and, in the Company's sole discretion, a one-year post-employment noncompetition agreement (the "**Separation Agreement"**) and (ii) the Separation Agreement becoming irrevocable, all within 60 days after the date of termination (or such shorter period as set forth in the Separation Agreement), which shall include a seven business day revocation period. No amounts will be paid or provided under Section 5.2 or Section 5.3 until the Separation Agreement becomes effective. Executive shall be deemed to have resigned from all officer and board member positions that the Executive holds with the Company or any of its respective subsidiaries and affiliates upon the termination of Executive's employment for any reason. Executive shall execute any documents in reasonable form as may be requested to confirm or effectuate any such resignations.

7. Section 409A.

7.1 Anything in this Agreement to the contrary notwithstanding, if at the time of Executive's separation from service within the meaning of Section 409A of the Code, the Company determines that Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that Executive becomes entitled to under this Agreement or otherwise on account of Executive's separation from service would be considered deferred compensation otherwise subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after Executive's separation from service, or (B) Executive's death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six- month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule.

7.2 All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year (except for any lifetime or other aggregate limitation applicable to medical expenses). Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

7.3 To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon Executive's termination of employment, then such payments or benefits shall be payable only upon Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

7.4 The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2). The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

7.5 The Company makes no representation or warranty and shall have no liability to Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

8. Definitions.

8.1 Cause. For purposes of this Agreement, "**Cause**" for termination will mean: (a) conviction of or please of guilty or *nolo contendere* to any felony or any crime involving dishonesty; (b) participation in any fraud against the Company; (c) material breach of any Company's policy or procedure after written notice from the Company and a reasonable period of not less than twenty-one (21) calendar days in which to cure such breach (if deemed curable); (d) persistent failure or refusal to perform Executive's job duties after written notice from the Company and a reasonable period of not less than twenty-one (21) calendar days in which to cure such performance issues (if deemed curable); (e) intentional damage to any property of the Company; (f) willful misconduct, or other violation of Company policy that causes harm; (g) breach of any written agreement by and between Executive and the Company; and (h) conduct by Executive which in the good faith and reasonable determination of the Company demonstrates gross unfitness to serve.

8.2 Change of Control. For purposes of this Agreement, "**Change of Control**" shall mean: a "Sale Event," as defined in the Company's 2020 Stock Option and Incentive Plan.

8.3 Disability. For purposes of this Agreement, "**Disability**" shall mean Executive's physical or mental condition that renders Executive unable to substantially perform for a period of ninety (90) aggregate days (regardless of whether or not continuous) during any three hundred sixty (360) day period, Executive's regular responsibilities hereunder, with or without a reasonable accommodation.

8.4 Good Reason. For purposes of this Agreement, "**Good Reason**" shall mean: (a) a material reduction in Executive's Base Salary (unless pursuant to a salary reduction applicable generally to the Company's similarly situated employees); or (b) the relocation of Executive's place of work for the Company that is more than 40 miles from Executive's primary place of work, unless mutually agreed upon. Notwithstanding the foregoing, no act or omission described in subclauses (a) or (b) above shall constitute "Good Reason" unless: (1) Executive first gives the Company written notice of such act or omission within forty-five (45) days of the later of the occurrence of such act or omission or Executive's first becoming aware thereof, (2) the Company fails to cure such act or omission within twenty-one (21) days after receiving such written notice from Executive, and (3) Executive resigns from employment (and all other positions, including as a member of the Board) within ten (10) days after the end of the cure period.

9. Other Obligations.

9.1 Restrictive Covenants. In connection with Executive's employment with the Company, Executive will continue to receive access to Company confidential information and trade secrets and develop valuable goodwill with the Company's customers, partners and vendors. To protect the Company's legitimate business interests, Executive executed the Employee Confidentiality, Assignment and Nonsolicitation Agreement on March 5, 2019 (the "**Confidentiality Agreement**"). In connection with Executive's execution of this Amended and Restated Employment Agreement and in further consideration of Executive's employment with the Company, Executive agrees to execute a Non-Competition Agreement (the "Non-Competition Agreement") in a form acceptable to the Company, which Executive will do in or around September 2020. Executive herein acknowledges and agrees that (i) the Confidentiality Agreement shall continue in full force and effect in accordance with its terms, and (ii) Executive will abide by the terms of the Confidentiality Agreement and the Non-Competition Agreement at all times.

9.2 Third-Party Agreements and Information. Executive represents and warrants that Executive's employment by the Company does not conflict with any prior employment or consulting agreement or other agreement with any third party, and that Executive will perform Executive's duties to the Company without violating any such agreement. Executive represents and warrants that Executive will not use or disclose confidential information arising out of prior employment, consulting, or other third party relationships, in connection with Executive's employment by the Company, except as expressly authorized by that third party. During Executive's employment by the Company, Executive will use in the performance of Executive's duties only information which is generally known and used by persons with training and experience comparable to Executive's own, common knowledge in the industry, otherwise legally in the public domain, or obtained or developed by the Company or by Executive in the course of Executive's work for the Company.

10. Outside Activities During Employment.

10.1 Non-Company Business. Except with the prior written consent of the Board, Executive will not during the term of Executive's employment with the Company undertake or engage in any other employment, occupation or business enterprise, other than ones in which Executive is a passive investor. In any event, Executive may engage in civic and not-for-profit activities so long as such activities do not materially interfere with the performance of Executive's duties hereunder.

10.2 No Adverse Interests. Executive agrees not to acquire, assume or participate in, directly or indirectly, any position, investment or interest known to be adverse or antagonistic to the Company, its business or prospects, financial or otherwise.

11. General Provisions.

11.1 Notices. Any notices provided must be in writing and will be deemed effective upon the earlier of personal delivery (including personal delivery by fax) or the next day after sending by overnight carrier, to the Company at its primary office location and to Executive at the address as listed on the Company payroll.

11.2 Severability. Whenever possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be invalid, illegal or unenforceable in any respect under any applicable law or rule in any jurisdiction, such invalidity, illegality or unenforceability will not affect any other provision or any other jurisdiction, but this Agreement will be reformed, construed and enforced in such jurisdiction to the extent possible in keeping with the intent of the parties.

11.3 Waiver. Any waiver of any breach of any provisions of this Agreement must be in writing to be effective, and it shall not thereby be deemed to have waived any preceding or succeeding breach of the same or any other provision of this Agreement.

11.4 Complete Agreement. This Agreement, together with the Confidentiality Agreement, constitutes the entire agreement between Executive and the Company and is the complete, final, and exclusive embodiment of the Parties' agreement and supersedes all prior agreements between the parties concerning such subject matter, including the Prior Agreement. This Agreement is entered into without reliance on any promise or representation, written or oral, other than those expressly contained herein, and it supersedes any other such promises, warranties or representations. It is entered into without reliance on any promise or representation other than those expressly contained herein, and it cannot be modified or amended except in a writing signed by a duly authorized officer of the Company.

11.5 Counterparts. This Agreement may be executed in separate counterparts, any one of which need not contain signatures of more than one party, but all of which taken together will constitute one and the same Agreement.

11.6 Headings. The headings of the paragraphs hereof are inserted for convenience only and shall not be deemed to constitute a part hereof nor to affect the meaning thereof.

11.7 Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of and be enforceable by Executive and the Company, and their respective successors, assigns, heirs, executors and administrators, except that Executive may not assign any of his duties hereunder and he may not assign any of his rights hereunder without the written consent of the Company, which shall not be withheld unreasonably.

11.8 Tax Withholding and Indemnification. All payments and awards contemplated or made pursuant to this Agreement will be subject to withholdings of applicable taxes in compliance with all relevant laws and regulations of all appropriate government authorities. Executive acknowledges and agrees that the Company has neither made any assurances nor any guarantees concerning the tax treatment of any payments or awards contemplated by or made pursuant to this Agreement. Executive has had the opportunity to retain a tax and financial advisor and fully understands the tax and economic consequences of all payments and awards made pursuant to the Agreement.

11.9 Choice of Law. All questions concerning the construction, validity and interpretation of this Agreement will be governed by the laws of the Commonwealth of Massachusetts.

IN WITNESS WHEREOF, the Parties have executed this Agreement on the day and year first above written.

PRAXIS PRECISION MEDICINES, INC.

By: /s/ Marcio Souza
Name: Marcio Souza
Title: CEO

Date: 10/14/2020

Executive

/s/ Bernard Ravina
Name: Bernard Ravina

Date: 10/14/2020

PRAXIS PRECISION MEDICINES, INC.

AMENDED AND RESTATED EMPLOYMENT AGREEMENT
for Nicole Sweeny

This Amended and Restated Executive Employment Agreement (the "**Agreement**") is made between Praxis Precision Medicines, Inc. (the "**Company**") and Nicole Sweeny ("**Executive**") (collectively, the "**Parties**") and is effective as of the closing of the Company's first underwritten public offering of its equity securities pursuant to an effective registration statement under the Securities Act of 1933, as amended (the "**Effective Date**"). This Agreement supersedes in all respects all prior agreements between Executive and the Company regarding the subject matter herein, including without limitation, the Offer Letter between Executive and the Company dated July 3, 2020 (the "**Prior Agreement**").

WHEREAS, the Company desires Executive to continue to provide services to the Company, and wishes to provide Executive with certain compensation and benefits in return for such employment services; and

WHEREAS, Executive wishes to continue to be employed by the Company and to provide personal services to the Company in return for certain compensation and benefits;

NOW, THEREFORE, in consideration of the mutual promises and covenants contained herein and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties hereto agree as follows:

1. Employment by the Company.

1.1 Position and Duties. Executive shall continue to serve as the Company's Chief Commercial Officer (the "**Position**"). During the term of Executive's employment with the Company, Executive shall devote one hundred percent of Executive's business time on behalf of the Company and, on a full time basis, use Executive's skills and render services to the best of Executive's abilities on behalf of the Company, and shall comply fully with the policies and procedures of the Company. Executive shall report directly to the Company's **Chief Executive Officer (the "CEO")**. Executive shall perform those duties typically associated with the Position and such other duties consistent with the Position as may be assigned by the **CEO**, including but not limited to executive responsibility for business and executive leadership. Notwithstanding the foregoing, nothing herein shall preclude Executive from (i) serving, with the prior written consent of the **CEO**, as a member of the boards of directors or advisory boards of non-competitive businesses and charitable organizations, (ii) engaging in charitable activities and community affairs, and (iii) managing Executive's personal investments and affairs; *provided*, *however*, that the activities set out in clauses (i), (ii), and (iii) shall be limited by Executive so as not to materially interfere, individually or in the aggregate, with the performance of Executive's duties and responsibilities hereunder and shall not, in the judgment of the **CEO** pose a conflict of interest with Executive's duties to the Company or its affiliates.

1.2 Location of Work. Executive shall work in Cambridge, Massachusetts, USA. The Company reserves the right to reasonably require Executive to perform Executive's duties at places other than Executive's primary office location from time to time, and to require reasonable business travel.

1.3 Policies and Procedures. The employment relationship between the Parties shall be governed by the general employment policies and practices of the Company, except that when the terms of this Agreement differ from or are in conflict with the Company's general employment policies or practices, this Agreement shall control.

2. Compensation.

2.1 Salary. For services to be rendered hereunder, Executive shall receive an initial base salary at the rate of $360,000 per year, subject to standard payroll deductions and withholdings and payable in accordance with the Company's regular payroll schedule (the "**Base Salary**"). Executive's Base Salary will be reviewed annually by the Board or the Compensation Committee of the Board (the "**Compensation Committee**").

2.2 Annual Cash Bonus. Executive will be eligible for an annual cash bonus with a target amount of thirty-five percent (35%) of Executive's Base Salary (the "**Annual Bonus**"). Whether Executive receives an Annual Bonus for any given year, and the amount of any such Annual Bonus, will be determined by the Board or the Compensation Committee based upon the Company's and Executive's achievement of objectives and milestones to be determined by the Board or the Compensation Committee on an annual basis. Except as otherwise provided herein or in applicable incentive compensation plan that may be in effect from time to time, Executive will not be eligible for, and will not earn, any Annual Bonus if Executive is not employed by the Company on the payment date (regardless of the reason for the separation from employment).

2.3 Equity. The stock options and other stock-based awards held by Executive shall continue to be governed by the terms and conditions of the Company's applicable equity incentive plan(s) and the applicable award agreement(s) governing the terms of such stock options and other stock-based awards (collectively, the "**Equity Documents**"); *provided*, *however*, and notwithstanding anything to the contrary in the Equity Documents, Section 5.3(ii)(b) of this Agreement shall apply in the event of a termination of Executive's employment by the Company without Cause or by Executive for Good Reason, in either case within the Change of Control Period (as such terms are defined below).

3. Standard Company Benefits. Executive shall be entitled to participate in all employee benefit programs for which Executive is eligible under the terms and conditions of the benefit plans that may be in effect from time to time and provided by the Company to its employees. The Company reserves the right to cancel or change the benefit plans or programs it offers to its employees at any time.

4. Expenses. The Company will reimburse Executive for reasonable travel, entertainment or other expenses incurred by Executive in furtherance or in connection with the performance of Executive's duties hereunder, in accordance with the Company's expense reimbursement policy as in effect from time to time.

5. Termination of Employment; Severance.

5.1 At-Will Employment. Executive's employment relationship is at- will. Either Executive or the Company may terminate the employment relationship at any time, with or without cause subject to the terms of this Agreement.

5.2 Severance Pay and Benefits Upon a Termination Without Cause or Resignation for Good Reason Outside the Change of Control Period.

(i) The Company may terminate Executive's employment with the Company at any time without Cause. Executive may terminate Executive's employment with the Company at any time for any reason, including for Good Reason.

(ii) In the event that Executive's employment with the Company is terminated by the Company without Cause or by Executive for Good Reason, in either case outside of the Change of Control Period, then, provided that Executive remains in compliance with the terms of this Agreement, the Company shall provide Executive with the following severance benefits:

(a) The Company shall pay Executive, as severance, 9 months of Executive's Base Salary in effect as of the date of Executive's employment termination, subject to standard payroll deductions and withholdings (the "**Severance**"). Subject to Section 5.2(iii) below, the Severance will be paid in equal installments on the Company's regular payroll schedule over the 9 month period following Executive's termination of employment.

(b) Provided Executive timely elects continued coverage under COBRA, the Company shall pay the Company's portion of Executive's COBRA premiums, equal to the percentage of health premiums paid by the Company prior to Executive's termination, to continue Executive's coverage (including coverage for eligible dependents, if applicable) ("**COBRA Premiums**") through the period (the "**COBRA Premium Period**") starting on Executive's date of termination and ending on the earliest to occur of: (i) the 9 month anniversary of Executive's date of termination; (ii) the date Executive becomes eligible for group health insurance coverage through a new employer; or (iii) the date Executive ceases to be eligible for COBRA continuation coverage for any reason, including plan termination. In the event Executive becomes covered under another employer's group health plan or otherwise ceases to be eligible for COBRA during the COBRA Premium Period, Executive must immediately notify the Company of such event. Notwithstanding the foregoing, if the Company determines, in its sole discretion, that it cannot pay the COBRA Premiums without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company instead shall pay to Executive, on the first day of each calendar month, a fully taxable cash payment equal to the applicable COBRA premiums for that month (including premiums for Executive and Executive's eligible dependents who have elected and remain enrolled in such COBRA coverage), subject to applicable tax withholdings (such amount, the "**Special Cash Payment**"), for the remainder of the COBRA Premium Period. Executive may, but is not obligated to, use such Special Cash Payments toward the cost of COBRA premiums.

(iii) The amounts payable under this Section 5.2, to the extent taxable, shall be paid or commence to be paid within 60 days after the date of termination; *provided, however*, that if the 60-day period begins in one calendar year and ends in a second calendar year, such payments to the extent they qualify as "non-qualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "**Code**"), shall be paid or commence to be paid in the second calendar year by the last day of such 60-day period.

5.3 Severance Pay and Benefits Upon Termination Without Cause or Resignation for Good Reason Within the Change of Control Period.

(i) The provisions of this Section 5.3 shall apply in lieu of, and expressly supersede, the provisions of Section 5.2 regarding severance pay and benefits upon a termination of employment by the Company without Cause or by Executive for Good Reason if such termination of employment occurs on or within 12 months after the occurrence of the first event constituting a Change of Control (such period, the "**Change of Control Period**"). These provisions shall terminate and be of no further force or effect after the Change of Control Period

(ii) In the event that Executive's employment with the Company is terminated by the Company without Cause or by Executive for Good Reason, in either case during the Change of Control Period, then, provided Executive remains in compliance with the terms of this Agreement, the Company shall provide Executive with the following severance benefits:

(a) The Company shall pay Executive, as severance, a lump sum in cash in an amount equal to 1 times the sum of (A) Executive's then current Base Salary (or Executive's Base Salary in effect immediately prior to the Change of Control, if higher) plus (B) Executive's Annual Bonus for the then-current year (or Executive's Annual Bonus in effect immediately prior to the Change of Control, if higher) (the "**Change of Control Severance**").

(b) Notwithstanding anything to the contrary in any applicable option agreement or other stock-based award agreement, all time-based stock options and other stock-based awards subject to time-based vesting held by Executive (the "**Time-Based Equity Awards**") shall immediately accelerate and become fully exercisable or nonforfeitable as of the later of (i) the date of termination or (ii) the effective date of the Separation Agreement (as defined below) (the "**Accelerated Vesting Date**"); *provided* that any termination or forfeiture of the unvested portion of such Time-Based Equity Awards that would otherwise occur on the date of termination in the absence of this Agreement will be delayed until the effective date of the Separation Agreement and will only occur if the vesting pursuant to this subsection does not occur due to the absence of the Separation Agreement becoming fully effective within the time period set forth therein. Notwithstanding the foregoing, no additional vesting of the Time-Based Equity Awards shall occur during the period between Executive's date of termination and the Accelerated Vesting Date.

(c) Provided Executive timely elects continued coverage under COBRA, the Company shall pay the Company's portion of Executive's COBRA premiums, equal to the percentage of health premiums paid by the Company prior to Executive's termination, to continue Executive's coverage (including coverage for eligible dependents, if applicable) ("**COC COBRA Premiums**") through the period (the "**COC COBRA Premium Period**") starting on Executive's date of termination and ending on the earliest to occur of: (i) the 12 month anniversary of Executive's date of termination; (ii) the date Executive becomes eligible for group health insurance coverage through a new employer; or (iii) the date Executive ceases to be eligible for COBRA continuation coverage for any reason, including plan termination. In the event Executive becomes covered under another employer's group health plan or otherwise ceases to be eligible for COBRA during the COC COBRA Premium Period, Executive must immediately notify the Company of such event. Notwithstanding the foregoing, if the Company determines, in its sole discretion, that it cannot pay the COC COBRA Premiums without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health

Service Act), the Company instead shall pay to Executive, on the first day of each calendar month, a fully taxable cash payment equal to the applicable COBRA premiums for that month (including premiums for Executive and Executive's eligible dependents who have elected and remain enrolled in such COBRA coverage), subject to applicable tax withholdings (such amount, the "**COC Special Cash Payment**"), for the remainder of the COC COBRA Premium Period. Executive may, but is not obligated to, use such COC Special Cash Payments toward the cost of COBRA premiums.

(iii) The amounts payable under this Section 5.3, to the extent taxable, shall be paid or commence to be paid within 60 days after the date of termination; *provided*, *however*, that if the 60-day period begins in one calendar year and ends in a second calendar year, such payments to the extent they qualify as "non-qualified deferred compensation" within the meaning of Section 409A of the Code, shall be paid or commence to be paid in the second calendar year by the last day of such 60-day period.

(iv) Additional Limitation.

(a) Anything in this Agreement to the contrary notwithstanding, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 280G of the Code, and the applicable regulations thereunder (the "**Aggregate Payments**"), would be subject to the excise tax imposed by Section 4999 of the Code, then the Aggregate Payments shall be reduced (but not below zero) so that the sum of all of the Aggregate Payments shall be $1.00 less than the amount at which Executive becomes subject to the excise tax imposed by Section 4999 of the Code; *provided* that such reduction shall only occur if it would result in Executive receiving a higher After Tax Amount (as defined below) than Executive would receive if the Aggregate Payments were not subject to such reduction. In such event, the Aggregate Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Aggregate Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (1) cash payments not subject to Section 409A of the Code; (2) cash payments subject to Section 409A of the Code; (3) equity-based payments and acceleration; and (4) non-cash forms of benefits; *provided* that in the case of all the foregoing Aggregate Payments, all amounts or payments that are not subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c).

(b) For purposes of this Section 5.3(iv), the "**After Tax Amount**" means the amount of the Aggregate Payments less all federal, state, and local income, excise and employment taxes imposed on Executive as a result of Executive's receipt of the Aggregate Payments. For purposes of determining the After Tax Amount, Executive shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes.

(c) The determination as to whether a reduction in the Aggregate Payments shall be made pursuant to Section 5.3(iv)(a) shall be made by a nationally recognized accounting firm selected by the Company (the "**Accounting Firm**"), which shall provide detailed supporting calculations both to the Company and Executive within 15 business days of the date of termination, if applicable, or at such earlier time as is reasonably requested by the Company or Executive. Any determination by the Accounting Firm shall be binding upon the Company and Executive.

5.4 Termination for Cause; Resignation without Good Reason; Death or Disability.

(i) The Company may terminate Executive's employment with the Company at any time for Cause. Further, Executive may resign at any time for any reason other than Good Reason. Executive's employment with the Company may also be terminated due to Executive's death or Disability (as defined below).

(ii) If Executive resigns without Good Reason, or the Company terminates Executive's employment for Cause, or upon Executive's death or Disability, then (i) all payments of compensation by the Company to Executive hereunder will terminate immediately (except as to amounts already earned), and (ii) Executive will not be entitled to any severance benefits, including (without limitation) the Severance, COBRA Premiums, the Change of Control Severance or the COC COBRA Premiums.

6. Conditions to Receipt of Severance, COBRA Premiums, Special Cash Payments and Vesting Acceleration. The receipt of the payments and benefits described in Section 5.2 and Section 5.3 will be subject to subject to (i) Executive signing a separation agreement and release in a form and manner satisfactory to the Company, which shall include, without limitation, a general release of claims against the Company and all related persons and entities and, in the Company's sole discretion, a one-year post-employment noncompetition agreement (the "Separation Agreement") and (ii) the Separation Agreement becoming irrevocable, all within 60 days after the date of termination (or such shorter period as set forth in the Separation Agreement), which shall include a seven business day revocation period. No amounts will be paid or provided under Section 5.2 or Section 5.3 until the Separation Agreement becomes effective. Executive shall be deemed to have resigned from all officer and board member positions that the Executive holds with the Company or any of its respective subsidiaries and affiliates upon the termination of Executive's employment for any reason. Executive shall execute any documents in reasonable form as may be requested to confirm or effectuate any such resignations.

7. Section 409A.

7.1 Anything in this Agreement to the contrary notwithstanding, if at the time of Executive's separation from service within the meaning of Section 409A of the Code, the Company determines that Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that Executive becomes entitled to under this Agreement or otherwise on account of Executive's separation from service would be considered deferred compensation otherwise subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after Executive's separation from service, or (B) Executive's death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six- month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule.

7.2 All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year (except for any lifetime or other aggregate limitation applicable to medical expenses). Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

7.3 To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon Executive's termination of employment, then such payments or benefits shall be payable only upon Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

7.4 The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2). The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

7.5 The Company makes no representation or warranty and shall have no liability to Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

8. Definitions.

8.1 Cause. For purposes of this Agreement, "**Cause**" for termination will mean: (a) conviction of or please of guilty or *nolo contendere* to any felony or any crime involving dishonesty; (b) participation in any fraud against the Company; (c) material breach of any Company's policy or procedure after written notice from the Company and a reasonable period of not less than twenty-one (21) calendar days in which to cure such breach (if deemed curable); (d) persistent failure or refusal to perform Executive's job duties after written notice from the Company and a reasonable period of not less than twenty-one (21) calendar days in which to cure such performance issues (if deemed curable); (e) intentional damage to any property of the Company; (f) willful misconduct, or other violation of Company policy that causes harm; (g) breach of any written agreement by and between Executive and the Company; and (h) conduct by Executive which in the good faith and reasonable determination of the Company demonstrates gross unfitness to serve.

8.2 Change of Control. For purposes of this Agreement, "**Change of Control**" shall mean: a "Sale Event," as defined in the Company's 2020 Stock Option and Incentive Plan.

8.3 Disability. For purposes of this Agreement, "**Disability**" shall mean Executive's physical or mental condition that renders Executive unable to substantially perform for a period of ninety (90) aggregate days (regardless of whether or not continuous) during any three hundred sixty (360) day period, Executive's regular responsibilities hereunder, with or without a reasonable accommodation.

8.4 Good Reason. For purposes of this Agreement, "**Good Reason**" shall mean: (a) a material reduction in Executive's Base Salary (unless pursuant to a salary reduction applicable generally to the Company's similarly situated employees); or (b) the relocation of Executive's place of work for the Company that is more than 40 miles from Executive's primary place of work, unless mutually agreed upon. Notwithstanding the foregoing, no act or omission described in subclauses (a) or (b) above shall constitute "Good Reason" unless: (1) Executive first gives the Company written notice of such act or omission within forty-five (45) days of the later of the occurrence of such act or omission or Executive's first becoming aware thereof, (2) the Company fails to cure such act or omission within twenty-one (21) days after receiving such written notice from Executive, and (3) Executive resigns from employment (and all other positions, including as a member of the Board) within ten (10) days after the end of the cure period.

9. Other Obligations.

9.1 Restrictive Covenants. In connection with Executive's employment with the Company, Executive will continue to receive access to Company confidential information and trade secrets and develop valuable goodwill with the Company's customers, partners and vendors. To protect the Company's legitimate business interests, Executive executed the Employee Confidentiality, Assignment and Nonsolicitation Agreement on July 20, 2020 (the "**Confidentiality Agreement**"). In connection with Executive's execution of this Amended and Restated Employment Agreement and in further consideration of Executive's employment with the Company, Executive agrees to execute a Non- Competition Agreement (the "Non-Competition Agreement") in a form acceptable to the Company, which Executive will do in or around September 2020. Executive herein acknowledges and agrees that (i) the Confidentiality Agreement shall continue in full force and effect in accordance with its terms, and (ii) Executive will abide by the terms of the Confidentiality Agreement and the Non-Competition Agreement at all times.

9.2 Third-Party Agreements and Information. Executive represents and warrants that Executive's employment by the Company does not conflict with any prior employment or consulting agreement or other agreement with any third party, and that Executive will perform Executive's duties to the Company without violating any such agreement. Executive represents and warrants that Executive will not use or disclose confidential information arising out of prior employment, consulting, or other third party relationships, in connection with Executive's employment by the Company, except as expressly authorized by that third party. During Executive's employment by the Company, Executive will use in the performance of Executive's duties only information which is generally known and used by persons with training and experience comparable to Executive's own, common knowledge in the industry, otherwise legally in the public domain, or obtained or developed by the Company or by Executive in the course of Executive's work for the Company.

10. Outside Activities During Employment.

10.1 Non-Company Business. Except with the prior written consent of the Board, Executive will not during the term of Executive's employment with the Company undertake or engage in any other employment, occupation or business enterprise, other than ones in which Executive is a passive investor. In any event, Executive may engage in civic and not-for-profit activities so long as such activities do not materially interfere with the performance of Executive's duties hereunder.

10.2 No Adverse Interests. Executive agrees not to acquire, assume or participate in, directly or indirectly, any position, investment or interest known to be adverse or antagonistic to the Company, its business or prospects, financial or otherwise.

11. General Provisions.

11.1 Notices. Any notices provided must be in writing and will be deemed effective upon the earlier of personal delivery (including personal delivery by fax) or the next day after sending by overnight carrier, to the Company at its primary office location and to Executive at the address as listed on the Company payroll.

11.2 Severability. Whenever possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be invalid, illegal or unenforceable in any respect under any applicable law or rule in any jurisdiction, such invalidity, illegality or unenforceability will not affect any other provision or any other jurisdiction, but this Agreement will be reformed, construed and enforced in such jurisdiction to the extent possible in keeping with the intent of the parties.

11.3 Waiver. Any waiver of any breach of any provisions of this Agreement must be in writing to be effective, and it shall not thereby be deemed to have waived any preceding or succeeding breach of the same or any other provision of this Agreement.

11.4 Complete Agreement. This Agreement, together with the Confidentiality Agreement, constitutes the entire agreement between Executive and the Company and is the complete, final, and exclusive embodiment of the Parties' agreement and supersedes all prior agreements between the parties concerning such subject matter, including the Prior Agreement. This Agreement is entered into without reliance on any promise or representation, written or oral, other than those expressly contained herein, and it supersedes any other such promises, warranties or representations. It is entered into without reliance on any promise or representation other than those expressly contained herein, and it cannot be modified or amended except in a writing signed by a duly authorized officer of the Company.

11.5 Counterparts. This Agreement may be executed in separate counterparts, any one of which need not contain signatures of more than one party, but all of which taken together will constitute one and the same Agreement.

11.6 Headings. The headings of the paragraphs hereof are inserted for convenience only and shall not be deemed to constitute a part hereof nor to affect the meaning thereof.

11.7 Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of and be enforceable by Executive and the Company, and their respective successors, assigns, heirs, executors and administrators, except that Executive may not assign any of his duties hereunder and he may not assign any of his rights hereunder without the written consent of the Company, which shall not be withheld unreasonably.

11.8 Tax Withholding and Indemnification. All payments and awards contemplated or made pursuant to this Agreement will be subject to withholdings of applicable taxes in compliance with all relevant laws and regulations of all appropriate government authorities. Executive acknowledges and agrees that the Company has neither made any assurances nor any guarantees concerning the tax treatment of any payments or awards contemplated by or made pursuant to this Agreement. Executive has had the opportunity to retain a tax and financial advisor and fully understands the tax and economic consequences of all payments and awards made pursuant to the Agreement.

11.9 Choice of Law. All questions concerning the construction, validity and interpretation of this Agreement will be governed by the laws of the Commonwealth of Massachusetts.

IN WITNESS WHEREOF, the Parties have executed this Agreement on the day and year first above written.

PRAXIS PRECISION MEDICINES, INC.

By: /s/ Marcio Souza
Name: Marcio Souza
Title: CEO

Date: 10/14/2020

Executive

/s/ Nicole Sweeny
Name: Nicole Sweeny

Date: 10/14/2020

PRAXIS PRECISION MEDICINES, INC.

NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

The purpose of this Non-Employee Director Compensation Policy (the "Policy") of Praxis Precision Medicines, Inc. (the "Company") is to provide a total compensation package that enables the Company to attract and retain, on a long-term basis, high-caliber directors who are not employees or officers of the Company or its subsidiaries ("Outside Directors"). This Policy will become effective as of the effective time of the registration statement for the Company's initial public offering of equity securities (the "Effective Date"). In furtherance of the purpose stated above, all Outside Directors shall be paid compensation for services provided to the Company as set forth below:

Cash Retainers

Annual Retainer for Board Membership: $40,000 for general availability and participation in meetings and conference calls of our Board of Directors, to be paid quarterly in arrears, pro-rated based on the number of actual days served by the director during such calendar quarter. No additional compensation will be paid for attending individual meetings of the Board of Directors.

Additional Annual Retainer for Non-Executive Chair: $30,000

Additional Annual Retainers for Committee Membership:

Audit Committee Chair: $16,000

Audit Committee member: $8,000

Compensation Committee Chair: $12,000

Compensation Committee member: $6,000

Nominating and Corporate Governance Committee Chair: $8,000

Nominating and Corporate Governance Committee member: $4,000

Science and Technology Committee Chair: $8,000

Science and Technology Committee member: $4,000

Chair and committee member retainers are in addition to retainers for members of the Board of Directors. No additional compensation will be paid for attending individual committee meetings of the Board of Directors.

Equity Retainers

Initial Award: An initial, one-time stock option award (the "Initial Award") to purchase a number of shares equal to 0.1% of the total number of shares of the Company's common stock issued and outstanding on the date of grant will be granted to each new Outside Director upon his or her election to the Board of Directors, which shall vest in equal monthly installments over three years from the date of grant; provided, however, that all vesting shall cease if the director resigns from the Board of Directors or otherwise ceases to serve as a director of the Company. The Initial Award shall expire ten years from the date of grant, and shall have a per

share exercise price equal to the Fair Market Value (as defined in the Company's 2020 Stock Option and Incentive Plan) of the Company's common stock on the date of grant. This Initial Award applies only to Outside Directors who are first elected to the Board of Directors subsequent to the Effective Date.

Annual Award: On each date of each Annual Meeting of Stockholders of the Company following the Effective Date (the "Annual Meeting"), each continuing Outside Director, other than a director receiving an Initial Award, will receive an annual stock option award (the "Annual Award") to purchase a number of shares equal to 0.05% of the total number of shares of the Company's common stock issued and outstanding on the date of grant, which shall vest in twelve equal monthly installments from the date of grant; provided, however, that all vesting shall cease if the director resigns from the Board of Directors or otherwise ceases to serve as a director, unless the Board of Directors determines that the circumstances warrant continuation of vesting. Such Annual Award shall expire ten years from the date of grant, and shall have a per share exercise price equal to the Fair Market Value (as defined in the Company's 2020 Stock Option and Incentive Plan) of the Company's common stock on the date of grant.

Sale Event Acceleration: All outstanding Initial Awards and Annual Awards held by an Outside Director shall become fully vested and exercisable upon a Sale Event (as defined in the Company's 2020 Stock Option and Incentive Plan).

Expenses

The Company will reimburse all reasonable out-of-pocket expenses incurred by non-employee directors in attending meetings of the Board of Directors or any committee thereof.

Maximum Annual Compensation

The aggregate amount of compensation, including both equity compensation and cash compensation, paid by the Company to any Outside Director in a calendar year for services as an Outside Director shall not exceed $750,000; provided, however, that such amount shall be $1,000,000 for the calendar year in which the applicable Outside Director is initially elected or appointed to the Board of Directors and such amount shall be $1,500,000 for the non-executive Chair of the Board of Directors; (or such other limits as may be set forth in Section 3(b) of the Company's 2020 Stock Option and Incentive Plan or any similar provision of a successor plan). For this purpose, the "amount" of equity compensation paid in a calendar year shall be determined based on the grant date fair value thereof, as determined in accordance with FASB ASC Topic 718 or its successor provision, but excluding the impact of estimated forfeitures related to service-based vesting conditions. Notwithstanding the foregoing, the independent members of the Board may make exceptions to these limits in exceptional circumstances, provided that the Non-Employee Director receiving such additional compensation may not participate in the decision to award such compensation.

Adopted September 9, 2020, as amended January 5, 2022.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement and related prospectus (Form S-3 No. 333-260726) of Praxis Precision Medicines, Inc., and

(2) Registration Statement (Form S-8 Nos. 333-254410 and 333-249522) pertaining to the 2017 Stock Incentive Plan, the 2020 Stock Option and Incentive Plan, and 2020 Employee Stock Purchase Plan of Praxis Precision Medicines, Inc.;

of our reports dated February 28, 2022, with respect to the consolidated financial statements of Praxis Precision Medicines, Inc. and the effectiveness of internal control over financial reporting of Praxis Precision Medicines, Inc. included in this Annual Report (Form 10-K) of Praxis Precision Medicines, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 28, 2022

Exhibit 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

I, Marcio Souza, certify that:

1. I have reviewed this Annual Report on Form 10-K of Praxis Precision Medicines, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2022

By: /s/ MARCIO SOUZA

Marcio Souza
Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 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

I, Timothy Kelly, certify that:

1. I have reviewed this Annual Report on Form 10-K of Praxis Precision Medicines, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2022

By: /s/ TIMOTHY KELLY

Timothy Kelly
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Praxis Precision Medicines, Inc. (the "Company") for the fiscal year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of their knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 28, 2022 By: /s/ MARCIO SOUZA

Marcio Souza
Chief Executive Officer
(Principal Executive Officer)

Date: February 28, 2022 By: /s/ TIMOTHY KELLY

Timothy Kelly
Chief Financial Officer
(Principal Financial Officer)