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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2022

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 001-39062

FREQUENCY THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**47-2324450**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
75 Hayden Avenue, Suite 300 Lexington, MA	**02421**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code: (781) 315-4600

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

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

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

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

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

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

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

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

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

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

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

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

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

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. ☐

The aggregate market value of common stock held by non-affiliates of the registrant based on the closing price of the registrant's common stock as reported on the Nasdaq Global Select Market on June 30, 2022, was $46.8 million.

The number of shares of Registrant's Common Stock outstanding as of February 28, 2023 was 35,286,837.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the registrant's 2023 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

Auditor Firm ID: 49 Auditor Name: RSM US LLP Auditor Location: Boston, Massachusetts, USA

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, product candidates, clinical development plans and expectations, prospective products, product approvals, research and development costs, timing and likelihood of success, and plans and objectives of management for future operations and results, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important 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 the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this Annual Report are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of important factors that could cause actual results to differ materially from those in the forward-looking statements, including the risks, uncertainties and assumptions described under the sections in this Annual Report titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” These forward-looking statements are subject to numerous risks, including, without limitation, the following:

- the initiation, timing, progress and results of our preclinical and clinical trials and research and development of programs, including our planned Phase 1 study in our remyelination in multiple sclerosis program, and any other future clinical trials for any product candidates;
- our ability to continue to develop our progenitor cell activation, or PCA, approach and identify additional product candidates;
- our ability to successfully complete clinical trials of any product candidate and obtain regulatory approval for it;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization, marketing and manufacture of any product candidate, if approved;
- the pricing and reimbursement of any product candidate, if approved;
- the rate and degree of market acceptance and clinical utility of any products for which we receive regulatory approval;
- the implementation of our strategic plans for our business, product candidates, and technology, including our reduction in force and changes to senior management;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, PCA approach, and technology;
- estimates of our expenses, future revenues, capital requirements, and our need for additional financing;
- our ability to establish collaborations;
- the impact and any future impact of public health emergencies, such as COVID-19, on our ongoing and planned clinical trials, our research and development activities and our business and financial markets;
- our ability to protect our network from cybersecurity threats;
- our financial performance and the sufficiency of our financial resources; and
- developments relating to our competitors and our industry, including the impact of government regulation.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances, or otherwise.

You should read this Annual Report and the documents that we reference in this Annual Report completely and with the understanding that our actual future results may be materially different from what we expect. We qualify that all of our forward-looking statements by these cautionary statements.

RISK FACTORS SUMMARY

Our business is subject to numerous risks and uncertainties, including those described in Part I Item 1A. “Risk Factors” in this Annual Report on Form 10-K. You should carefully consider these risks and uncertainties when investing in our common stock. The principal risks and uncertainties affecting our business include the following:

- We are heavily dependent on the success of our remyelination in multiple sclerosis program, or MS Program, which is still under development. If our MS Program does not receive regulatory approval or is not successfully commercialized, our business will be materially adversely harmed;
- We utilize our PCA approach to develop product candidates that are designed to activate progenitor cells, which is a new approach to therapeutic intervention and, as a result, successful development, approval, and commercialization of any product candidates, including from our MS Program, is uncertain;
- Clinical trials are expensive, time consuming, and difficult to design and implement, and involve an uncertain outcome. The results of preclinical studies and early clinical trials are not always predictive of future results. Our FX-322 Phase 2b results (FX-322-208), for example, showed no statistically significant difference at day 90 between those administered FX-322 versus those receiving placebo in the proportion of individuals that demonstrated an improvement in speech perception. Any other product candidate that we advance into clinical trials may also not achieve favorable results in later clinical trials, if any, or receive marketing approval;
- We may be impacted by general economic, political, and geopolitical conditions such as recessions, interest rates, inflation rates, labor shortages, supply chain difficulties, fuel prices, sanctions, and acts of war or terrorism, including the recent hostilities between Russia and Ukraine. For example, the recent sanctions imposed by the United States on Russia may impede our ability to pay fees related to Russian patents making the future of such patents uncertain;
- The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our MS Program or any other product candidates, our business will be substantially harmed;
- We may not be successful in our efforts to identify additional product candidates. Due to our limited resources and access to capital, we must prioritize development of certain product candidates, the choice of which may prove to be wrong and adversely affect our business;
- We will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of our MS Program and additional product candidates;
- We face significant competition from biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively;
- If we are unable to establish sales and marketing capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing any product candidate we develop, if approved;
- Public health emergencies, including COVID-19, have caused and could continue to cause disruptions to our business, including our preclinical studies, clinical trials and operations and could adversely impact our financial condition and results of operations;
- We are currently subject to securities class action and other shareholder litigation and could be subject to similar or other litigation in the future; and
- Our organizational changes undertaken to better align our workforce with the needs of our business and focus more of our capital resources on our research and development programs may not achieve our intended outcome.

PART I

Item 1. Business.

Overview

We are pioneering a new category in regenerative medicine that aims to restore human function by developing therapeutics that activate a person's innate regenerative potential within the body through the activation of progenitor cells. Our lead preclinical program is designed to activate oligodendrocyte precursor cells with the goal of inducing remyelination and potential functional recovery for individuals living with multiple sclerosis, or MS.

Our proprietary approach, called progenitor cell activation, or PCA, uses small molecules to activate progenitor cells within the body to create functional tissue. These progenitor cells, which are similar to stem cells, already reside in the target tissues in the body and can develop and differentiate into specific cell types within an organ. We believe this approach provides us the opportunity to pursue multiple proposed indications and develop potential treatments for an array of degenerative diseases throughout the body.

Our first application of this technology was for the restoration of the cochlea, with a focus on treating a condition called sensorineural hearing loss, or SNHL, which is the most prevalent type of hearing loss. Our lead cochlear regeneration program, FX-322, was designed to treat the underlying cause of SNHL by regenerating cells in the inner ear required for hearing through the activation of progenitor cells already present in the cochlea. Since 2019, we ran five FX-322 clinical studies, all with the aim of understanding safety as well as severities and etiologies that FX-322 might treat and the appropriate dose regime. In several of these studies, we had observed that a single dose of FX-322 was associated with statistically significant improvements in hearing function as measured by improved speech perception in subjects with SNHL giving us confidence in the potential of FX-322 as a potential drug candidate for hearing loss.

In 2021 we commenced our sixth study, a Phase 2b clinical trial of FX-322 (FX-322-208), a randomized, placebo-controlled, multi-center study designed to evaluate the impact of a single administration of FX-322 on speech perception in 124 subjects, ultimately enrolling 142 subjects, with either noise-induced or sudden SNHL, the same hearing loss severities and etiologies as those subjects in which statistically significant improvements in speech perception were observed in prior FX-322 clinical trials. The study's primary endpoint was speech perception, a measure of sound clarity and understanding speech. In a Type-C meeting, the FDA agreed that speech perception is an acceptable primary efficacy endpoint. For the statistically powered study, we assumed 5% of placebo subjects would show an improvement. Therefore, our treatment effect was targeted to be 20% at day 90. Consequently, a sample size of 112 subjects at 80% power to detect this 20% difference at a significance level of 0.05 resulted in enrollment of 142 subjects to account for potential subject attrition.

In February 2023, we announced results of the Phase 2b clinical trial of FX-322 (FX-322-208) and that the study failed to achieve its primary efficacy endpoint of an improvement in speech perception. Data showed no statistically significant difference at day 90 between those administered FX-322 versus those receiving placebo in the proportion of individuals that demonstrated an improvement in speech perception. There were also no measurable improvements observed in any of the study's secondary endpoints. As a result of this outcome, we decided to discontinue the FX-322 development program.

Simultaneously, we were working on a second hearing program, called FX-345, which we believed might expand the opportunity to treat different types of SNHL as FX-345 was designed to achieve exposure at desired drug concentrations through a large portion of the cochlea. Cochlear pharmacokinetic measures and human modeling data in a preclinical setting showed that FX-345 achieved exposure at desired concentrations through a larger portion of the cochlea for longer time as compared to FX-322 and therefore we believe that greater coverage of the cochlea using FX-345 may extend the reach of our approach. The FX-345 program commenced dosing in a Phase 1b study completing an initial safety cohort. Given the outcome of the FX-322-208 study data and the similarities of the two candidates in design, intended mechanism of action and clinical design components, the decision was made to also cease development of FX-345 and our hearing program overall and to now focus our resources to advance the remyelination in MS program, or MS Program, into the clinic.

While exiting hearing was a difficult decision, we continue to strongly believe our PCA approach can impact a wide range of degenerative diseases. We are now working to rapidly advance discovery efforts using our PCA approach to potentially remyelinate neurons in individuals with MS. MS induces demyelination, stripping axons of the myelin sheaths that support neuronal signal conduction and axonal survival. We previously reported that we had identified a novel target relevant to myelination. Modulation of this target induces robust oligodendrocyte differentiation and expression of myelin proteins in vitro. We have identified multiple novel chemical entities that induce robust remyelination following demyelination in an adult in vivo animal model.

The MS Program is independent of the now discontinued hearing program, with a distinct molecular target, mechanism, progenitor cell population, and small molecule drug candidates. Further, a well-defined clinical path with objective biomarkers such as visual evoked potential (VEP) and magnetic resonance imaging (MRI) exist for studying the performance of remyelination therapies in MS patients. Our novel agents substantially outperform other clinically studied remyelination agents in head-to-head in vivo studies. We plan to begin our clinical program for remyelination in the first half of 2024. Refer to *Our multiple sclerosis (MS) program* below for detailed information on our internal program and ongoing sponsored research.

Concurrent with the release of the FX-322 Phase 2b clinical trial (FX-322-208) results in February 2023, the Company also announced it will immediately reduce headcount as part of an overall restructuring, downsizing personnel by approximately 55 percent. The Company believes that the restructuring will generate sufficient cost savings to extend its runway into 2025 and enable it to complete a first clinical trial of its MS Program in the second half of 2024.

Our team and history

Our company was founded in 2014 with the goal of creating medicines based on breakthrough research focused on activating the body's regenerative potential. In their groundbreaking research, Professors Robert S. Langer at the Massachusetts Institute of Technology and Jeffrey Karp at Harvard Medical School decoded the natural signals between cells that make the intestine one of the most regenerative organs in the body through the continuous activation of progenitor cells. Recognizing that similar progenitor cells were present but inactive in other organs, they discovered how to adapt these natural signals using small molecules to temporarily activate progenitor cells in other organs and create a localized healing response.

Our leadership team includes experienced biotech executives David L. Lucchino, our Chief Executive Officer and co-founder, Christopher R. Loose, our Chief Scientific Officer and co-founder, and Quentin McCubbin, our Chief Manufacturing Officer. As a result of our restructuring, Carl P. LeBel, Chief Development Officer, and Wendy S. Arnold, Chief People Officer, will be leaving the Company effective March 31, 2023 while Susan Stewart, Chief Regulatory Officer, will be leaving the Company effective April 30, 2023. We have also assembled a world-class team of leaders in regenerative biology, drug development, and drug delivery with a Remyelination Advisory Board comprised of leading experts from across the neurosciences. Our PCA Regenerative Medicine Advisory Board members are at the forefront of scientific discovery on the activation of progenitor cells and their potential application to therapeutic interventions in diseases of multiple tissues and organs.

Our strategy

We intend to create and commercialize therapeutics to potentially transform the lives of individuals by repairing or reversing damage done to cells, tissue, and organs. To do so, we are implementing the following strategies:

- ***Advance a remyelination therapy using our PCA approach.*** We believe our PCA approach has the potential to address a wide range of clinical applications. We will continue to invest in research and development to enhance our PCA approach with the goal of delivering new therapeutics in additional indications. We identified MS as a disease where PCA has the potential to produce a restorative effect by stimulation of oligodendrocyte precursor cells, or OPCs, to myelinate axons. We established an internal research program using PCA to induce remyelination as a potential therapy for MS and have generated several preclinical stage compounds that, based on *in vivo* models, have shown significantly greater remyelinating effect than published comparator approaches. Our efforts are focused on advancing these compounds in preclinical safety studies to enable a first human trial to begin in the first half of 2024.
- ***Continue to build strategic collaborative relationships***. Given the broad potential opportunity of our PCA approach, we believe entering into strategic research, development, and commercial collaborations in select therapeutic areas may provide an attractive avenue to facilitate the capital-efficient development of our PCA approach and product pipeline. We believe these strategic collaborations could potentially provide significant funding to advance our product candidates while allowing us to benefit from the development and therapeutic area expertise of our collaborators. We may collaborate with large pharmaceutical companies, biotechnology companies, and academic institutions to maximize the potential of our PCA approach to create new therapies for patients.

Our approach: Progenitor cell activation within the body

We are pioneering a new class of small molecule therapeutics designed to activate progenitor cells already present within the body to create healthy functional tissues and organs. We developed our PCA approach to identify small molecules that selectively activate progenitor cells to regenerate tissues. Our current therapeutic focus is remyelination in MS. We believe that our preclinical studies in MS have validated the potential of our PCA approach to provide a new methodology to regenerative medicine.

Relationship between stem cells and progenitor cells

All cells in the human body arise from a single unspecialized, or undifferentiated, cell type called a pluripotent stem cell. Two of the key characteristics of pluripotent stem cells are their ability to renew themselves through cell division and the ability to differentiate into any cell type. Progenitor cells have similar self-renewal properties as pluripotent stem cells. However, progenitor cells are programmed to develop and differentiate into specific cell types within an organ. The progenitor cells are programmed to create specific cell types and, in some cases, allow mature tissue and organs to repair and renew. However, researchers have discovered that many organs throughout the human body that do not spontaneously regenerate do contain inactive progenitor cells that, if stimulated, are potentially available to induce regeneration.

We believe that our PCA approach bypasses the challenges presented by stem cell therapies by utilizing small molecule therapeutics to temporarily reactivate progenitor cells that are already located at the tissue target site within the body and are pre-programmed to make specific cell types.

Key attributes of our PCA approach

Our discoveries in regenerative medicine allow us to activate the innate capabilities of progenitor cells. We believe our PCA approach represents a transformative step in the evolution of regenerative medicine by providing the following key advantages compared to other regenerative approaches:

- ***Harnesses innate biology***. We overcome the major challenge of delivering and integrating cells into the proper location within tissue. Our small molecule therapeutic candidates activate the body's own progenitor cells at the desired location in targeted tissues.
- ***Ease of manufacturing***. We eliminate the need to remove and grow live cells *ex vivo*, which can be costly and complex to manufacture and may pose potential safety risks. In contrast, our small molecule therapeutic candidates will be produced using standard pharmaceutical manufacturing methods.
- ***No change to genome***. Instead of altering genes, our small molecules are designed to temporarily activate the biochemical pathways that play a central role in the development of organs and tissues. This small molecule approach could create a disease-modifying or restorative effect without changing the body's genetic code. In addition, we believe we avoid the risk of acquiring immune reactivity to our therapeutics, which is commonly associated with genetically modifying cells.

Our therapeutic discovery process

We utilize a proprietary process to identify small molecule combinations for activating progenitor cells.

- ***Discovery in the right context***. Traditional drug screening uses immortalized cell lines that are convenient for use in a laboratory but may not reflect the complex biology of tissue-specific cell types in the body. One of our core capabilities is using primary progenitor cell assays that are designed to maintain these cells in their natural state in order to increase the likelihood of successful drug discovery and translation into an effective tissue-specific therapeutic.
- ***Decoding and controlling activation pathways for progenitor cells***. We use our accumulated insights into progenitor cell signaling and aging to identify biological pathways that may activate a specific progenitor cell. We then design and apply small molecules to modulate the chosen biological pathways and achieve PCA.

By assessing our small molecule combinations in a highly relevant context, we and our collaborators have applied this discovery process to identify compounds that activate progenitor cells in numerous tissues.

Our multiple sclerosis (MS) program

Overview of multiple sclerosis

The symptoms of MS include numbness or tingling, weakness, dizziness and vertigo, spasticity, vision problems, sexual problems, bladder or bowel problems, pain, cognitive changes, emotional changes, and depression. Initially, most individuals experience a relapsing-remitting experience course of disease, with periods of new or relapsing symptoms followed by recovery and periods of remission. Early in the disease course, the individuals are partially able to remyelinate the demyelinated nerves. As the disease progresses the ability of the body to remyelinate axons significantly decreases leading to progressive and irreversible neurological deficits. According to the National Multiple Sclerosis Society, nearly one million people in the United States are living with MS.

The FDA has approved a number of disease-modifying therapies for MS that reduce the immune system attack on myelin, which may reduce the number of relapses, delay progression of disability, and limit new disease activity. However, none of these products directly induce the remyelination of the nerve fibers. There are no FDA approved remyelinating therapies for MS and we believe this remains the largest unmet medical need in individuals with MS. Our program aims to induce OPCs to differentiate into oligodendrocytes and replace the myelin lost to multiple sclerosis.

Our novel compounds

We believe our PCA approach can impact a wide range of degenerative diseases, including MS. MS induces demyelination, stripping axons of the myelin sheaths that support nerve signal conduction and axonal survival. Our program focuses on inducing remyelination by activating oligodendrocyte progenitor cells, or OPCs, in the central nervous system to generate new oligodendrocytes and regenerate myelin, potentially repairing the damage caused by MS. Our efforts are focused on advancing proprietary Frequency compounds in preclinical safety studies to begin our clinical program in the first half of 2024.

The potential for pharmacologic therapy to induce remyelination in MS has been supported by multiple clinical trials. Clinical trials testing clemastine, histamine receptor 3 inverse agonists, anti-LINGO antibodies, and bexarotene have shown modest improvements in electrophysiological or MRI measures of MS.

However, to maximize the benefit to individuals with MS, we believe it is likely that significantly more effective remyelinating agents will be necessary. To create such a therapeutic, we established an independent internal research program to explore the biology underlying remyelination and develop novel chemical entities, or NCEs. We have identified and are pursuing a novel target that modulates oligodendrocyte differentiation and remyelination. Our internal discovery efforts have yielded a number of potential Novel Chemical Entities (NCEs) that have shown encouraging remyelination inducing activity in preclinical studies. We compared some of our internally discovered preclinical stage compounds to three known compounds, thyroid hormone, anti-LINGO antibody, and clemastine, in *in vivo* models. In these models, our internally discovered preclinical stage compounds induced significantly more oligodendrocyte differentiation (Exhibit 1) and remyelination (Exhibit 2) *in vivo* than the published comparator compounds. Our internally discovered preclinical stage compounds were shown to be effective even in aged animals and drove remyelination in both white and gray matter, which are critical in motor, sensory and cognitive aspects of MS.

Exhibit 1:

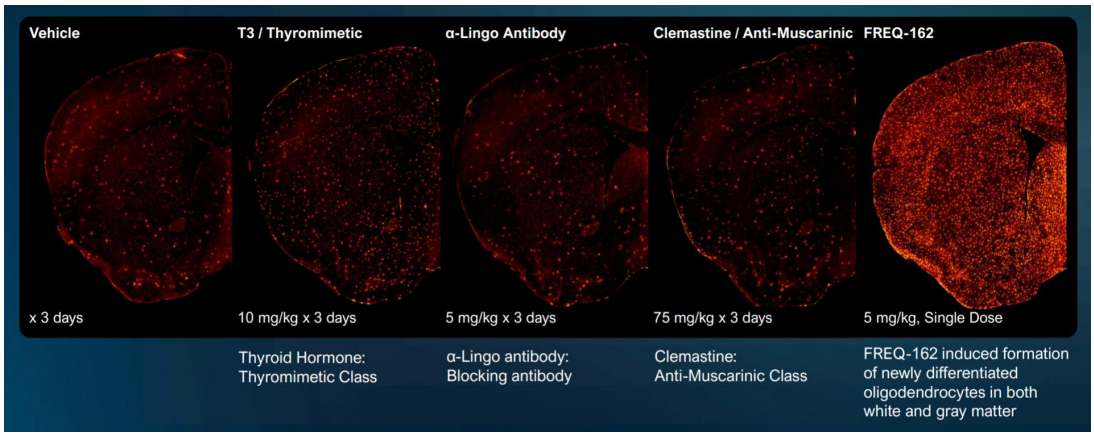
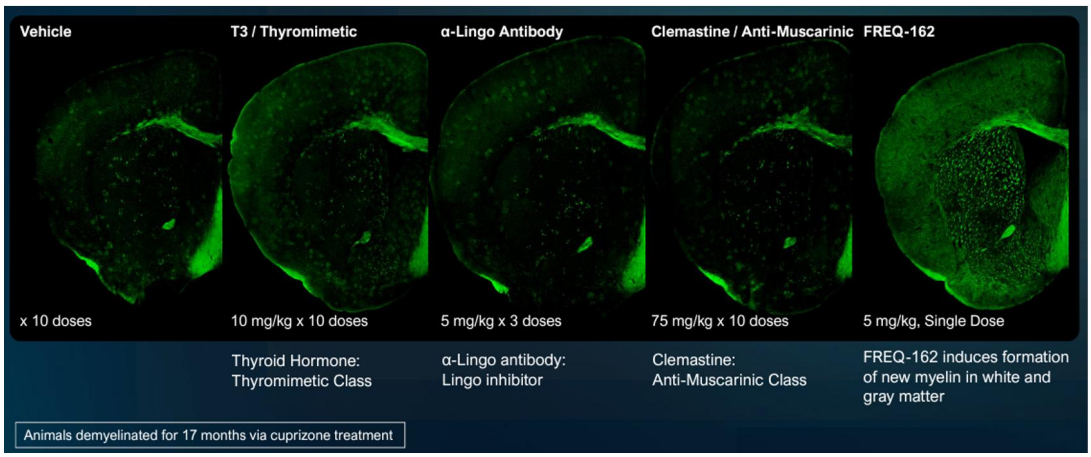


Exhibit 2:



Leveraging our PCA approach for future applications

In addition to our MS Program, we believe our PCA approach has the potential to address a wide range of clinical applications. In directing our internal research, research collaborations, and in-licensing efforts, we intend to target areas of high unmet medical need for which the underlying disease process involves loss or degeneration of key cells that could be reversed using PCA. We believe the PCA approach could further be applied to diseases of the muscle, gastrointestinal tract, skin, and bone. We intend to continue to identify areas with high unmet need where our PCA approach and novel approach to regenerative medicine could lead to potentially disease-modifying therapeutics that create healthy functional tissues and improve peoples' lives.

Manufacturing

Our product candidates consist of small chemical compounds to stimulate cell and tissue regeneration *in vivo*. As a result, we can rely on the well-established and available manufacturing and drug-delivery technologies developed over decades by the pharmaceutical industry. We source our active pharmaceutical ingredients from contract manufacturers with a track record of FDA-compliant GMP manufacturing. After rigorous internal and external quality control testing, we release these materials to additional contract manufacturers for formulation and packaging into final drug product for use in clinical testing. We expect to use a similar hybrid of internal and contract resources for commercialization of our products, at least until our operations reach a scale sufficient to justify investment in internal manufacturing capacity.

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 by seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets, confidential information and know-how, continuing technological innovation, and in-licensing opportunities to develop, strengthen, and maintain our proprietary position in our field.

Our future commercial success depends, in part, on our ability to: obtain and maintain patent and other proprietary protection for commercially important technology, inventions, and know-how related to our business; defend and enforce our intellectual property rights, in particular our patent rights; preserve the confidentiality of our trade secrets; and operate without infringing, misappropriating, or violating the valid and enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell, or importing products identical or similar to ours may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The patent positions of biotechnology and pharmaceutical companies like ours are generally uncertain and can involve complex legal, scientific, and factual issues. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. We also cannot ensure that patents will issue with respect to any patent applications that we or our licensors may file in the future, nor can we ensure that any of our owned or licensed patents or future patents will be commercially useful in protecting our product candidates and methods of manufacturing the same. In addition, the coverage claimed in a patent application may be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any of our products will be protected or remain protectable by enforceable patents. Moreover, any patents that we hold may be challenged, circumvented, or invalidated by third parties. See “Risk factors—Risks related to our intellectual property” for a more comprehensive description of risks related to our intellectual property.

In an effort to secure our intellectual property positions we generally file patent applications directed to our programs. As of February 1, 2023, we owned, licensed, or have an option to license 34 patent families. These patent families include 31 U.S. patents, 128 ex-U.S. patents, 23 pending U.S. utility patent applications, 110 pending ex-U.S. utility applications, and 1 PCT patent application.

The intellectual property portfolio as of February 1, 2023 is summarized below. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U.S. Patent and Trademark Office may be significantly narrowed before issuance, if issued at all. We expect this may be the case with respect to some of our pending patent applications referred to below.

Multiple sclerosis program

We own intellectual property directed to the treatment of MS and we advise on an exclusively in-licensed portfolio of intellectual property directed to the treatment of MS from The Scripps Research Institute. As of February 1, 2023, no development candidate has been designated, but the intellectual property portfolio for our MS research program currently includes 3 patent families including 4 U.S. patents, 15 ex-U.S. patents, 1 pending U.S. utility patent application, 10 ex-U.S. patent applications, and 1 PCT patent application. While we believe that the specific and generic claims, contained in our U.S. and ex-U.S. patents provide protection for the claimed pharmaceutical compositions and methods of use third parties may nevertheless challenge such claims. If any such claims are invalidated or rendered unenforceable for any reason, we will lose valuable intellectual property rights, and our ability to prevent others from competing with us would be impaired. Any U.S. or ex-U.S. patents that may issue from pending applications that we own or exclusively in-licensed, if any, for our MS program are projected to have a statutory expiration date between 2032 and 2042, excluding any additional term for patent term adjustments or patent term extensions. The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

Hearing loss

The patent portfolio for hearing loss is based upon our owned and in-licensed patent families that include patents and patent applications directed generally to compositions of matter, pharmaceutical compositions, and methods of using the same to treat hearing loss; and specifically directed to compositions of matter of FX-322, pharmaceutical compositions of FX-322 and methods of using the same to treat hearing loss. The in-licensed patents and patent applications are subject to license agreements with Massachusetts Institute of Technology and Massachusetts Eye and Ear described herein. As of February 1, 2023, we have rights to, through ownership and in-licensing, 30 patent families, including 27 U.S. patents, 112 ex-U.S. patents, 22 pending U.S. utility patent applications, and 93 pending ex-U.S. patent applications related to treating hearing loss, generally and a subset are related to FX-322. While we believe that the specific and generic claims contained in some of our issued U.S. patents provide protection for the composition of matter and the method of using FX-322 to treat hearing loss and/or diseases associated with the absence or lack of certain tissue cells, third parties may nevertheless challenge such claims in our patents. If any such claims are invalidated or rendered unenforceable for any reason, we will lose valuable intellectual property rights, and our ability to prevent others from competing with us would be impaired. Any U.S. or ex-U.S. patents that may issue from pending applications that we control, if any, for hearing loss are projected to have a statutory expiration date in between 2035 and 2040, excluding any additional term for patent term adjustments or patent term extensions, if applicable.

In the United States, the term of a patent covering an FDA-approved drug may, in certain cases, be eligible for a patent term extension under the Hatch-Waxman Act as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years, but the remaining term of a patent cannot be extended beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering the use of products from our intellectual property may be entitled to patent term extensions. If our use of drug candidates or the drug candidate itself receive FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved use or drug candidate. We also intend to seek patent term extensions in any jurisdictions where available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and, even if granted, the length of such extensions.

In addition to patent protection, we rely upon trade secrets, confidential information and know-how, and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and confidential information and know-how are difficult to protect. We seek to protect our proprietary information, in part, using confidentiality agreements with any collaborators, scientific advisors, employees, and consultants; and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected consultants, scientific advisors, and collaborators. These agreements may not provide meaningful protection. These agreements may also be breached, and we may not have an adequate remedy for any such breach. In addition, our trade secrets and/or confidential information and know-how may become known or be independently developed by a third party, or misused by any collaborator to whom we disclose such information. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to copy aspects of our products or obtain or use information that we regard as proprietary. Although we take steps to protect our proprietary information, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses, or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drugs may have an adverse impact on us. If third parties have prepared and filed patent applications prior to March 16, 2013, in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the United States Patent and Trademark Office, or USPTO, to determine priority of inventions. See “Risk factors—Risks related to our intellectual property” for a more comprehensive description of risks related to our intellectual property.

License and collaboration agreements

Astellas Pharma Inc.

In July 2019, we entered into the Astellas Agreement with Astellas, under which we granted Astellas an exclusive, royalty-bearing, sub-licensable, nontransferable license to certain patent rights to research, develop, manufacture, have manufactured, use, seek and secure regulatory approval for, commercialize, offer for sale, sell, have sold and import, and

otherwise exploit licensed products containing both a GSK-3 inhibitor and an HDAC inhibitor, or the Astellas licensed products, including our product candidate FX-322, outside of the United States. We also granted Astellas a right of first negotiation and a right of last refusal if we enter into any negotiation or agreement of any kind (other than an acquisition of all of our stock or assets) with any third party under which such third party would obtain the right to develop, manufacture, or commercialize Astellas licensed products in the United States.

We and Astellas have agreed to jointly develop the Astellas licensed products, including potentially carrying out joint studies. Each party has agreed to use commercially reasonable efforts to carry out development activities assigned to it under an agreed-upon development plan. Astellas has agreed to use commercially reasonable efforts to obtain regulatory approval for at least one Astellas licensed product in SNHL and in age-related hearing loss, in each case, in one major Asian country and one major European country. We have agreed to use commercially reasonable efforts to obtain regulatory approval for at least one Astellas licensed product in the United States. Astellas has the sole right to commercialize the Astellas licensed products outside of the United States, and we have the sole right to commercialize the Astellas licensed products in the United States. Astellas has agreed to use commercially reasonable efforts to commercialize Astellas licensed products in a major Asian country and a major European country following receipt of regulatory approval in such countries.

As consideration for the licensed rights under the Astellas agreement, Astellas paid us an upfront payment of $80.0 million in July 2019 and has agreed to pay potential development milestone payments up to $230.0 million. Specifically, we would receive development milestone payments of $65.0 million and $25.0 million upon the first dosing of a subject in a Phase 2b clinical trial for SNHL in Europe and Asia, respectively, and $100.0 million and $40.0 million upon the first dosing of a subject in a Phase 3 clinical trial for SNHL in Europe and Asia, respectively. If the Astellas licensed products are successfully commercialized, we would be eligible for up to $315.0 million in potential commercial milestone payments and also tiered royalties at rates ranging from low- to mid-teen percentages.

The Astellas Agreement remains in effect until the expiration of all royalty obligations. Royalties are paid on a licensed product-by-licensed product and country-by-country basis until the latest of (i) the expiration of the last valid claim in the licensed patent rights with respect to such Astellas licensed product in such country or (ii) a set number of years from the first commercial sale of such Astellas licensed product in such country. Astellas may terminate the Astellas Agreement at will upon 60 days' written notice. Each party has the right to terminate the Astellas Agreement due to the other party's material breach if such breach remains uncured for 90 days (or 45 days in the case of nonpayment) or if the other party becomes bankrupt.

Massachusetts Institute of Technology

In December 2016, we entered into an Exclusive Patent License Agreement, or the MIT License, with the Massachusetts Institute of Technology, or MIT, under which we received an exclusive, worldwide, royalty-bearing license to certain patent rights to develop, make, have made, use, sell, offer to sell, lease, and import products, or the MIT licensed products, and to develop and perform processes, or the MIT licensed processes, which incorporate the licensed technology for the treatment of disease, including, but not limited to, the prevention and remediation of hearing loss. We also have the right to grant sublicenses under the MIT License. MIT and Brigham and Women's Hospital retain the right on behalf of themselves and all other nonprofit research institutions to practice the licensed patent rights for nonclinical research, teaching, and educational purposes.

We are required to use diligent efforts to develop and commercialize the MIT licensed products or processes and to make such products or processes reasonably available to the public. We are also subject to certain development obligations with regards to a first MIT licensed product. We have satisfied certain obligations related to preclinical and clinical studies and the filing of an IND for a first MIT licensed product with our development activities related to FX-322. Our future development obligations are: (i) to commence a Phase 3 clinical trial for such Product within five years of the IND filing for such product, (ii) to file a New Drug Application or equivalent with the FDA or comparable European regulatory agency for such Product within nine years of the IND filing for such Product, and (iii) to make a first commercial sale of such Product within 11 years of the IND filing for such Product. We also have certain development obligations with regards to a second MIT licensed product. If we fail to meet our development obligations, other than those relating to a second MIT licensed product, MIT may terminate the MIT License. In the event that we have failed to fulfill our development timeline obligation with respect to a second MIT licensed product and fail to cure such breach within 90 days of written notice by MIT, MIT may restrict the licensed field to the prevention and remediation of hearing loss in humans and animals. We do not have the right to control prosecution of the in-licensed patent applications, and our rights to enforce the in-licensed patents are subject to certain limitations.

Upon entering the MIT License, we paid a $50 thousand license fee payment and issued to MIT shares of our common stock equal to 5% of our then-outstanding capital stock. We are required to pay certain annual license maintenance fees

ranging from $30 thousand to $0.1 million per year prior to first commercial sale of a MIT licensed product and an annual license maintenance fee of $0.2 million every year afterwards, which may be credited to running royalties during the same calendar year, if any. We are also required to make potential milestone payments in an aggregate amount of up to $2.9 million on each MIT licensed product or process. In addition, we agreed to pay a low single-digit royalty on the MIT licensed products and processes and a 20% royalty on sub-license revenues.

The MIT License will remain in effect until the expiration or abandonment of all licensed issued patents and filed patent applications, unless terminated earlier. We have the right to terminate for any reason upon three months' prior written notice. MIT has the right to terminate immediately if we cease to carry on any business related to the MIT License. MIT may also terminate the MIT License for our material breach if such breach remains uncured for 90 days (or 30 days in the case of nonpayment). MIT may also terminate the MIT License if we or our affiliates commence any action against MIT to declare or render any claim of the licensed patent rights invalid, unpatentable, unenforceable, or not infringed, or if our sub-licensee commences such actions and we do not terminate such sub-license within 30 days after MIT's demand. MIT has the right to increase all payments due by us, instead of terminating the MIT License in the case of a patent challenge.

In May 2019, we entered into an amendment with MIT, updating the diligence milestones for a second Licensed Product.

In March 2022, we entered into an amendment with MIT, removing a patent and certain patent applications from the MIT License Agreement which were unrelated to our hearing and MS programs and which we were not utilizing.

Massachusetts Eye and Ear (Formerly Massachusetts Eye and Ear Infirmary)

In February 2019, we entered into an Non-Exclusive Patent License Agreement, or the MEE License, with the Massachusetts Eye and Ear, or MEE, under which we received a non-exclusive, non-sub-licensable, worldwide, royalty-bearing license to certain patent rights to develop, make, have made, use, sell, offer to sell, lease and import products and to develop and perform processes that incorporate the licensed technology for the treatment or prevention of hearing loss, or the MEE licensed products. We are obligated to use diligent efforts to develop and commercialize the MEE licensed products. We met one of our milestone timeline obligations by dosing a first subject in a Phase 2 trial by December 31, 2020. We are still subject to a milestone timeline obligation to dose a first subject in a Phase 3 trial by December 31, 2024. We do not control the filing, prosecution, enforcement, and defense of any licensed patent rights.

Upon entering the MEE License, we made a $20 thousand license fee payment. We are obligated to pay certain annual license maintenance fees between $5 thousand and $7.5 thousand per each MEE patent family case number included in the licensed MEE patent rights prior to first commercial sale of an MEE licensed product. We are also obligated to pay a minimum annual royalty payment of $15 thousand per each MEE patent family case number included in the licensed MEE patent rights after first commercial sale of an MEE licensed product. We are also obligated to make milestone payments up to $350 thousand on each product or process that incorporates the licensed patent rights. In addition, we have agreed to pay a low single-digit royalty on products and processes that incorporate the licensed patent rights.

The MEE License remains in effect until all issued patents and filed patent applications within the licensed patent rights have expired or been abandoned, unless terminated earlier. We have the right to terminate the MEE License at will by 30 business days' advance written notice to MEE. MEE has the right to terminate the MEE License (i) if we fail to make any payment due within 30 business days after MEE notifies us of such failure, (ii) if we fail to maintain required insurance, (iii) upon 45 business days' written notice if we become insolvent, or (iv) for any other default by us that is not cured within 60 business days of receipt of written notice. MEE also has the right to terminate if we or our affiliates challenge the validity of the licensed patent rights.

The Scripps Research Institute (California Institute for Biomedical Research)

In September 2018, we entered into a license agreement, or the CALIBR License, with the California Institute for Biomedical Research, or CALIBR, a division of Scripps, under which we received an exclusive, worldwide, royalty-bearing license to certain patent rights to make, have made, use, sell, offer to sell, and import products, or the CALIBR licensed products, which incorporate licensed technology for the treatment of MS. We also have the right to grant sublicenses under the CALIBR License. CALIBR reserves the right to use for itself and the right to grant nonexclusive licenses to other nonprofit or academic institutions for any internal research and educational purposes.

We have agreed to use commercially reasonable efforts to develop, manufacture, and sell at least one CALIBR licensed product. We are also subject to certain milestone timeline obligations, which may be extended in certain circumstances as set

forth in the CALIBR License. In October 2021, we entered into an amendment with CALIBR which updated the milestone obligations to: (i) initiate a Phase 2 clinical trial (or equivalent) for a CALIBR licensed product by December 31, 2023 and (ii) initiate a Phase 3 clinical trial (or equivalent) for a CALIBR licensed product by December 31, 2025. We do not have the right to control prosecution of the in-licensed patent applications, and our rights to enforce the in-licensed patents are subject to certain limitations.

Upon entering the CALIBR license, we made a $1.0 million license fee payment, and are required to make milestone payments in an aggregate amount of up to $26.0 million for each category of CALIBR licensed products. Category 1 is any CALIBR licensed products containing a compound that modulates any muscarinic receptor, and Category 2 is any CALIBR licensed products not included in Category 1 that could differentiate oligodendrocyte precursor cells from *in vitro* studies and/or are active in animal models relevant to MS. We are also required to pay a mid-single-digit royalty on CALIBR licensed products and a royalty on sub-license revenues ranging from a low-teen percentage to 50%.

The CALIBR License continues in effect until expiration of all our obligations to pay royalties. Royalties are payable by us on a country-by-country and licensed-product-by-licensed product basis upon the later of (i) the expiration or abandonment of all valid claims of the licensed patent rights in such country and (ii) 10 years from the first commercial sale of each CALIBR licensed product in such country. We may terminate the CALIBR License at will upon 30 days' prior written notice. We may also elect to terminate our license to one or more licensed patents in any or all jurisdictions by giving 90 days' prior written notice to CALIBR. CALIBR may terminate the CALIBR License for our material breach if such breach remains uncured for 30 days. CALIBR has the right to terminate or reduce the license to a non-exclusive license if we fail to use diligent efforts to develop and commercially exploit CALIBR licensed products.

Cambridge Enterprise Limited

In December 2019, we entered into an Exclusive Patent License Agreement, or the Cambridge License, with Cambridge Enterprise, under which we received an exclusive, worldwide, royalty-bearing license to certain patent rights to make, have made, use, sell, offer to sell, and import products, or the Cambridge licensed products, which incorporate licensed technology for the treatment of demyelinating diseases. Under the Cambridge License, we also had the right to grant sublicenses. Upon entering into the Cambridge License, we made a $50 thousand license fee payment and were obligated to pay an annual license fee of $50 thousand. One June 28, 2022, we sent Cambridge Enterprise a notice stating that we would be terminating the Cambridge License in 90 days' time, and on September 26, 2022 this termination became effective. We are not subject to any payments or costs as a result of this termination.

Competition

As a clinical-stage biotechnology company, we face competition from a wide array of companies in the pharmaceutical and biotechnology industries. These include both small companies and large companies with much greater financial and technical resources and far longer operating histories than our own. We also compete with the intellectual property, technology, and product development efforts of academic, governmental, and private research institutions.

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

The key competitive factors affecting the success of any product candidates that we develop, if approved, are likely to be their efficacy, safety, convenience, price, and the availability of reimbursement from government and other third-party payors. Our commercial opportunity for any of our product candidates could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours and may commercialize products more quickly than we are able to.

There are multiple therapeutic options for treating the symptoms of MS, as well as the underlying disease. However, all approved therapies are directed at blocking demyelination, and, to our knowledge, there are no approved therapies that are designed to promote remyelination. We are aware of numerous efforts to identify drugs or biologics that can stimulate

oligodendrocyte regeneration and myelin repair in the central nervous system. These include companies such as Clene Inc., which has an ongoing Phase 2 trial of CNM-Au8, a gold nanocrystal suspension, and Pipeline Therapeutics, which completed a Phase 1 trial for PIPE-307, a selective M1 receptor antagonist to treat multiple sclerosis and other demyelinating disorders. In March 2022, Pipeline received IND clearance to initiate a Phase 1b/2a study of PIPE-307. Idorsia Pharma completed two Phase 1 studies in 2019 and 2020 for ACT-1004-1239, a small molecule CXCR7 inhibitor involved in OPC differentiation. NervGen Pharma is developing NVG-291, a therapeutic peptide which is a mimetic of the intracellular domain of protein tyrosine phosphatase (PTPσ). In October 2022, NervGen Pharma announced plans to initiate a Phase 2 trial of NVG-291 in 2023 in patients with RRMS. This is an active research area with a number of entities researching compounds, antibodies, and proteins which may enhance remyelination.

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 drugs, such as those we are developing. These agencies and other federal, state, and local entities 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 our product candidates.

U.S. drug development process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process, or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending new drug applications, NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties.

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 and formulation studies, as well as animal safety studies, in compliance with the FDA's good laboratory practice, or GLP, regulations, as appropriate;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, 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 indication;
- submission to the FDA of an NDA;
- endorsement by an FDA advisory committee, if applicable;
- satisfactory completion of an FDA inspection of the clinical site(s), and related services involved in the conduct of the clinical studies to assess compliance with good clinical practices, or GCP;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice, or cGMP, requirements, and to assure that the facilities, methods, and controls are adequate to preserve the drug's identity, strength, quality, and purity;
- FDA review and approval of the NDA prior to commercial marketing or sale of the drug in the United States; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, or to conduct a post-approval study or studies.

Preclinical studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity, and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with

manufacturing information, analytical data, and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the submission including to one or more proposed clinical trials and places the clinical trial on a partial or full clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about on-going or proposed clinical trials or noncompliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators 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. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific time frames to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website.

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

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion, and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases, and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unreasonable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution 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. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

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

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA, and more frequently if serious adverse events occur. Phase 1, Phase 2, and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. There are also requirements governing the registration of, reporting of ongoing clinical trials and completed trial results to public registries.

Marketing approval

Assuming successful completion of the required clinical testing, the results of the 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. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes 12 months from the date the NDA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision. Specifically, 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 resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the submitted information supports that the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged, or held meets standards designed to assure the product's continued safety, quality, and purity.

The FDA also may require submission of a REMS plan to ensure that for certain medications with serious safety concerns the benefits of the drug outweigh its risks. The REMS plan 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 may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or 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 to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a Complete Response Letter, or CRL. A CRL generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for the FDA to reconsider the application for approval. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

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 a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing 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.

The Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver, or the indication sought is for an orphan condition. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or the FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a noncompliance 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. In some situations, the requirement for studies in pediatric populations can be waived if there is no relevant use.

FDA-expedited development and review programs

The FDA has various programs, including orphan drug designation, rare pediatric disease designation, fast track designation, accelerated approval priority review, and breakthrough therapy designation, which are intended to expedite or simplify the process for the development and the FDA review of drugs that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition, demonstrates the potential to address an unmet medical need, and is actively developing the drug for the disease. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The FDA may review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

The FDA may give a priority review designation to drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of 10 months under current PDUFA guidelines. Under the new PDUFA agreement, these six- and 10-month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review, and, if relevant, accelerated approval.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act, or FDASIA, passed in July 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for priority review and accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. The designation includes all the benefits of a fast track designation. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met.

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 decide that the time period for FDA review or approval will not be shortened. Furthermore, fast track designation, priority review, and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process. We may explore some of these opportunities for our product candidates as appropriate.

Post-approval requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion, and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and

approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

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 and local agencies and are subject to periodic unannounced inspections by government agencies for compliance with cGMP and other 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. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warning or other safety information about the product;
- fines, warning letters, or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

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

Marketing exclusivity

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

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

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

Other healthcare laws and compliance requirements

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the state, local, and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, U.S. federal and state anti-kickback, fraud and abuse, false claims, consumer fraud, pricing reporting, and transparency laws and regulations, as well as similar foreign laws in the jurisdictions outside the U.S. State laws may require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, as well as require the registration of pharmaceutical sales representatives and the reporting of pricing information and marketing expenditures. Violations of such laws, or any other governmental regulations that apply, may result in penalties, including, without limitation, civil and criminal penalties, damages, fines, additional reporting and oversight obligations, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs, and individual imprisonment.

Foreign regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials in those countries, if relevant, and market application approval by foreign countries or economic areas, such as the European Union, or EU, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Non-clinical Studies and Clinical Trials

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

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization, or ICH, guidelines on Good Clinical Practices, or GCP, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU countries, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member

states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

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

Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice, or GMP. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorization

In order to market our product candidates in the EU and many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization, or MA. To obtain regulatory approval of a product candidate under EU regulatory systems, we must submit a MA application, or MAA. The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs:

- "Centralized MAs" are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and are valid throughout the EU. The centralized procedure is mandatory for certain types of products, such as (i) medicinal products derived from biotechnology processes, (ii) designated orphan medicinal products, (iii) advanced therapy medicinal products, or ATMPs (such as gene therapy, somatic cell therapy and tissue engineered products) and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune, and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU; for products that constitute a significant therapeutic, scientific or technical innovation; or for products that are in the interest of public health in the EU. National MAs" are issued by the competent authorities of the EU member states and only cover their respective territory, and are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure, an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.
- Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops.

Under the above described procedures, in order to grant the MA, the EMA or the competent authorities of the EU member states make an assessment of the risk benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. MAs have an initial duration of five years. After these five years, the authorization may be renewed on the basis of a reevaluation of the risk-benefit balance.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EU assess the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety, and efficacy.

Data and Marketing Exclusivity

As in the United States, it may be possible in foreign countries to obtain a period of market and/or data exclusivity that would have the effect of postponing the entry into the marketplace of a competitor's generic product. For example, in the EU new products authorized for marketing (*i.e.*, reference products) generally receive eight years of data exclusivity and an additional two years of marketing exclusivity upon MA. If granted, the data exclusivity period prevents generic and biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial MA of the reference product in the EU. The overall ten-year market exclusivity period can be extended to a maximum of eleven years, if during the data exclusivity period (the first eight years of the ten year marketing exclusivity period) the MA holder obtains an authorization for one or more new therapeutic indications that are deemed to bring a significant clinical benefit compared to existing therapies. In Japan, our products may be eligible for eight years of data exclusivity. There can be no assurance that a product candidate will qualify for such regulatory exclusivity, or that such exclusivity will prevent competitors from seeking approval solely on the basis of their own studies.

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

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Brexit and the Regulatory Framework in the United Kingdom

Since the end of the Brexit transition period on January 1,2021, Great Britain (England, Scotland and Wales) has not been subject to EU laws. However under the terms of the Ireland/Northern Ireland Protocol, Northern Ireland continues to follow EU law. The EU laws that have been transposed into United Kingdom, or UK, law through secondary legislation remain applicable in Great Britain. However, under the Retained EU Law (Revocation and Reform) Bill 2022, which is currently before the UK parliament, any retained EU law not expressly preserved and "assimilated" into domestic law or extended by ministerial regulations (to no later than 23 June 2026) will automatically expire and be revoked by December 31, 2023. In addition, new legislation such as the EU CTR is not applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an 'appropriate authority' to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, is the UK's standalone medicines and medical devices regulator. The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in Great Britain (only), free of charge on January 1, 2021, unless the MA holder chose to opt-out. After Brexit, companies established in the UK cannot use the centralized procedure and instead must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the UK. For a period of three years from 1 January 2021, the MHRA may rely on a decision taken by the EU Commission on the approval of a new (centralized procedure) MA when determining an application for a Great Britain authorization; or use the MHRA's decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in Great Britain.

Coverage and reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufactures to provide scientific and clinical support for the use of a product to each payor separately, and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. 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. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, third-party payors are increasingly reducing reimbursements for pharmaceutical products and services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement, and requirements for substitution of generic products. Third-party payors are more and more challenging the prices charged, examining the medical necessity, and reviewing the cost effectiveness of pharmaceutical products, in addition to questioning their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. 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. 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. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products and may also compete with imported foreign products. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available, or that the third-party payors' reimbursement policies will not adversely affect the ability of manufacturers to sell products profitably.

Healthcare reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect the pharmaceutical industry. In March 2010, the Affordable Care Act (ACA) was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States. The ACA contained a number of provisions of particular import to the pharmaceutical industry, including those governing enrollment in federal healthcare programs, reimbursement adjustments, and fraud and abuse changes. Additionally, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; required the collection of rebates for drugs paid by Medicaid managed care organizations; imposed a nondeductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs; implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded the eligibility criteria for Medicaid programs; created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conducts comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, executive and Congressional 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. Prior to the Supreme Court's decision, President Biden issued an executive order initiating 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.

Legislative changes have been proposed and adopted since the ACA was enacted. On March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, or AMP, beginning January 1, 2024. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries, and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated.

Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference-pricing systems and publication of discounts and list prices.

Data privacy and security laws

Numerous state, federal and foreign laws, including consumer protection laws and regulations, 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, and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Cybersecurity

In the normal course of business, we may collect and store personal information and other sensitive information, including proprietary and confidential business information, trade secrets, intellectual property, information regarding trial participants in connection with clinical trials, sensitive third-party information and employee information. To protect this information, our existing cybersecurity policies require monitoring and detection programs, network security precautions, encryption of critical data, and security assessment of vendors. We maintain various protections designed to safeguard against cyberattacks. We have established and test our disaster recovery plan and we protect against business interruption by backing up our major systems. In addition, we scan our environment for any vulnerabilities, perform penetration testing and engage third parties to assess effectiveness of our data security practices. A third party security consultant conducts regular network security reviews, scans and audits.

Our cybersecurity program is comprised of Company employees and a third-party cybersecurity vendor, all of whom are highly skilled cybersecurity professionals. Our program incorporates industry-standard frameworks, policies and practices designed to protect the privacy and security of our sensitive information.

Despite the implementation of our cybersecurity program, our security measures cannot guarantee that a significant cyberattack will not occur. A successful attack on our information technology systems could have significant consequences to the business. While we devote resources to our security measures to protect our systems and information, these measures cannot provide absolute security. See "Risk Factors – risks related to our employees, managing our growth and our operations" for additional information about the risks to our business associated with a breach or compromise to our information technology systems.

Environmental, Social, and Governance Initiatives

Corporate sustainability and environmental responsibility

We understand the importance of reducing our environmental impact. We are proud to be headquartered in a LEED certified building, a globally recognized symbol of sustainability achievement and leadership. We continue to promote sustainability within our office by limiting single-use plastic and implementing compost and recycling programs. Our current hybrid work model allows employees to work remotely for a portion of the week, decreasing the emissions associated with employees commuting to the office.

Diversity & Inclusion

We are committed to creating and maintaining a workplace free from discrimination or harassment on the basis of color, race, sex, national origin, ethnicity, religion, age, disability, sexual orientation, gender identification or expression, or any other status protected by applicable law. Our management team and employees are expected to exhibit and promote honest, ethical and respectful conduct in the workplace. All of our employees must adhere to a code of conduct that sets standards for appropriate behavior and are required to attend training upon hire and at our request to help prevent, identify, report and stop any type of discrimination and harassment. Ongoing acknowledgment of our anti-harassment policy is required on an annual basis. Our recruitment, hiring, development, training, compensation and advancement at our company is based on qualifications, performance, skills and experience without regard to gender, race and ethnicity. Our Diversity, Equity & Inclusion (DEI) Committee is an employee-led group that works to raise awareness for DEI initiatives and identify ways we can continue to promote inclusion within our corporate culture. Although we are a smaller reporting company, our Board of Directors meets the requirements under NASDAQ's Board Diversity Rule for accelerated and large-accelerated filers with two diverse directors.

Employees and Human Capital Resources

As of February 1, 2023, we had 48 employees, including 46 full-time employees. Women represent approximately 46% of our employees and 29% of our senior management level/leadership roles. Thirty-eight percent of our employees have a Ph.D. or doctorate. From time to time, we also retain independent contractors to support our organization. None of our employees are represented by a labor union or covered by collective bargaining agreements, and we believe our relationship with our employees is good.

We strive to provide pay, comprehensive benefits and services that help meet the varying needs of our employees. Our total rewards package includes competitive pay; comprehensive healthcare benefits package for employees, with family member healthcare benefits covered at 90%; a health savings account with company contribution; unlimited paid time off and paid holidays; family medical leave; and flexible work schedules. In addition, we offer every full-time employee, both exempt and non-exempt, the benefit of equity ownership in the company through stock option grants, restricted stock units, and our employee stock purchase plan. We also sponsor a 401(k) plan with a 5% match.

We focus on attracting, retaining, and cultivating talented individuals. We emphasize employee development and training by providing access to a wide range of online and instructor led development and continual learning programs. Employees are encouraged to attend scientific, clinical and technological meetings and conferences and have access to broad resources they need to be successful.

On February 13, 2023, we announced a reduction in force of approximately 55% of our workforce, which will take place in phases and is expected to be completed by April 30, 2023.

Safety

The safety, health and wellness of our employees is a top priority. In response to public health emergencies, including COVID-19, we have implemented safety protocols including a flexible hybrid work schedule for non-lab based employees, optional wearing of masks, regular cleaning procedures and readily available hand sanitizer. These protocols are designed to comply with health and safety standards as required by federal, state and local government agencies, taking into consideration guidelines of the Centers for Disease Control and Prevention and other public health authorities.

Our Corporate Information

We were incorporated under the laws of the state of Delaware in November 2014. Our principal executive offices are located at 75 Hayden Avenue, Suite 300, Lexington, Massachusetts 02421 and our telephone number is (781) 315-4600. Our corporate website address is *www.frequencytx.com*. The information contained in, or accessible through, our website is not incorporated by reference into this Annual Report and you should not consider information on our website to be a part of this Annual Report. We have included our website address in this Annual Report solely as an inactive textual reference.

Where you can find more information

We are subject to the information requirements of the Securities Exchange Act of 1934, as amended. The SEC maintains an internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically, such as ourselves, with the SEC at http://www.sec.gov.

Item 1A. Risk Factors.

Our future operating results could differ materially from the results described in this Annual Report on Form 10-K due to the risks and uncertainties described below. You should consider carefully the following information about risks below in evaluating our business. If any of the following risks actually occur, our business, financial conditions, results of operations and future growth prospects would likely be materially and adversely affected. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. In these circumstances, the market price of our common stock would likely decline. In addition, we cannot assure investors that our assumptions and expectations will prove to be correct. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements. See "Forward Looking Statements" for a discussion of some of the forward-looking statements that are qualified by these risk factors. Factors that could cause or contribute to such differences include those factors discussed below.

Risks related to our financial position and need for additional capital

We have incurred significant losses since inception and anticipate that we will continue to incur losses for the foreseeable future. We are not currently profitable, and we may never achieve or sustain profitability. If we are unable to achieve or sustain profitability, the market value of our common stock will likely decline.

We are a clinical-stage biotechnology company with a limited operating history. As a result, we are not profitable and have incurred significant losses since our formation. We had net losses of $81.6 million and $84.7 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $261.7 million. 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 gain regulatory approval and become commercially viable. We have not commercialized any products and have never generated revenue from the commercialization of any product. To date, we have devoted most of our financial resources to licensing technologies and research and development, including our preclinical platform development activities and clinical trials.

We expect to incur significant additional operating losses for the next several years, at least, as we advance a potential therapeutic candidate for multiple sclerosis, or MS, and any other product candidate through clinical development, complete clinical trials, seek regulatory approval and commercialize an MS therapeutic or any other product candidate, if approved. The costs of advancing product candidates into each clinical phase tend to increase substantially over the duration of the clinical development process. Therefore, the total costs to advance any product candidate to marketing approval in even a single jurisdiction are substantial. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of any product candidates or achieve or maintain profitability. Our expenses will also increase substantially if and as we:

- continue to develop and commence clinical trials of our remyelination program in MS;
- expand our development programs based on our progenitor cell activation, or PCA, approach;
- continue to develop our PCA approach;
- seek regulatory approvals for an MS therapeutic and any other product candidates;
- secure a commercial manufacturing source and supply chain capacity sufficient to produce commercial quantities of any product candidate for which we obtain regulatory approval;
- establish a sales, marketing and distribution infrastructure to commercialize an MS therapeutic, if approved, and for any other product candidates for which we may obtain marketing approval;
- maintain, expand, and protect our intellectual property portfolio; and
- acquire or in-license other product candidates or technologies.

Furthermore, our ability to successfully develop, commercialize and license any product candidates and generate product revenue is subject to substantial additional risks and uncertainties, as described under "—Risks related to development, clinical testing, manufacturing, and regulatory approval" and "—Risks related to commercialization." As a result, we expect to continue to incur net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. The amount of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. If we are unable to develop and commercialize one or more product candidates, either alone or through collaborations, or if revenues from any product that receives marketing approval are insufficient, we will not achieve

profitability. Even if we successfully commercialize an MS therapeutic or any other product candidates, we may continue to incur substantial research and development and other expenses to identify and develop other product candidates. Even if we do achieve profitability, we may not be able to sustain profitability or meet outside expectations for our profitability. If we are unable to achieve or sustain profitability or to meet outside expectations for our profitability, the value of our common stock will be materially adversely affected.

We will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of an MS therapeutic or explore additional product candidates.

We expect to spend substantial amounts to complete the development of, seek regulatory approvals for and, if approved, commercialize an MS therapeutic and any other product candidates. These expenditures include and will include, as the case may be, preclinical development costs and costs related to trials we conduct to support the development of an MS therapeutic and any other product candidates.

We will require additional capital to enable us to develop an MS therapeutic, which we may acquire through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our development efforts.

Based upon our current operating plan, and as a result of the realignment of the Company to focus on the MS program, including cost saving measures such as our reduction in force during the first half of 2023, we believe that our existing cash, cash equivalents, and marketable securities of $83.1 million will enable us to fund our operating expenses and capital expenditure requirements into 2025. This estimate and our expectation regarding the sufficiency of our current financial resources to advance the development of an MS therapeutic and any other product candidates are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect, or our planned Phase 1 study in our program for remyelination in MS may be more expensive, time consuming or difficult to design or implement than we currently anticipate. Changing circumstances, including any unanticipated expenses, could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Because the length of time and scope of activities associated with successful development of an MS therapeutic or any product candidate we may develop is highly uncertain, we are unable to estimate the actual funds we will require for development and any marketing and commercialization activities. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs and results of our clinical trials through all phases of development, including the planned Phase 1 study in our MS Program, and the development of any other product candidates including any unforeseen costs we may incur as a result of the COVID-19 global pandemic or other causes;
- the outcome, timing and cost of meeting regulatory requirements established by the U.S. Food and Drug Administration, or the FDA, and other comparable foreign regulatory authorities, including any clinical trials required by the FDA or other comparable foreign regulatory authorities;
- the willingness of the FDA and other comparable foreign regulatory authorities to accept our clinical trial designs, as well as data from our planned clinical trials and preclinical studies, as the basis for review and approval of an MS therapeutic and any other product candidates;
- the cost of filing, prosecuting, defending, and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us;
- the effect of competing technological and market developments;
- the cost and timing of completion of commercial-scale manufacturing activities;
- the costs of operating as a public company;
- the extent to which we in-license or acquire other product candidates or technologies;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates, if approved; and
- the initiation, progress, and timing of our commercialization of an MS therapeutic, if approved, or our other product candidates.

Depending on our business performance, the economic climate and market conditions, we may be unable to raise additional funds through any sources. Market volatility resulting from the COVID-19 global pandemic, the conflict in Ukraine, the escalation of tensions between China and Taiwan, global supply chain issues, and increased inflation could also adversely impact our ability to access capital as and when needed. 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 an MS therapeutic or any other product candidates, or potentially discontinue operations.

We have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We were established and began operations in 2014. Our operations to date have been limited to financing and staffing our company, licensing technologies, developing our PCA approach, developing and conducting preclinical and clinical studies of FX-322 for the treatment of SNHL, and developing a pipeline of preclinical and research programs, including FX-345 and our remyelination program in MS. We have not yet demonstrated the ability to successfully complete a large-scale, pivotal clinical trial, obtain marketing approval, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges. Our FX-322 Phase 2b results (FX-322-208), for example, showed no statistically significant difference at day 90 between those administered FX-322 versus those receiving placebo in the proportion of individuals that demonstrated an improvement in speech perception. We will eventually need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition and, as a result, our business may be adversely affected.

As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, the results of any quarterly or annual period are not necessarily indicative of future operating performance.

Our ability to use our net operating loss carryforwards to offset future taxable income, or tax credit carryforwards to offset future income tax liabilities, may be subject to certain limitations.

As of December 31, 2022, we had net operating loss carryforwards, or NOLs, of $174.1 million for federal income tax purposes and $141.3 million for state income tax purposes, which may be available to offset our future taxable income, if any. Our NOLs expire in various amounts through 2042, provided that federal NOLs generated in taxable years beginning after December 31, 2017 will not be subject to expiration. As of December 31, 2022, we also had federal and state research and development and other tax credit carryforwards of approximately $8.2 million and $3.6 million, respectively, available to reduce future income tax liabilities. Our tax credit carryforwards expire at various dates through 2042. These NOLs and tax credit carryforwards could expire unused, to the extent subject to expiration, and be unavailable to offset future taxable income or income tax liabilities, as applicable. In addition, in general, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an “ownership change” is subject to limitations on its ability to use its pre-change NOLs and tax credit carryforwards to offset future taxable income. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation’s stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a specified testing period. Similar rules may apply under state tax laws. We believe we have experienced ownership changes in 2017 and 2019 and may experience ownership changes in the future as a result of future transactions in our stock, some of which may be outside our control. As a result of the ownership changes in 2017 and 2019, $0.01 million and $0.04 million of NOL carryforwards are limited under Section 382 of the Code. If we undergo additional ownership changes, our ability to use our NOLs and tax credit carryforwards could be further limited. For these reasons, we may not be able to use a material portion of our NOLs or tax credit carryforwards, even if we attain profitability. Furthermore, federal NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely but may only be used to offset 80% of our taxable income in years beginning after December 31, 2020, which may require us to pay federal income taxes in future years despite generating federal NOLs in prior years. We have recorded a full valuation allowance related to our NOLs and other deferred tax assets due to the uncertainty of the ultimate realization of the future tax benefit of such assets.

Risks related to development, clinical testing, manufacturing, and regulatory approval

We are heavily dependent on the success of our MS Program, which is still under development, and if an MS therapeutic does not receive regulatory approval or is not successfully commercialized, our business will be materially adversely harmed.

To date, we have invested a significant portion of our efforts and financial resources in the development of FX-322 for the treatment of SNHL. We recently discontinued our FX-322 and FX-345 development programs following the results of our FX-322 Phase 2b study which showed no statistically significant difference at day 90 between those administered FX-322 versus those receiving placebo in the proportion of individuals that demonstrated an improvement in speech perception. Our future success is substantially dependent on our ability to successfully complete development for, obtain regulatory approval for, and successfully commercialize an MS therapeutic, which may never occur. We currently have no products that are approved for commercial sale and may never be able to develop a marketable product. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to our MS program, which will require additional clinical development, management of clinical and manufacturing activities, regulatory approval, establishing commercial scale manufacturing, and significant sales, marketing, and distribution efforts before we can generate any revenues from any commercial sales. We cannot be certain that we will be able to successfully complete any of these activities or that, even if it receives regulatory approval, a remyelinating therapeutic will be as effective as anticipated at treating MS.

The research, testing, manufacturing, labeling, approval, sale, packaging, marketing, and distribution of drug products are subject to extensive regulation by the FDA and comparable regulatory authorities in other countries. We are not permitted to market an MS therapeutic until we receive regulatory approval from the FDA or comparable regulatory authorities in other countries, and we may never receive such regulatory approval. As a result, our financial position will be materially adversely affected, and we may not be able to generate sufficient revenue to continue our business.

We utilize our PCA approach to develop product candidates that are designed to activate progenitor cells, which is a new approach to therapeutic intervention and, as a result, successful development, approval, and commercialization of any product candidates, including an MS therapeutic, is uncertain.

We utilize our PCA approach to develop product candidates, including in our MS Program. Our PCA approach is designed to identify pathways to activate progenitor cells already present in the body to treat conditions or diseases through cellular regeneration. We have not, nor to our knowledge has any other company, received regulatory approval utilizing this mechanism of cellular regeneration. Given the novelty of our approach, we could encounter a longer than expected regulatory review process, increased development costs, or unexpected delays in, or even prevention of, the regulatory approval and commercialization of our product candidates, and we cannot be certain that our approach will lead to the development of any approvable or marketable products.

Clinical trials are expensive, time consuming, and difficult to design and implement, and involve an uncertain outcome. The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate that we advance into clinical trials may not achieve favorable results in later clinical trials, if any, or receive marketing approval.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and completed clinical trials are not necessarily predictive of future results, and any product candidates we develop may not be further developed or may have additional unfavorable results in later studies or trials. Clinical trial failure may result from a multitude of factors, including, but not limited to, flaws in study design, dose selection, placebo effect, subject enrollment criteria, selection of subjects based on subject misrepresentations, and failure to demonstrate favorable safety or efficacy traits. As such, failure in clinical trials can occur at any stage of testing. Several companies in the pharmaceutical industry have suffered setbacks in the advancement of their drug candidates into later-stage clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding favorable results in earlier preclinical studies or clinical trials. Our FX-322 Phase 2b results (FX-322-208), for example, showed no statistically significant difference at day 90 between those administered FX-322 versus those receiving placebo in the proportion of individuals that demonstrated an improvement in speech perception. Based upon negative or inconclusive results or a need for additional information, we may decide, or regulatory authorities may require us, to conduct additional clinical trials or preclinical studies.

We may experience delays in initiating and completing any clinical trials that we intend to conduct, and we do not know whether our clinical trials will begin on time, need to be redesigned, enroll subjects on time, or be completed on

schedule, or at all. For example, a number of clinical trial sites for our completed Phase 2a clinical trial of FX-322 (FX-322-202) temporarily halted subject enrollment during the first and second quarter of 2020 in response to the COVID-19 pandemic. Enrollment in other planned clinical trials could be adversely affected by the pandemic. Clinical trials can be delayed for a variety of reasons, including delays related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical studies;
- obtaining regulatory approval to commence a trial;
- reaching an 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 trial sites;
- obtaining Institutional Review Board, or IRB, approval at each site within the United States, or Independent Ethics Committee, or IEC, approval at sites outside the United States;
- business interruptions resulting from the COVID-19 pandemic;
- recruiting suitable subjects to participate in a trial in a timely manner and in sufficient numbers;
- having subjects complete a trial or return for post-treatment follow-up;
- imposition of a clinical hold by regulatory authorities, including as a result of unforeseen safety issues or side effects or failure of trial sites or investigators to adhere to regulatory requirements or follow trial protocols;
- clinical sites deviating from the trial protocol or dropping out of a trial;
- addressing subject safety concerns that arise during a trial;
- adding a sufficient number of clinical trial sites; or
- manufacturing sufficient quantities of a product candidate for use in clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs or IECs of the institutions in which such trials are being conducted, the FDA or other regulatory authorities, or recommended for termination by a Data and Safety Monitoring Board, or DSMB, for such trial. Such authorities may impose a suspension or termination or recommend an alteration 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 other 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.

Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and, while we have agreements governing their committed activities, we have limited influence over their actual performance, as described in the section titled "—Risks related to our dependence on third parties."

Our MS Program is still in development and will require the successful completion of several trials before we are prepared to submit an NDA for regulatory approval by the FDA.

If we experience delays in the commencement or completion of any clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of any product candidate we develop could be harmed, and our ability to generate revenues may be delayed. In addition, any delays in our clinical trials could increase our costs, slow the development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may materially harm our business, financial condition, and results of operations. In addition, many of the factors that may 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.

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

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during a product candidate's clinical development and may vary among

jurisdictions. The approval process may also be delayed by changes in government regulation, the impact of the COVID-19 pandemic, future legislation or administrative action. We have not obtained regulatory approval for any product candidate and it is possible that we will never obtain regulatory approval for any product candidate. We are not permitted to market any of our product candidates in the United States until we receive approval of an NDA from the FDA.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authority, that such product candidates are safe and effective for their intended uses. In addition, data obtained from preclinical trials and clinical trials are susceptible to varying interpretations, and regulatory authorities may not interpret our data as favorably as we do, which may further delay, limit, or prevent development efforts, clinical trials, or marketing approval. Furthermore, as more competing drug candidates within a class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other comparable regulatory authorities.

The FDA or any foreign regulatory authority can delay, limit, or deny approval of an MS therapeutic that we develop or require us to conduct additional preclinical or clinical testing or abandon a program for many reasons, including:

- 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;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates, or other products containing an active ingredient in our product candidates;
- negative or ambiguous results from our clinical trials or results that 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 acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and we may be required to conduct additional clinical trials;
- the FDA's or the applicable foreign regulatory authority's disagreement regarding the formulation, the labeling, and/or the specifications of our product candidates;
- the FDA or comparable foreign regulatory authorities may fail to approve or find deficiencies with the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- 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; and
- significant regulatory GxP non-compliance or data integrity findings from FDA Bioresearch Monitoring inspections or pre-approval inspections inclusive of clinical investigator sites, contracted partners and their company's quality management system and execution thereof.

Of the large number of drugs in development, only a small percentage successfully complete the regulatory approval processes and are commercialized. 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 our product candidates, which would significantly harm our business, results of operations, and prospects.

In addition, the FDA or the applicable foreign regulatory authority also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or applicable foreign regulatory authority 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 circumstances could materially harm the commercial prospects for our product candidates and our business.

Enrollment and retention of individuals in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of subjects who remain in the study until its conclusion. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of subjects to complete any of our clinical trials, and even once enrolled, we may be unable to retain a sufficient number of subjects to complete any of our trials.

Subject enrollment and retention in clinical trials depends on many factors, including:

- the extent of the ongoing COVID-19 pandemic, see *—"The COVID-19 pandemic could adversely impact our business, including our preclinical studies, clinical trials and operations"*;
- the subject eligibility criteria defined in the protocol;
- the size of the subject population required for analysis of the trial's primary endpoints;
- the nature of the trial protocol, trial design, side effects or other results that may arise in development;
- the existing body of safety and efficacy data with respect to the product candidate;
- the proximity of subjects to clinical sites;
- our ability to recruit clinical trial investigators with the appropriate competencies, motivation and experience;
- clinicians' and subjects' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- competing clinical trials being conducted by other companies or institutions;
- our ability to obtain and maintain subject consents; and
- the risk that subjects 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 subjects available to us, because some people who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Furthermore, any negative results we may report in clinical trials of any product candidate may make it difficult or impossible to recruit and retain people in other clinical trials of that same product candidate. Delays or failures in planned subject enrollment or retention may result in increased costs or program delays, which could have a harmful effect on our ability to develop a product candidate or could render further development impossible.

Results of preclinical studies, clinical trials, or analyses may not be indicative of results that may be obtained in later trials or preclinical studies.

The results of preclinical studies, clinical trials, or analyses of the results from such trials may not be predictive of the results of later preclinical studies or clinical trials. Product candidates in later clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and prior clinical trials or having shown promising results based on analyses of data from earlier trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding earlier promising results. Our FX-322 Phase 2b results (FX-322-208), for example, showed no statistically significant difference at day 90 between those administered FX-322 versus those receiving placebo in the proportion of individuals that demonstrated an improvement in speech perception. In addition, conclusions based on promising data from analyses of clinical results, such as the prospective and *post hoc* analysis of data from our Phase 1/2 clinical trial of FX-322 for the treatment of SNHL (FX-322-201), may be shown to be incorrect in subsequent clinical trials that have pre-specified end points or may not be considered adequate by regulatory authorities. Further, we have in the past and may in the future abandon product candidates that we initially advanced for development based on positive preclinical results due to unfavorable results from additional preclinical studies. For example, we recently discontinued our FX-322 and FX-345 development programs after the results of the FX-322-208 clinical trial. Even if we complete later clinical trials as planned, we cannot be certain that their results will support the safety and efficacy requirements sufficient to obtain regulatory approval, and, as a result, our clinical development plans may be materially harmed.

Interim and preliminary "top-line" data from our clinical trials that we announce or publish from time to time may change as more subject 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 interim, top-line or preliminary data from our clinical trials, which is 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 top-line 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. Top-line or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the top-line or preliminary data we previously published. As a result, top-line and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose 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 subject enrollment continues and more subject data become available. Adverse differences between interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors 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 or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, top-line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Any of our product candidates or component of a product candidate that we develop or the administration thereof, may cause serious adverse events or undesirable side effects, which may halt their clinical development, delay or prevent marketing approval, or, if approved, require them to be taken off the market, include safety warnings, or otherwise limit their sales.

Serious adverse events or undesirable side effects caused by our product candidates or component of a product candidate we develop 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 other comparable foreign regulatory authorities. Results of any clinical trial we conduct could reveal a high and unacceptable severity and prevalence of side effects.

If unacceptable side effects arise in the development of any product candidate, we, the FDA, or the IRBs or IECs at the institutions in which our studies are conducted, or the DSMB, if constituted for our clinical trials, could recommend a suspension or termination of our clinical trials, or the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of a product candidate for any or all targeted indications. In addition, drug-related side effects could affect subject recruitment or the ability of enrolled subjects to complete a trial or result in potential product liability claims. These side effects also may not be appropriately recognized or managed by the treating medical staff. We may have to train medical personnel regarding the proper administration protocol for our product candidates and to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in subject injury or death. Any of these occurrences may harm our business, financial condition, and prospects significantly.

Additionally, if an MS therapeutic or any other product candidates we develop receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may suspend, withdraw, or limit approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require us to recall a product or we may decide to initiate a voluntary recall of a product;

- regulatory authorities may require additional warnings on the label, such as a “black box” warning or contraindication;
- additional restrictions may be imposed on the marketing of the product or the manufacturing processes for the product or any component thereof;
- we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to subjects;
- we may be required to conduct post-market studies or agree to post marketing commitments;
- we could be sued and held liable for harm caused to subjects;
- the product may become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of a product candidate, if approved, and could significantly harm our business, results of operations, and prospects.

Disruptions at the FDA and other government agencies caused by funding shortages, changes in the federal administration or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, 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 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 to be reviewed or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs or the FDA experiences other delays, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of foreign and domestic manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays.

Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic or issue guidance materially affecting the conduct of clinical trials. If a prolonged government shutdown occurs, or if global health concerns continue to 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 to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

We may not be successful in our efforts to identify additional product candidates. Due to our limited resources and access to capital, we must prioritize development of certain product candidates, the choice of which may prove to be wrong and adversely affect our business.

Although we intend to explore additional product candidates based on our PCA approach, we may fail to identify viable new product candidates for clinical development for several reasons. If we fail to identify additional potential product candidates, our business could be materially harmed.

Research programs to develop additional product candidates based on our PCA approach require substantial technical, financial, and human resources whether or not they are ultimately successful. Our research programs may initially show promise in identifying potential indications or product candidates, yet fail to yield results for clinical development for several reasons, including:

- the research methodology used may not be successful in identifying potential indications or product candidates;

- potential product candidates may, after further study, be shown to have harmful or unexpected adverse effects or other characteristics that indicate they are unlikely to be effective drugs; or
- it may take greater human and financial resources than we possess to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, thereby limiting our ability to develop, diversify, and expand our product portfolio.

Because we have limited financial and human resources, we intend to initially focus on research programs and product candidates for a limited set of indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that could have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, which could materially adversely affect our future growth and prospects. For example, we may encounter delays in the process of selecting a product candidate for the treatment of MS and we may not achieve the timeline we currently anticipate for submitting an IND or comparable foreign equivalent. We may focus our efforts and resources on potential product candidates or other potential programs that ultimately prove to be unsuccessful.

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

We have never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any NDAs that we submit for our product candidates or may conclude after review of our data that our applications are insufficient to obtain marketing approval of our product candidates. We believe our approach of activating progenitor cells to treat conditions or diseases through cellular regeneration is novel and, as a result, the process for, and the outcome of, FDA approval is especially uncertain. If the FDA does not accept or approve our NDAs for our product candidates, it may require that we conduct additional clinical, preclinical, or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any NDA that we submit may be delayed or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs.

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

Even if we obtain FDA approval for a product candidate in the United States, we may never obtain approval for or commercialize the product candidate in any other jurisdiction, which would limit our ability to realize its full market potential.

In order to market any product in a particular jurisdiction, we or our collaborators must establish and comply with numerous and varying regulatory requirements regarding safety and efficacy on a country-by-country basis. Approval by the FDA in the United States does not ensure approval by comparable regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our or our collaborators' ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could 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. We do not have any product candidates approved for sale in any jurisdiction, including in 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, or if regulatory approvals in international markets are delayed, our target market will be reduced and we will be unable to realize the full market potential of any product we develop.

Even if we obtain regulatory approval for any product candidate, we will still face extensive and ongoing regulatory requirements and obligations, which may result in significant additional expense, and any product candidates, if approved, may face future development and regulatory difficulties.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, and advertising and promotional activities for such product, among other things, will be subject to extensive and ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements, continued compliance with current Good Manufacturing Practice, or cGMP, requirements relating to manufacturing, quality control, quality assurance, and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping and Good Clinical Practice, or GCP, and requirements for any clinical trials that we conduct post-approval.

Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product candidate may be marketed or to the conditions of approval, including a requirement to implement a REMS. If a product candidate receives marketing approval, the accompanying label may limit the approved indicated use of the product, which could limit sales of the product. The FDA may also require costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use, and if we market our products for uses beyond their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act, or FDCA, relating to the promotion of prescription drugs, may lead to FDA enforcement actions and investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

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

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of products;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recalls or market withdrawals of products;
- fines, restitution, or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions, consent decrees, or the imposition of civil or criminal penalties.

Further, the FDA's policies may change, and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of a product candidate. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects, and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. The policies of the FDA and of other comparable regulatory authorities may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of a product candidate. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action, and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition, and results of operations. Furthermore, noncompliance by us or any collaborator with regulatory

requirements, including safety monitoring or pharmacovigilance, may also result in significant financial penalties, which would adversely affect our business.

We may seek Fast Track designation by the FDA for any future product candidates, but we might not receive such a designation. However, such designation may not lead to a faster development or regulatory review or approval process.

If a drug is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, a drug sponsor may qualify for FDA Fast Track designation. Fast Track designation provides increased opportunities for sponsor meetings with the FDA during preclinical and clinical development, in addition to the potential for rolling review and priority review once a marketing application is filed. The FDA has broad discretion whether to grant Fast Track designation, and we may not receive such a designation for all of the product candidates for which we may request it. Moreover, even if we receive Fast Track designation, Fast Track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular time frame. We may not experience a faster development or regulatory review or approval process with Fast Track designation compared to conventional FDA procedures. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures.

We may seek a Breakthrough Therapy designation for an MS therapeutic or other product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster development or regulatory review or approval process.

We may seek a Breakthrough Therapy designation for an MS therapeutic if results from future clinical trials support such designation and we may seek a Breakthrough Therapy designation for other product candidates we may develop. A Breakthrough Therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA may also be eligible for priority review if supported by clinical data at the time the NDA is submitted to the FDA.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe that a product candidate meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such a designation. Even if we receive Breakthrough Therapy designation, the receipt of such designation may not result in a faster development or regulatory review or approval process compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if a product candidate qualifies as a Breakthrough Therapy, the FDA may later decide that it no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Potential product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

The use of any product candidate we may develop in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical trials;
- significant costs to defend the litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize a product candidate;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;

- decreased market demand for any product; and
- loss of revenue.

The product liability insurance we currently carry, and any additional product liability insurance coverage we acquire in the future, may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for any product candidate, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim, or series of claims, brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operation and business, including preventing or limiting the commercialization of any product candidates we develop.

The COVID-19 pandemic has caused and could continue to cause disruptions to our business, including our preclinical studies, clinical trials and operations and could adversely impact our financial condition and results of operations.

The COVID-19 pandemic, and government measures taken in response, have had a significant impact, both direct and indirect, on business and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen.

Since March 2020, the majority of our employees have continued to work from home two to three days per week, while our laboratory employees have largely resumed a full in-person schedule in our Lexington, MA facility. We have also taken steps consistent with the FDA's updated industry guidance for conducting clinical trials.

If COVID-19 or its variants again spread in the United States and worldwide, and measures to mitigate the ongoing effects of the pandemic, such as stay home orders and/or advisories persist or are reintroduced, we may continue to experience disruptions and other effects on our business that could severely impact our business, operations, preclinical studies and clinical trials, including:

- delays, difficulties or postponement in enrolling and retaining subjects in our planned clinical trials;
- delays, difficulties or postponement in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- interruptions in planned trials due to restricted or limited operations at our laboratory facility;
- continual changes to operating requirements and related expenses, limitations in employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people and resulting losses of productivity and employee work culture;
- risk that participants enrolled in our clinical trials will acquire COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- refusal of the FDA, or other government agencies, to accept data from clinical trials in these affected geographies;
- interruption or delayed to our sourced discovery and clinical activities, and;
- inability to obtain additional financing or access the financial markets.

The global outbreak of COVID-19 continues to rapidly evolve and continues to have indeterminable adverse effects on general commercial activity and the world economy. Due to the uncertain nature of the effects of the outbreak, particularly in the United States, enrollment, participation and retention in our planned trials may be reduced, and for a number of the clinical sites, halted for an unknown period of time. Any reduction in enrollment, participation and retention and any halts may delay our planned clinical trials and our development plans for an MS therapeutic and any other product candidates, which could have an adverse impact on our business and results of operations.

The extent to which COVID-19 may continue to impact our business, preclinical studies, planned clinical trials and operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ongoing and ultimate geographic spread of the disease, duration of the outbreak, including future waves of infection, new variant strains of the underlying virus, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, adoption and effectiveness of vaccines and other actions taken in the United States and other countries to contain, treat and mitigate the spread of COVID-19. In addition, if we or any of the third parties with whom we engage were to experience shutdowns or additional business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted, which could have a material adverse effect on our business and our financial results. The COVID-19 pandemic has resulted in a widespread health crisis that has adversely affected the economies and financial markets worldwide, resulting in an economic downturn that could continue to significantly impact our business, financial condition and results of operations. To the extent the COVID-19 pandemic adversely affects our business, financial condition and results of operations, it may also have the effect of heightening many of the other risks described in this "Risk Factors" section.

Risks related to commercialization

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

The biotechnology and pharmaceutical industries are highly competitive and subject to significant and rapid technological change. Our success is highly dependent on our ability to acquire, develop, and obtain marketing approval for new products on a cost-effective basis and to market them successfully. If a product candidate we develop is approved, we will face intense competition from a variety of businesses, including large, fully integrated pharmaceutical companies, specialty pharmaceutical companies, and early-stage companies, particularly if the early-stage company has a collaborative arrangement with a large and established company. We are aware of several companies developing programs with research and development efforts to treat MS through the regeneration of myelin. If we successfully develop and, if approved, commercialize an MS therapeutic, it may compete, or potentially be used in conjunction with, currently marketed therapeutics and any new therapeutics that may become available in the future.

Competition could render any product candidate we develop obsolete, less competitive, or uneconomical. Our competitors may, among other things:

- have significantly greater name recognition and financial, manufacturing, marketing, product development, technical, and human resources than we do, with mergers and acquisitions in the biotechnology and pharmaceutical industries resulting in even more resources being concentrated in our competitors;
- more effectively recruit and retain qualified scientific and management personnel;
- more effectively establish clinical trial sites and subject registration;
- develop and commercialize products that are safer, more effective, less expensive, more convenient, or easier to administer, or have fewer or less severe side effects;
- obtain quicker regulatory approval;
- better protect their patents and intellectual property or acquire technologies that are complementary to, or necessary for, our programs;
- implement more effective approaches to sales, marketing, pricing, coverage, and reimbursement; or
- form more advantageous strategic alliances or collaborations.

If we are not able to effectively compete for any of the foregoing reasons, our business will be materially harmed.

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

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers, and other third-party payors are essential for most patients to be able to afford prescription medications. Our ability to achieve acceptable levels of coverage and reimbursement for products or procedures using our products by governmental authorities, private health insurers and other organizations will influence our ability to successfully commercialize any product candidates we develop. Assuming we obtain coverage for any product candidates or procedures using our products 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 or elsewhere will be available for any product we commercialize, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and the current presidential administration and Congress have introduced several proposals related to drug pricing. Many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar, or a less expensive therapy is available. Although there are currently no FDA approved drugs for the treatment of MS through the regeneration of myelin, it is possible that a third-party payor may consider such a drug as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy, pricing of existing drugs may limit the amount we will be able to charge for any product we commercialize. Payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize a satisfactory return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates and may not be able to obtain a satisfactory financial return on our product candidates. Additionally, our ability to obtain a satisfactory financial return depends on what, if any, proposals related to drug pricing may be implemented and, if implemented, when they might take effect.

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

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor, and one third-party payor's decision to cover a product does not ensure that other payors will also provide similar coverage. Additionally, the process for determining whether a third-party payor will provide coverage for a product is typically separate from the process for setting the price of such product or establishing the reimbursement rate that the payor will pay for the product once coverage is approved. As a result, the determination of coverage and reimbursement is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Moreover, increasing efforts by governmental and third-party payors in the United States 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 any product we commercialize. We expect to experience pricing pressures in connection with the sale of any product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations, and additional legislative, administrative, or regulatory changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

We may also be subject to extensive governmental price controls and other market regulations outside of the United States, and we believe the increasing emphasis on cost-containment initiatives in other countries have and will continue to put pressure on the pricing and usage of medical products. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for products we commercialize. Accordingly, in markets outside the United States, the reimbursement for products we or commercialize may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Even if a product candidate we develop receives marketing approval, it may fail to achieve market acceptance by physicians, patients, third-party payors, or others in the medical community necessary for commercial success.

If a product candidate we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, and others in the medical community. For example, current MS treatments are well established in the medical community, and physicians may continue to rely on these treatments to the exclusion of ours. In addition, physicians, patients, and third-party payors may prefer other novel products to ours. If a product candidate does not achieve an adequate level of acceptance, we may not generate significant product revenues or become profitable. The degree of market acceptance of our product candidates, if approved, will depend on several factors, including, but not limited to:

- the efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our product together with other medications.

Because we expect sales of our product candidates, if approved, to generate substantially all our revenues for the foreseeable future, the failure of our product candidates to find market acceptance would harm our business and could require us to seek additional financing.

If we are unable to establish sales and marketing capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing any product candidate we develop, if approved.

In order to market and successfully commercialize any product candidate we develop, if approved, we must build our sales and marketing capabilities or enter into collaborations with third parties for these services. We currently have no sales, marketing or distribution capabilities and as a company have no experience in marketing products. We intend to directly market and commercialize an MS therapeutic, if approved, by entering into collaborations for the sales and marketing of our product candidates, if approved. To the extent that we depend on collaborators for sales and marketing activities, any revenues we receive will depend upon the success of those collaborators' sales and marketing teams and the collaborators' prioritization of our product and compliance with applicable regulatory requirements, and there can be no assurance that the collaborators' efforts will be successful.

If we are unable to enter into a collaboration for the commercialization of product candidates we develop, if approved, we may be forced to delay the commercialization of our product candidates or reduce the scope of our sales or marketing activities, which would have an adverse effect on our business, operating results and prospects.

A variety of risks associated with operating internationally could materially adversely affect our business.

Our business strategy includes potentially expanding internationally if any of our product candidates receive regulatory approval. Doing business internationally involves several risks, including, but not limited to:

- multiple, conflicting, and changing laws and regulations, such as data privacy and security laws and regulations, tax laws, export and import restrictions, economic sanctions laws and regulations, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses, including, among others, expenses for travel, translation, and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, its books and records provisions, or its anti-bribery provisions, as well as other applicable laws and regulations prohibiting bribery and corruption.

Any of these factors could significantly harm any future international expansion and operations and, consequently, our results of operations.

Risks related to our dependence on third parties

We intend to continue to collaborate with third parties for the development and commercialization of any product candidates. We may not succeed in establishing and maintaining collaborations, which may significantly limit our ability to successfully develop and commercialize our other product candidates, if at all.

We may seek collaborations for the development and commercialization of any product candidates. The process of establishing and maintaining collaborative relationships is difficult, time-consuming, and involves significant uncertainty, such as:

- a collaborator may shift its priorities and resources away from our product candidates due to a change in business strategies, or a merger, acquisition, sale, or downsizing;
- a collaborator may seek to renegotiate or terminate its relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- a collaborator may cease development in therapeutic areas which are the subject of our collaboration;
- a collaborator may not devote sufficient capital or resources towards our product candidates, or may fail to comply with applicable regulatory requirements;
- a collaborator may change the success criteria for a product candidate, thereby delaying or ceasing development of such candidate;
- a significant delay in initiation of certain development activities by a collaborator will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- a collaborator could develop a product that competes, either directly or indirectly, with our product candidate;
- a collaborator with commercialization obligations may not commit sufficient financial resources or personnel to the marketing, distribution, or sale of a product;

- a collaborator with manufacturing responsibilities may encounter regulatory, resource, or quality issues and be unable to meet demand requirements;
- a collaborator may terminate a strategic alliance;
- a dispute may arise between us and a collaborator concerning the research, development, or commercialization of a product candidate resulting in a delay in milestones or royalty payments or termination of the relationship and possibly resulting in costly litigation or arbitration, which may divert management's attention and resources; and
- a collaborator may use our products or technology in such a way as to invite litigation from a third party.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing, or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborations on acceptable terms or to successfully transition away from terminated collaborations, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense, or find alternative sources of capital, which would have a material adverse impact on our clinical development plans and business.

Our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with development and commercialization may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

Our employees and independent contractors, including principal investigators, CROs, consultants, vendors, and any third parties we may engage in connection with development and commercialization of our product candidates, could engage in misconduct, including intentional, reckless, or negligent conduct or unauthorized activities that violate applicable laws, rules, and regulations including: the laws and regulations of the FDA or other similar regulatory requirements of other authorities, including those laws that require the reporting of true, complete, and accurate information to such authorities; manufacturing standards; data privacy, security, fraud and abuse, and other healthcare laws and regulations; or laws that require the reporting of true, complete, and accurate financial information and data. Specifically, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Activities subject to these or other laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials, or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person or government agency could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us or them 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 significant civil, criminal, and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

We currently intend to rely on third-party contract manufacturing organizations, or CMOs, for the production of clinical supply and the production of commercial supply of our future product candidates, as well as to supply raw materials necessary to produce our product candidates. Our dependence on CMOs may impair the development of our product candidates and may impair their commercialization, which would adversely impact our business and financial position.

We do not own facilities for manufacturing any product candidate. Instead, we rely on and expect to continue to rely on CMOs for the supply of cGMP grade clinical trial materials of any product candidates we develop and, in future, for commercial quantities. Reliance on CMOs may expose us to more risk than if we were to manufacture our product candidates ourselves. If any CMO we engage is unable to provide sufficient supply of any product candidate we develop, we may be unable to arrange for an alternative supply or to do so on commercially reasonable terms or in a timely manner, which could delay any clinical trials, the commercial launch of our product candidates, if approved, or, regarding any commercial supply, result in a shortage in supply that could negatively impact our revenues.

The facilities used to manufacture any product candidates we develop must be inspected by the FDA and comparable foreign regulatory authorities. While we provide oversight of manufacturing activities, we do not and will not control the execution of manufacturing activities by, and are or will be dependent on, our CMOs for compliance with cGMP requirements for the manufacture of any product candidates. As a result, we are subject to the risk that any product candidates may have manufacturing defects that we have limited ability to prevent. If a CMO cannot successfully manufacture material that conforms to our specifications and the regulatory requirements, we will not be able to secure or maintain regulatory approval for the use of our product candidates in clinical trials, or for commercial distribution of any product candidates, if approved. We have limited control over the ability of our CMOs to maintain adequate quality control, quality assurance, and qualified personnel, and we were not involved in developing our CMOs' policies and procedures.

If the FDA or comparable foreign regulatory authority finds deficiencies with or does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval or finds deficiencies in the future, we may need to find alternative manufacturing facilities, which would delay our development program and significantly impact our ability to develop, obtain regulatory approval for, or commercialize our product candidates, if approved. In addition, any failure to achieve and maintain compliance with laws, regulations, and standards related to manufacturing could subject us to risks, including the risk that we may have to suspend the manufacture of our product candidates, that obtained approvals could be revoked, and that the FDA or another governmental regulatory authority may take enforcement actions, including untitled letters, warning letters, seizures, injunctions, or product recalls. Furthermore, CMOs may breach existing agreements they have with us because of factors beyond our control. They may also terminate or refuse to renew their agreement at a time that is costly or otherwise inconvenient for us. If we were unable to find an adequate CMO or another acceptable solution in time, our clinical trials could be delayed, or our commercial activities could be harmed.

We contract for the supply of the active pharmaceutical ingredient, or API, and other raw material necessary to produce any product candidates we develop. Supplies of API or other raw material could be interrupted from time to time and we cannot be certain that alternative supplies could be obtained within a reasonable time frame, at an acceptable cost, or at all. 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 mitigate the spread of COVID-19 or treat its effects and may cause delays. In addition, a disruption in the supply of API or other raw material could delay the commercial launch of our product candidates, if approved, or result in a shortage in supply, which would impair our ability to generate revenues. Growth in the costs and expenses of API or other raw material may also impair our ability to cost-effectively manufacture our product candidates. In addition, there may be a limited number of suppliers for API or other raw material that we may use to manufacture our product candidates, and we cannot be certain that we will be able to engage such suppliers in a timely manner or at all. If we are unable to do so, clinical development of our product candidates, commercialization for any approved product, or our business could be adversely affected.

Finding new CMOs or third-party suppliers involves additional cost and requires our management's time and focus. In addition, there is typically a transition period when a new CMO commences work. Although we have not, and do not intend to, begin a clinical trial unless we believe we have on hand, or will be able to obtain, a sufficient supply of our product candidates to complete the clinical trial, any significant delay in the supply of our product candidates or the raw materials needed to produce our product candidates, could considerably delay conducting our clinical trials and potential regulatory approval of our product candidates.

As part of their manufacture of our product candidates, our CMOs and third-party suppliers are expected to comply with and respect the proprietary rights of others. If a CMO or third-party supplier fails to acquire the proper licenses or otherwise infringes the proprietary rights of others in the course of providing services to us, we may have to find alternative CMOs or third-party suppliers or defend against claims of infringement, either of which would significantly impact our ability to develop, obtain regulatory approval for, or commercialize our product candidates, if approved.

We intend to rely on third parties to conduct, supervise, and monitor our clinical trials. If those third parties do not successfully carry out their contractual duties, or if they perform in an unsatisfactory manner, it may harm our business.

We have relied, and will continue to rely, on CROs, CRO-contracted vendors, and clinical trial sites to ensure the proper and timely conduct of our clinical trials, including our planned Phase 1 study in our MS Program, and any future clinical trials of other product candidates. Our reliance on CROs and clinical trial sites for clinical development activities limits our control over these activities and we were not involved in developing their policies and procedures, but we remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol and legal, regulatory, and scientific standards. For example, we have identified and corrected errors made by a clinical trial site and a CRO in the FX-322-111 and FX-322-113 trials, respectively.

We and our CROs will be required to comply with the Good Laboratory Practice requirements for our preclinical studies and GCP requirements for our clinical trials, which are regulations and guidelines enforced by the FDA and are also required by comparable foreign regulatory authorities. Regulatory authorities enforce GCP requirements through periodic inspections of trial sponsors, principal investigators, and clinical trial sites. If we or our CROs fail to comply with GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, our clinical trials must be conducted with product produced under cGMP requirements. Accordingly, if our CROs fail to comply with these requirements, we may be required to repeat clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we do not control whether they devote sufficient time and resources to our clinical trials. Our CROs 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 harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, or fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If our relationship with any CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management's time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. While the COVID-19 pandemic and government measures taken in response have had a significant impact on our CROs and their ability to conduct clinical trials, there is potential they will face disruption in the future, which may affect our ability to initiate and complete our clinical trials. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have an adverse impact on our business, financial condition, and prospects.

Risks related to healthcare laws and other legal compliance matters

Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates, if approved, and may affect the prices we may set.

In the United States and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes, and additional proposed changes, to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of health care. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the biotechnology and pharmaceutical industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and biologics that are inhaled, infused, instilled, implanted, or injected;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial 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. Prior to the Supreme Court's decision, President Biden issued an executive order initiating 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. It is unclear how healthcare reform measures, if any, will impact our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In March 2021, the American Rescue Plan Act of 2021 was signed into law, which, among other things, eliminated the statutory cap on drug manufacturers' Medicaid Drug Rebate Program rebate liability, effective January 1, 2024. Under current law enacted as part of the ACA, drug manufacturers' Medicaid Drug Rebate Program rebate liability is capped at 100% of the average manufacturer price for a covered outpatient drug. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been administration efforts, Congressional inquiries and proposed federal and state legislation designed to bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient assistance programs and reform government program reimbursement methodologies for drugs. Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. We expect that additional U.S. federal healthcare reform measures will be implemented in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions 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. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices. These reforms could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In markets outside of the United States, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. 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 any other jurisdiction. 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.

Our business operations and current and future relationships with contractors, investigators, healthcare professionals, consultants, third-party payors, patient organizations, customers, and others will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with contractors, investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell, and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving, or providing any remuneration (including any kickback, bribe, or certain 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 for, or the purchase, lease, order, or recommendation of, any good, facility, item or service for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The U.S. federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other hand;
- the U.S. federal false claims, including the civil False Claims Act, or FCA, which, among other things, impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. A claim includes "any request or demand" for money or property presented to the federal government. In addition, pharmaceutical 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 U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation:
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics, and medical devices;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products;
- the U.S. federal legislation commonly referred to as the Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics, and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants and certified nurse midwives) and teaching hospitals, as well as ownership and investment interests held by such physicians and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales, and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities;

- similar healthcare laws and regulations in the European Union, or EU, and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers; and
- laws and regulations prohibiting bribery and corruption such as the FCPA, which, among other things, prohibits U.S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations or foreign government-owned or affiliated entities, candidates for foreign public office, and foreign political parties or officials thereof.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our business activities, including our consulting agreements and other relationships with healthcare providers, some of whom receive stock or stock options as compensation for their services, could be subject to challenge under one or more of such laws. Ensuring that our current and future internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance, or case law involving applicable fraud and abuse or other healthcare laws and regulations.

If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to actions including the imposition of civil, criminal, and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid, and other federal healthcare programs, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements, or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time consuming, and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

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 data, such as information that we may collect in connection with clinical trials in the U.S. 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.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. We may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly regulated under HIPAA, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPAA. Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners.

Further, we may also be or become subject to other state laws governing the privacy, processing and protection of personal information. For example, the California Consumer Privacy Act, or CCPA, went 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, passed in California and it significantly amends the CCPA. It 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 went into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia, Connecticut, Utah and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, 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.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For example, in Europe, the EU General Data Protection Regulation, or GDPR, went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. 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; in July 2020, the Court of Justice of the EU, or CJEU, limited how organizations could lawfully transfer personal data from the EU/EEA to the United States by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses, or SCCs. In March 2022, the US and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-US Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. European court and regulatory decisions subsequent to the CJEU decision of July 16, 2020 have taken a restrictive approach to international data transfers. 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, from January 1, 2021, companies have had to comply with the GDPR and also the United Kingdom GDPR, or the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, i.e., fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. The relationship between the United Kingdom and the European Union in relation to certain aspects of data protection law remains unclear, and it is unclear how United Kingdom data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the United Kingdom will be regulated in the long term. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities.

Our operations, including our development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws and regulations. These laws and regulations govern, among other things, the controlled

use, handling, release, and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds, and compounds that have a toxic effect on reproduction, laboratory procedures and exposure to blood-borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions.

As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third-party manufacturers or our development efforts may be interrupted or delayed.

Risks related to our intellectual property

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

Our success depends in large part on our ability to obtain and maintain protection of the intellectual property we may own solely and jointly with others, or may license from others, particularly patents, in the United States and other countries with respect to any proprietary technology and product candidates we develop. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our technologies and product candidates that are important to our business and by in-licensing intellectual property related to such technologies and product candidates. If we are unable to obtain or maintain patent protection with respect to any proprietary technology or product candidate, our business, financial condition, results of operations and prospects could be materially harmed.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, defend, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing, and prosecution of patent applications, or to maintain, enforce, and defend the patents, covering technology that we license from third parties. Therefore, these in-licensed patents, and applications may not be prepared, filed, prosecuted, maintained, defended, and enforced in a manner consistent with the best interests of our business.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the scope of patent protection outside of the United States is uncertain and laws of foreign countries may not protect our rights to the same extent as the laws of the United States or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. With respect to both owned and in-licensed patent rights, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not published at all. Therefore, neither we nor our licensors can know with certainty whether either we or our licensors were the first to make the inventions claimed in the patents and patent applications we own or in-license now or in the future, or that either we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability, and commercial value of our owned and in-licensed patent rights are uncertain. Moreover, our owned and in-licensed pending and future patent applications may not result in patents being issued that protect our technology and product candidates, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents and our ability to obtain, protect, maintain, defend, and enforce our patent rights, narrow the scope of our patent protection and, more generally, could affect the value or narrow the scope of our patent rights.

Moreover, we or our licensors may be subject to a third-party pre-issuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, *inter partes* review, post-grant review, or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. If the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome,

it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Additionally, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if our owned and in-licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us, or otherwise provide us with any competitive advantage. The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our management and employees, even if the eventual outcome is favorable to us. 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. Furthermore, our competitors may be able to circumvent our owned or in-licensed patents by developing similar or alternative technologies or products in a non-infringing manner. As a result, our owned and in-licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing technology and products similar or identical to any of our technology and product candidates.

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 United States non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing, and regulatory review of 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 are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation. 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.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could significantly harm our business, financial condition, results of operations, and prospects.

Additionally, if we fail to comply with our obligations under license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, or impede, or delay or prohibit the further development or commercialization of, one or more product candidates that rely on such agreements.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for any product candidates we may develop, our business may be materially harmed.

In the United States, the patent term of a patent that covers an FDA-approved drug may be eligible for limited patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. In addition, only one patent applicable to an approved drug may be extended, and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions may be available in Europe and certain other non-United States jurisdictions to extend the term of a patent that covers an approved drug. While, in the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates, there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. We may not be granted patent term extension either in the United States or in any foreign country 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 term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations, and prospects could be materially harmed.

It is possible that we will not obtain patent term extension under the Hatch-Waxman Act for a United States patent covering any of our product candidates that we may identify even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought. Further, for our licensed patents, we may not have the right to control prosecution, including filing with the USPTO, of a petition for patent term extension under the Hatch-Waxman Act. Thus, if one of our licensed patents is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether a petition to obtain a patent term extension is filed, or obtained, from the USPTO.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If one of our product candidates is approved and a patent covering that product candidate is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application filed with the FDA to obtain permission to sell a generic version of such product candidate.

Although we or our licensors are not currently involved in any litigation, we may become involved in lawsuits to protect or enforce our patent or other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our or our licensors' issued patents or other intellectual property. As a result, we or our licensors may need to file infringement, misappropriation or other intellectual property related claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke such parties to assert counterclaims against us alleging that we infringe, misappropriate, or otherwise violate their intellectual property. In addition, in a patent infringement proceeding, such parties could counterclaim that the patents we or our licensors have asserted are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may institute such claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). The outcome following legal assertions of invalidity and unenforceability is unpredictable.

An adverse result in any such proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly and could put any of our owned or in-licensed patent applications at risk of not yielding an issued patent. A court may also refuse to stop the third party from using the technology at issue in a proceeding on the grounds that our owned or in-licensed patents do not cover such technology. 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 or trade secrets could be compromised by disclosure during this type of litigation. Any of the foregoing could allow such third parties to develop and commercialize competing technologies and products and have a material adverse impact on our business, financial condition, results of operations, and prospects.

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. An unfavorable outcome 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. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs, and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

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. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

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

Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. There is considerable patent and other intellectual property litigation in the pharmaceutical and biotechnology industries. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and product candidates, including interference proceedings, post grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the European Patent Office. 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 pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our technologies or product candidates that we may identify may be subject to claims of infringement of the patent rights of third parties.

The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. The risks of being involved in such litigation and proceedings may increase if and as our product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of merit. We may not be aware of all such intellectual property rights potentially relating to our technology and product candidates and their uses, or we may incorrectly conclude that third party intellectual property is invalid or that our activities and product candidates do not infringe such intellectual property. Thus, we do not know with certainty that our technology and product candidates, or our development and commercialization thereof, do not and will not infringe, misappropriate or otherwise violate any third party's intellectual property.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the discovery, use or manufacture of the product candidates that we may identify or related to our technologies. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that the product candidates that we may develop may be found to infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, as noted above, there may be existing patents that we are not aware of or that we have incorrectly concluded are invalid or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover, for example, the manufacturing process of the product candidates that we may develop, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize the product candidates that we may identify. 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, pay royalties, redesign our infringing products, or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may choose to take a license or, if we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights, we could also be required to obtain a license from such third party to continue developing, manufacturing and marketing our technology and product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us and could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right and could be forced to indemnify our customers or collaborators. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. In addition, we may be forced to redesign our product candidates, seek new regulatory approvals, and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects.

Intellectual property litigation or other legal proceedings relating to intellectual property could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and may also have an advantage in such proceedings due to their more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of intellectual property litigation or other proceedings could compromise our ability to compete in the marketplace.

Obtaining and maintaining 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 noncompliance with these requirements.

Periodic maintenance, renewal and annuity fees and various other government fees on any issued patent and pending patent application must be paid to the USPTO and foreign patent agencies in several stages or annually over the lifetime of our owned and in-licensed patents and patent applications. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In certain circumstances, we rely on our licensing partners to pay these fees to, or comply with the procedural and documentary rules of, the relevant patent agency. With respect to our patents, we rely on an annuity service, outside firms, and outside counsel to remind us of the due dates and to make payment after we instruct them to do so. 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. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. Under certain circumstances, we may be unable to comply with requirements. For example, due to the sanctions imposed by the United States on Russia as a result of the conflict in Ukraine, it is not possible to pay fees on Russian patents and the future of such patents is uncertain. In such an event, potential competitors might be able to enter the market with similar or identical products or technology. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, it would have a material adverse effect on our business, financial condition, results of operations, and prospects.

Changes to patent laws in the United States and other 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 patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the maintenance, enforcement, or defense of our owned and in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution, and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 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. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory 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. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our 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 biologics and pharmaceuticals 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 patent rights and our ability to protect, defend and enforce our patent rights in the future.

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

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, and even where such protection is nominally available, judicial and governmental enforcement of such intellectual property rights may be lacking. 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 or licenses, but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, certain jurisdictions do not protect, to the same extent or at all, inventions that constitute new methods of treatment.

In addition, geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's conflict in Ukraine may limit or prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees from the United States without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Proceedings to enforce our intellectual property and proprietary 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, could put 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 and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

Finally, Europe is implementing a Unified Patent Court that may present uncertainties for our ability to protect and enforce our patent rights in Europe and the ability of third parties to do the same. In 2012, regulations were passed with the goal of providing a pan-European Unitary Patent and a new European Unified Patent Court, or UPC, for litigation involving European patents. Implementation is currently scheduled for June 1, 2023. Under the UPC, all European patents granted in countries that have ratified the UPC Agreement, including those patents issued prior to the UPC, will automatically fall under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke European patents, and allow for the possibility of a competitor to obtain injunctions in multiple European countries in a single UPC action. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by the UPC. Note that we will have the option to opt our patents out of the UPC over the first seven years of the court's existence, but doing so may preclude us from realizing the benefits of the new unified court.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

We are party to license and funding agreements that impose, and we may enter into additional licensing and funding arrangements with third parties that may impose, diligence, development, and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Under our existing licensing and funding agreements, we are obligated to pay royalties on net product sales of product candidates or related technologies to the extent they are covered by the agreements. If we fail to comply with such obligations under current or future license and funding agreements, our counterparties may have the right to terminate these agreements or require us to grant them certain rights. Such an occurrence could materially adversely affect the value of any product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

- the scope of rights granted under the license agreement and other interpretation related issues;
- the extent to which our 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 technology and product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

Our current or future licensors may have relied on third-party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents and patent applications we in-license. If other third parties have ownership rights to patents and/or patent applications we in-license, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize product candidates and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products and technologies identical to ours. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

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

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets, or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Detecting the disclosure or misappropriation of a trade secret and enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely 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 registered and unregistered 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, which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trade names or trademarks that incorporate variations of our unregistered trade names or trademarks. Over the long term, if we are unable to successfully register our trade names and trademarks and establish name recognition based on our trade names and trademarks, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trade names and trademarks may

be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Intellectual property rights do not necessarily address all potential threats.

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

- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or in-licensed intellectual property rights;
- it is possible that our owned and in-licensed pending patent applications or those we may own or in-license in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates;
- we cannot ensure that any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable product candidates or will provide us with any competitive advantages;
- we cannot ensure that our commercial activities or product candidates will not infringe upon the patents of others;
- we cannot ensure that we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before the relevant patents that we own, or license expire;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks related to our employees, managing our growth and our operations

Our future success depends on our ability to retain our key personnel and to attract, retain and motivate qualified personnel.

We are highly dependent on the expertise of David L. Lucchino, our President and Chief Executive Officer, as well as the other principal members of our management, scientific, and clinical teams. Although we have employment agreements, offer letters or consulting agreements with our executive officers, these agreements do not prevent them from terminating their services at any time.

If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period 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 product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous biotechnology and pharmaceutical companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. We may also decide not to replace an executive officer, which may have an adverse effect on our operations. For

example, we do not have a Chief Financial Officer and do not currently intend to fill that position, which could adversely affect our financial reporting and operations.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by other companies or organizations and may have commitments that limit their availability. 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.

Our recent reduction in force undertaken to better align our workforce with the needs of our business and focus more of our capital resources on our pre-clinical program for remyelination in MS.

In February 2023, we implemented a reduction in force affecting approximately 55% of our workforce to better align our workforce with the needs of our business and focus more of our capital resources on our pre-clinical program for remyelination in MS. We believe these changes will preserve capital, ensuring that we are appropriately resourced to complete a first clinical trial of our MS Program. In connection with these actions, we will incur termination costs, which include severance costs and related expenses, which are estimated to be approximately $4.0 million in future cash outlays.

The reduction in force may result in unintended consequences and costs, such as the loss of institutional knowledge and expertise, attrition beyond the intended number of employees, decreased morale among our remaining employees, and the risk that we may not achieve the anticipated benefits of the reduction in force. In addition, while positions have been eliminated certain functions necessary to our operations remain, and we may be unsuccessful in distributing the duties and obligations of departed employees among our remaining employees. The reduction in workforce could also make it difficult for us to pursue, or prevent us from pursuing, new opportunities and initiatives due to insufficient personnel, or require us to incur additional and unanticipated costs to hire new personnel to pursue such opportunities or initiatives. If we are unable to realize the anticipated benefits from the reduction in force, or if we experience significant adverse consequences from the reduction in force, our business, financial condition, and results of operations may be materially adversely affected.

We may engage in transactions that could disrupt our business, cause dilution to our shareholders or reduce our financial resources.

In the future, we may enter into transactions to acquire or in-license rights to product candidates, products or technologies, or to acquire other businesses. If we do identify suitable candidates, we may not be able to enter into such transactions on favorable terms, or at all. Any such acquisitions or in-licenses may not strengthen our competitive position, and these transactions may be viewed negatively by analysts, investors, customers, or other third parties with whom we have relationships. We may decide to incur debt in connection with an acquisition, or in-license or issue our common stock or other equity securities as consideration for the acquisition, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the sellers of the acquired business. In addition, we may not be able to successfully integrate the acquired personnel, technologies, and operations into our existing business in an effective, timely, and nondisruptive manner. Such transactions may also divert management attention from day-to-day responsibilities, increase our expenses, and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or in-licenses or the effect that any such transactions might have on our operating results.

Our business and operations would suffer in the event of security breaches or information technology system failures.

In the ordinary course of our business, we and third parties with which we have relationships will continue to collect and store sensitive data, including clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in data centers and on networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite the implementation of security measures, our computer systems, as well as those of our CROs and other contractors and consultants, are vulnerable to attack, damage and interruption from computer viruses and malware (e.g. ransomware), malicious code, unauthorized access, malfeasance, natural and manmade disasters (including hurricanes), terrorism, war, and telecommunication, electrical failures, hacking, cyberattacks, phishing attacks and other social engineering schemes, employee theft of misuse, human error, fraud, denial or degradation of service attacks, sophisticated nation-state and nation-state-supported actors or unauthorized access or use by persons inside our organization, or persons with access to systems inside our organization.

Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. For instance, companies have experienced an increase in phishing and social engineering attacks from third parties in connection with COVID-19 global pandemic, and the recent hostilities between Russia and Ukraine may result in

increased attacks that could either directly or indirectly impact us. 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. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that our network has experienced any significant 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 delays and/or material disruptions of our research and development programs. For example, the loss of preclinical or clinical trial data from completed, ongoing, or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we currently rely and intend to rely in the future on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. If a security breach or other incident were to result in the unauthorized access to or unauthorized use, disclosure, release or other processing of personal information, it may be necessary to notify individuals, governmental authorities, supervisory bodies, the media and other parties pursuant to privacy and security laws. Any such access, disclosure, notifications, follow-up actions related to such a security breach or other loss of information could result in legal claims or proceedings, liability under data protection laws, and significant costs, including regulatory penalties, fines, and legal expenses, and such an event could disrupt our operations, cause us to incur remediation costs, damage our reputation, and cause a loss of confidence in us and our or such third parties' ability to conduct clinical trials, which could adversely affect our reputation and delay the clinical development of our product candidates.

Our employees work remotely and in a shared office with our sublessor, and we may be subject to heightened operational, confidentiality and cybersecurity risks.

Many of our employees work remotely from home at times. In addition, when in the office, our employees share an open, undivided office space with our sublessor. This subjects us to heightened operational risks. For example, technologies in our employees' homes may not be as robust and could cause the networks, information systems, applications, and other tools available to employees to be more limited or less reliable, and we may be subject to increased cybersecurity risk which could expose us to risks of data or financial loss. In our office, there are risks that individuals accessing our shared office space who are not associated with us may have access to confidential data, including from our clinical trials. There is no guarantee that the security and privacy safeguards we will put in place both for remote work and for our shared office space will be completely effective or that we will not encounter risks associated with unauthorized access to our data and information. If any of these risks were to occur, our business and operations could be materially adversely affected.

Risks related to our common stock

The market price of our common stock has been volatile and fluctuated and may in future fluctuate substantially, which could result in substantial losses for our stockholders.

The market price of our common stock has been highly volatile and subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this section titled "Risk factors" and elsewhere in this Annual Report on Form 10-K, these factors include:

- any delay in the enrollment or ultimate completion of the planned Phase 1 study in our MS Program;
- the results of the planned Phase 1 study in our MS Program, or any future clinical trials of our MS Program or clinical trials of our competitors for the same or similar indication. For example, the price of our common stock decreased significantly following the announcement of our FX-322 Phase 2a (FX-322-202) interim results and our FX-322 Phase 2b (FX-322-208) results;
- our ability to develop our remyelination program in MS, or any additional product candidates based on our PCA approach;
- any delay in submitting a regulatory filing and any adverse development or perceived adverse development with respect to the regulatory review of such filing;
- failure to successfully develop an MS therapeutic or any future product candidates;

- inability to obtain additional funding;
- regulatory or legal developments in the United States and other countries applicable to our PCA approach or any product candidate:
- adverse regulatory decisions;
- changes in the structure of healthcare payment systems;
- adverse developments concerning our CMOs or CROs;
- inability to obtain adequate product supply for our other product candidates, or the inability to do so at acceptable prices;
- introduction of new products, services or technologies by our competitors;
- our ability to effectively manage our growth;
- failure to meet or exceed financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- changes in the market valuations of companies similar to us;
- market conditions in the biotechnology and pharmaceutical sectors, and the issuance of new or changed securities analysts' reports or recommendations;
- announcements of significant acquisitions, strategic collaborations, joint ventures or capital commitments by us or our competitors;
- the termination of a collaboration agreement, licensing agreement or other strategic arrangement, or the inability to establish additional collaboration arrangements that we need on favorable terms, or at all;
- significant lawsuits and their outcomes, including patent or shareholder litigation, and disputes or other developments relating to our proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our product candidates and PCA approach;
- additions or departures of key scientific or management personnel;
- sales of our common stock by us or our shareholders in the future;
- trading volume of our common stock; and
- general economic, industry and market conditions, including the effects of recession or slow economic growth in the U.S. and abroad, interest rates, inflation rates, labor shortages, supply chain difficulties, fuel prices, international currency fluctuations, corruption, political instability, acts of war, including the hostilities between Russia and Ukraine and the escalation of tensions between China and Taiwan, acts of terrorism, and the ongoing COVID-19 pandemic or other public health crises.

In addition, the trading prices for common stock of biopharmaceutical companies continue to be highly volatile as a result of the COVID-19 pandemic and general market conditions, among other reasons. The COVID-19 pandemic and fluctuations in the global economy continue to evolve and remain unpredictable. The extent to which a public health emergency, such as the COVID-19 pandemic, may impact our business and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

Our directors, executive officers and shareholders affiliated with our directors and executive officers own a significant percentage of our common stock and, if they choose to act together, will be able to exert significant influence over matters subject to shareholder approval.

Our directors, executive officers, and shareholders affiliated with our directors and executive officers exert significant influence on us. As of December 31, 2022, these holders beneficially owned approximately 16.4% of the voting power of our outstanding common stock. As a result, these holders, acting together, have significant influence over all matters that require approval of our stockholders, including the election of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transactions. The interests of these holders may not always coincide with our corporate interests or the interests of other shareholders, and they may act in a manner with which our shareholders may not agree or that may not be in the best interests of our other shareholders.

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

We have never declared or paid any cash dividends on our common 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. In addition, our loan and security agreement with Silicon Valley Bank currently prohibits us from paying dividends on our equity securities, and any future debt agreements may likewise preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain on an investment in our common stock for the foreseeable future.

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

As a public company, and particularly after we no longer qualify as an emerging growth company, we will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, or SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Stock Market LLC, and other applicable securities rules and regulations impose various requirements on U.S. reporting public companies, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. For example, these rules and regulations may make it more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified senior management personnel or members for our board of directors. In addition, these rules and regulations are often subject to varying interpretations, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of SOX, or Section 404, we are required to furnish a report by our senior management on our internal control over financial reporting, and our independent registered public accounting firm is required to provide an attestation report on our internal control over financial reporting. However, while we remain an emerging growth company, our independent registered public accounting firm will not be required to provide the attestation report. To ensure compliance with Section 404, we continue to engage in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction on the price of our common stock in the market due to a loss of confidence in the reliability of our financial statements. Furthermore, if we are unable to conclude that our internal control over financial reporting is effective, our investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock could decline.

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

We are an "emerging growth company," as defined in the JOBS Act, and a "smaller reporting company" as defined under the rules promulgated under the Securities Act. As an emerging growth company and a smaller reporting company we may follow reduced disclosure requirements and do not have to make all the disclosures that public companies that are not emerging growth companies or smaller reporting companies do. We will remain an emerging growth company until the earlier of (a) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (b) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (c) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (d) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC, which means the market value of our voting and non-voting common stock that is held by non-affiliates exceeds $700 million as of the last business day of our second fiscal quarter. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404;
- an exemption from compliance with the requirement of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor's report on the financial statements;

- progressively adding to the number of years of audited financial statements required to be included in our periodic reports; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation, stockholder approval of any golden parachute payments not previously approved and having to disclose the ratio of the compensation of our chief executive officer to the median compensation of our employees.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for complying with new or revised accounting standards; and as a result of this election, our financial statements may not be comparable to companies that comply with public company effective dates.

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure, are exempt from the auditor attestation requirements of Section 404, 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.

We may choose to take advantage of some, but not all, of the available exemptions for emerging growth companies and smaller reporting companies. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our shares price may be more volatile.

Provisions in our restated certificate of incorporation and our amended and restated bylaws or Delaware law may discourage, delay or prevent a merger, acquisition or other change in control of our company that our shareholders may consider favorable, including transactions in which our shareholders might otherwise receive a premium for their shares.

Our restated certificate of incorporation and our amended and restated bylaws include certain anti-takeover provisions, including those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents shareholders from filling vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our restated certificate of incorporation regarding the election and removal of directors:
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president, or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors: and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a shareholders' meeting, which may discourage or deter a

potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors.

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 prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed
manner.

Our restated certificate of incorporation and amended and restated bylaws designates specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Our restated certificate of incorporation specifies that, unless we consent in writing to the selection of an alternative forum to the fullest extent permitted by law, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim for breach of a fiduciary duty owed by any of our directors, officers, or other employees to us or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware, our restated certificate of incorporation, or our amended and restated bylaws, (4) any action to interpret, apply, enforce, or determine the validity of our restated certificate of incorporation or our amended and restated bylaws, or (5) any action asserting a claim governed by the internal affairs doctrine. Under our restated certificate of incorporation, this exclusive forum provision will not apply to claims which are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. In addition, our amended and restated bylaws specifies that unless we consent 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 exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. For example, stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near the State of Delaware. The Court of Chancery may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation 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 amended and restated certificate of incorporation to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provisions contained in our amended and restated certificate of incorporation or amended and restated 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.

General Risk Factors

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

Until such time, if ever, as we can generate substantial revenues, we may finance our cash needs through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources. We do not currently have any committed external source of funds. 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 equity or convertible debt securities, our existing stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. In addition, 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. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, intellectual property, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. Furthermore, any capital raising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to advance research programs, product development activities or product candidates. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate product candidate development or future commercialization efforts.

We may be subject to claims by third parties asserting that our employees, consultants or contractors have wrongfully used or disclosed confidential information of third parties, or we have wrongfully used or disclosed alleged trade secrets of their current or former employers, or claims asserting we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at universities or other pharmaceutical or biotechnology companies, including our competitors or potential competitors. In addition, we share an undivided, open office space with our sublessor, and our employees or other individuals who are in our offices may have access to information regarding our sublessor's business, including potentially proprietary information. Although we try to ensure that our employees, consultants, and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our intellectual property assignment agreements with them may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our competitive business position and prospects. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

We are currently subject to securities class action and other shareholder litigation and could be subject to similar or other litigation in the future.

In the past, securities class action and other shareholder litigation has often been brought against companies following a decline in the market price of their securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant share price volatility in recent years. See Note 16, "*Commitments and contingencies – Legal Contingencies*", for a description of our material legal proceedings.

We can make no assurances as to the time or resources that will need to be devoted to these lawsuits or their final outcomes, or the impact, if any, of these lawsuits or any proceedings on our business, financial condition, results of operations and cash flows. While we are vigorously defending against all claims asserted, these lawsuits could result in substantial costs to us and a diversion of our management's attention and resources, which could harm our business. In addition, the uncertainty of the pending lawsuits or potential filing of additional lawsuits could lead to more volatility and a reduction in our stock price.

If securities or industry analysts issue an adverse or misleading opinion regarding our common stock, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical studies and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

The trading price of our common stock has been highly volatile.

The trading price of our common stock has been highly volatile, particularly over the last year. For example, on December 31, 2021, the closing price of our common stock was $5.13 per share and on December 31, 2022 it was $3.85 per share. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and economic factors that are beyond our control. In addition, while the stock market in general has experienced high volatility, biotechnology companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to operating performance. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Sales of a substantial number of shares of our common stock, or the perception that substantial sales might occur, could cause the price of our common stock to fall.

Sales of a substantial number of shares of our common stock, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. The shares of common stock that were sold in the initial public offering of our common stock are freely transferable without restrictions or further registration under the Securities Act of 1933, as amended, or the Securities Act, except for any shares acquired by our affiliates, as defined in Rule 144 under the Securities Act. The remaining shares of our common stock that are outstanding are either unrestricted or restricted as a result of securities laws. In addition, there are shares of common stock that are either subject to outstanding options or reserved for future issuance under our existing equity incentive plans and may become eligible for future sale subject to vesting, and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results.

There has been increasing public focus by investors, customers environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We may experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. We may experience increased costs in order to execute upon our sustainability goals and measure achievement of those goals, which could have an adverse impact on our business and financial condition.

In addition, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted.

Financial volatility or geopolitical instability outside of the U.S. may adversely impact the U.S.

We could be adversely affected by general conditions in the global economy and in the global financial markets. Global credit and financial markets have experienced volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, rising interest rates, declines in consumer confidence, declines in economic growth, increase in unemployment rates and uncertainty about economic stability. Our business and stock price may be adversely affected by any such economic downturn, volatile business environment or large-scale unpredictable or unstable market conditions, including the recent hostilities between Russia and Ukraine and the escalation of tensions between China and Taiwan which could have a lasting impact on regional and global economies.

Item 1B. Unresolved Staff Comments.

None

Item 2. Properties.

Our principal office is located at 75 Hayden Avenue, Lexington, Massachusetts 02421, where we lease approximately 61,307 square feet of office and laboratory space. The lease term commenced on December 11, 2020 and expires on May 31, 2031.

Item 3. Legal Proceedings.

See Note 16, "*Commitments and contingencies – Legal Contingencies*", for more information.

Item 4. Mine Safety Disclosures.

Not applicable

PART II

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

Market Information

Our common stock is traded under the symbol "FREQ" on the Nasdaq Global Select Market.

On February 1, 2023, there were approximately 67 registered holders of record 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. The number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid any dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will require approval from Silicon Valley Bank under the terms of our loan and security agreement. Investors should not purchase our common stock with the expectation of receiving cash dividends.

Equity Compensation Plan Information

Equity compensation plan information will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Recent Sales of Unregistered Equity Securities

During the period covered by this Annual Report on Form 10-K, we did not issue any securities which were unregistered under the Securities Act and required to be disclosed herein.

Use of Proceeds

In October 2019, we issued and sold 6,325,000 shares of our common stock in our initial public offering, or IPO, at a public offering price of $14.00 per share. The offer and sale of all the shares in the IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-233652), as amended, which was declared effective by the SEC on October 2, 2019.

The $79.7 million in net proceeds we received from the IPO have been invested in cash and cash equivalents. There has been no material change in the expected use of the net proceeds from our IPO as described in our final prospectus, dated October 2, 2019, filed with the SEC pursuant to Rule 424(b) relating to our registration statement on Form S-1 on October 4, 2019.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes and other financial information included elsewhere in this Annual Report on Form 10-K. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including those set forth under Item 1A. "Risk Factors" and under "Forward-Looking Statements" in this Annual Report. You should review the section titled "Risk factors" in this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described below.

Overview

We are pioneering a new category in regenerative medicine that aims to restore human function by developing therapeutics that activate a person's innate regenerative potential within the body through the activation of progenitor cells. We believe our progenitor cell activation, or PCA, approach can impact a wide range of degenerative diseases. Our lead preclinical program is designed to activate oligodendrocyte precursor cells with the goal of inducing remyelination and potential functional recovery for individuals living with multiple sclerosis (MS).

Our first application of this technology was for the restoration of the cochlea, with a focus on treating sensorineural hearing loss, or SNHL, which is the most prevalent type of hearing loss. Our lead cochlear regeneration program, FX-322, was designed to treat the underlying cause of SNHL by regenerating cells in the inner ear required for hearing through the activation of progenitor cells already present in the cochlea. Since 2019, we ran five FX-322 clinical studies, all with the aim of understanding safety as well as severities and etiologies that FX-322 might treat and the appropriate dose regime. In several of these studies, we observed that a single dose of FX-322 was associated with statistically significant improvements in hearing function as measured by improved speech perception in subjects with SNHL giving us confidence in the potential of FX-322 as a potential drug candidate for hearing loss.

In 2021 we commenced our sixth study, a Phase 2b clinical trial of FX-322 (FX-322-208), a randomized, placebo-controlled, multi-center study designed to evaluate the impact of a single administration of FX-322 on speech perception in 124 subjects, ultimately enrolling 142 subjects, with either noise-induced or sudden SNHL, the same hearing loss severities and etiologies as those subjects in which statistically significant improvements in speech perception were observed in prior FX-322 clinical trials. The study's primary endpoint was speech perception, a measure of sound clarity and understanding speech. In a Type-C meeting, the FDA agreed that speech perception is an acceptable primary efficacy endpoint. In February 2023, we announced results of FX-322-208 and that the study failed to achieve its primary endpoint of an improvement in speech perception. Data showed no statistically significant difference at day 90 between those administered FX-322 versus those receiving placebo in the proportion of individuals that demonstrated an improvement in speech perception. There were also no measurable improvements observed in any of the study's secondary endpoints. As a result of this outcome, we decided to discontinue the FX-322 development program.

Also in 2021, we introduced a second hearing program, called FX-345, which we believed might expand the opportunity to treat different types of SNHL as FX-345 was designed to achieve exposure at desired drug concentrations through a large portion of the cochlea. Cochlear pharmacokinetic measures and human modeling data in a preclinical setting showed that FX-345 achieved exposure at desired concentrations through a larger portion of the cochlea for longer time as compared to FX-322. The FX-345 program commenced dosing in a Phase 1b study (FX-345-101) in December 2022, completing an initial safety cohort. Given the outcome of the FX-322 study data and the similarities of the two candidates in design, intended mechanism of action, and clinical design components we decided to discontinue the FX-345 development program as well. Ceasing development of our hearing program, while a difficult decision, will allow us to focus our resources to advance the remyelination in MS program, or MS Program, into the clinic.

We are now working to rapidly advance discovery efforts using our PCA approach to potentially remyelinate neurons in individuals with MS. MS induces demyelination, stripping axons of the myelin sheaths that support neuronal signal conduction and axonal survival. We previously reported that we had identified a novel target relevant to myelination. Modulation of this target induces robust oligodendrocyte differentiation and expression of myelin proteins *in vitro*. We have identified multiple novel chemical entities that induce robust remyelination following demyelination in an adult *in vivo* animal model.

The MS Program is independent of the hearing program, with a distinct molecular target, mechanism, progenitor cell population, and small molecule drug candidates. Further, a well-defined clinical path with objective biomarkers such as visual evoked potential (VEP) and magnetic resonance imaging (MRI) exist for studying the performance of remyelination therapies in MS patients. Our novel agents substantially outperform other clinically studied remyelination agents in head-to-head *in vivo* studies. We plan to begin our clinical program for remyelination in MS in the first half of 2024.

On April 8, 2022, we announced a reduction in force of approximately 30% of our workforce to better align our workforce with the near-term needs of our business and focus more of our capital resources on our research and development programs for hearing and remyelination in MS. On February 13, 2023, we announced a restructuring of our business including the discontinuation our hearing program and a downsizing of personnel by approximately 55%. We believe these changes will generate sufficient cost savings to enable us to complete a first clinical trial of our MS Program in the second half of 2024 with cash runway into 2025.

Since our formation in 2014, we have devoted substantially all our resources to developing our PCA approach, conducting research and development activities, including product candidate development, recruiting skilled personnel, establishing our intellectual property portfolio, and providing general and administrative support for these operations. We have financed our operations primarily through private and public securities financings, a term loan, and amounts received under a collaboration agreement.

Since our formation, we have incurred significant operating losses and have not generated any revenue from the sale of products. Our ability to generate any product revenue or product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our product candidates. Our net losses were $81.6 million and $84.7 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $261.7 million. During the periods presented, we do not have any off-balance sheet arrangements.

Our operating expenses discussed in this section reflect our development programs around FX-322, FX-345, MS and any future programs as well as our operations as a public company. We will not generate revenue from product sales unless and until we successfully complete clinical development, obtain regulatory approval for, and successfully commercialize our product candidates, or until our collaborators do so, which could result in milestone payments or royalties to us. If we obtain regulatory approval for any of our product candidates, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing and distribution.

As a result of these anticipated expenditures, we will need additional financing to support our continuing operations. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our cash needs through a combination of public or private equity or debt financings and other sources, which may include current and new collaborations with third parties. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We cannot be sure that we will ever generate sufficient revenue to achieve profitability.
Because of the numerous risks and uncertainties associated with the development of therapeutics, 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 can generate revenue from 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 required to raise additional capital on terms that are unfavorable to us or we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

License and collaboration agreements

Astellas Pharma Inc.

In July 2019, we entered into the Astellas Agreement with Astellas, under which we granted Astellas an exclusive, royalty-bearing, sub-licensable, nontransferable license to certain patent rights to research, develop, manufacture, have manufactured, use, seek, and secure regulatory approval for, commercialize, offer for sale, sell, have sold and import, and otherwise exploit licensed products containing both a GSK-3 inhibitor and an HDAC inhibitor, or the Astellas licensed products, including our product candidate FX-322, outside of the United States. We and Astellas have agreed to jointly develop the Astellas licensed products, including carrying out joint studies. Each party has agreed to use commercially reasonable efforts to carry out development activities assigned to it under an agreed-upon development plan. Astellas has agreed to use commercially reasonable efforts to obtain regulatory approval for at least one Astellas licensed product in SNHL and in age-related hearing loss, in each case in one major Asian country and one major European country. We have agreed to use commercially reasonable efforts to obtain regulatory approval for at least one Astellas licensed product in the United States. Astellas has the sole right to commercialize the Astellas licensed products outside of the United States and we

have the sole right to commercialize the Astellas licensed products in the United States. Astellas has agreed to use commercially reasonable efforts to commercialize Astellas licensed products in a major Asian country and a major European country following receipt of regulatory approval in such countries.

As consideration for the licensed rights under the Astellas Agreement, Astellas paid us an upfront payment of $80.0 million in July 2019 and has agreed to pay potential development milestones up to $230.0 million. Specifically, we would receive development milestone payments of $65.0 million and $25.0 million upon the first dosing of a subject in Phase 2b clinical trial for SNHL in Europe and Asia, respectively and $100.0 million and $40.0 million upon the first dosing of a subject in a Phase 3 clinical for SNHL in Europe and Asia, respectively. If the Astellas Licensed Products are successfully commercialized, we would be eligible for up to $315.0 million in potential commercial milestone payments and tiered royalties at rates ranging from low to mid-teen percentages. The parties shall share equally, on a 50/50 basis, all out-of-pocket costs and joint study costs for all the joint activities conducted pursuant to the development plans or the joint manufacturing plan. Pursuant to our Exclusive Patent License Agreement, or the MIT License, with the Massachusetts Institute of Technology, or MIT, we are required to pay MIT a royalty on sublicense revenues. A royalty of $16.0 million related to the $80.0 million upfront payment received from Astellas was expensed in the quarter ended September 30, 2019 and paid in November 2019. The $80.0 million upfront payment received from Astellas in July 2019 was recorded as deferred revenue and recognized as revenue, using the input method, over the period from execution of the agreement through June 30, 2021, when the Phase 2a clinical trials were completed.

Massachusetts Institute of Technology

In December 2016, we entered into the MIT License, with MIT under which we received an exclusive, worldwide, royalty-bearing license to certain patent rights to develop, make, have made, use, sell, offer to sell, lease, and import products, or the MIT licensed products, and to develop and perform processes, or the MIT licensed processes, which incorporate the licensed technology for the treatment of disease, including but not limited to the prevention and remediation of hearing loss. We are required to use diligent efforts to develop and commercialize the MIT licensed products or processes, and to make such products or processes reasonably available to the public. We are also subject to certain development obligations with regards to a first MIT licensed product. We have satisfied certain obligations related to preclinical studies and the filing of an IND for a first MIT licensed product with our development activities related to FX-322. Our future development obligations are: (i) to commence a Phase 3 clinical trial for such product within five years of the IND filing for such product, (ii) to file a New Drug Application, or NDA, or equivalent with the FDA or comparable European regulatory agency for such product within nine years of the IND filing for such product, and (iii) to make a first commercial sale of such product within 11 years of the IND filing for such product. We also have certain development obligations with regards to a second MIT licensed product.

Upon entering into the MIT License, we paid a $50 thousand license fee payment and issued shares of our common stock equal to 5% of our then-outstanding capital stock to MIT. We are required to pay certain annual license maintenance fees ranging from $30 thousand to $0.1 million per year prior to first commercial sale of a MIT licensed product and an annual license maintenance fee of $0.2 million every year afterwards, which may be credited to running royalties during the same calendar year, if any. We are also required to make potential milestone payments in an aggregate amount of up to $2.9 million on each MIT licensed product or process. In addition, we agreed to pay a low single-digit royalty on the MIT licensed products and processes and a low-twenties royalty on sub-license revenues.

In May 2019, we entered into an amendment with MIT, updating the diligence milestones for a second Licensed Product.

In March 2022, we entered into an amendment with MIT, removing a patent and certain patent applications from the MIT License Agreement which were unrelated to our hearing and MS programs and which we were not utilizing.

Massachusetts Eye and Ear (Formerly Massachusetts Eye and Ear Infirmary)

In February 2019, we entered into an Non-Exclusive Patent License Agreement, or the MEE License, with the Massachusetts Eye and Ear, or MEE, under which we received a non-exclusive, non-sub-licensable, worldwide, royalty-bearing license to certain patent rights to develop, make, have made, use, sell, offer to sell, lease, and import products, and to develop and perform processes that incorporate the licensed technology for the treatment or prevention of hearing loss, or the MEE licensed products. We are obligated to use diligent efforts to develop and commercialize the MEE licensed products. We met one of our milestone timeline obligations by dosing a first subject in a Phase 2 trial by December 31, 2020. We are still subject to a milestone timeline obligation to dose a first subject in a Phase 3 trial by December 31, 2024.

Upon entering into the MEE License, we made a $20 thousand license fee payment. We are obligated to pay certain annual license maintenance fees between $5 thousand and $7.5 thousand per each MEE patent family case number included in the licensed MEE patent rights prior to first commercial sale of an MEE licensed product. We are also obligated to pay a minimum annual royalty payment of $15 thousand per each MEE patent family case number included in the licensed MEE patent rights after first commercial sale of an MEE licensed product. We are also obligated to make milestone payments up to $350 thousand on each product or process that incorporates the licensed patent rights. In addition, we have agreed to pay a low single-digit royalty on products and processes that incorporate the licensed patent rights.

The Scripps Research Institute (California Institute for Biomedical Research)

In September 2018, we entered into a license agreement, or the CALIBR License, with the California Institute for Biomedical Research, or CALIBR, a division of Scripps, under which we received an exclusive, worldwide, royalty-bearing license to certain patent rights to make, have made, use, sell, offer to sell, and import products, or the CALIBR licensed products, which incorporate licensed technology for the treatment of MS. We have agreed to use commercially reasonable efforts to develop, manufacture, and sell at least one CALIBR licensed product. We are also subject to certain milestone timeline obligations, which may be extended in certain circumstances as described in the CALIBR License. In October 2021, we entered into an amendment with CALIBR which updated the milestone obligations to: (i) initiate a Phase 2 clinical trial (or equivalent) for a CALIBR licensed product by December 31, 2023 and (ii) initiate a Phase 3 clinical trial (or equivalent) for a CALIBR licensed product by December 31, 2025.

Upon entering into the CALIBR License, we made a $1.0 million license fee payment, and are required to make milestone payments in an aggregate amount of up to $26.0 million for each category of CALIBR licensed products. Category 1 is any CALIBR licensed products containing a compound that modulates any muscarinic receptor, and Category 2 is any CALIBR licensed products not included in Category 1 that could differentiate oligodendrocyte precursor cells from *in vitro* studies and/or are active in animal models relevant to MS. We are also required to pay a mid-single-digit royalty on CALIBR licensed products and a royalty on sub-license revenues ranging from a low-teen percentage to 50%.

Components of our results of operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales in the foreseeable future. In July 2019, we entered into the Astellas Agreement and received an upfront license fee payment of $80.0 million. In accordance with ASC 606, we recognized the $80.0 million as revenue over the period that research and development services for the Phase 2a clinical study for FX-322 (FX-322-202) were being provided using the input method. These research and development services concluded in June 2021. As such, $14.1 million of the $80.0 million upfront fee was recognized as revenue in the year ended December 31, 2021. No revenue was recognized in the year ended December 31, 2022.

Research and development expenses

Research and development expenses presented in this section consist primarily of costs related to activities largely focused on hearing restoration and MS. These expenses include the following:

- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, and other third parties that conduct preclinical research and development activities and clinical trials on our behalf;
- costs to manufacture our clinical trial material for use in our preclinical studies and clinical trials;
- costs of outside consultants, including their fees and related travel expenses;
- costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials;
- option and license payments made to third parties, including MIT, Scripps, and MEE for intellectual property used in research and development activities; and

- facility-related expenses, which include direct depreciation costs and expenses for rent and maintenance of facilities and other operating costs if specifically, identifiable to research activities.

We track external research and development costs, including the cost of services, outsourced research and development, clinical trials, contract manufacturing, laboratory equipment and maintenance, and certain other development costs, by product candidate when the costs are specifically identifiable to a product candidate. Internal and external costs associated with infrastructure resources, other research and development costs, facility-related costs, and depreciation and amortization that are not identifiable to a specific product candidate are included in the platform development, early-stage research, and unallocated expenses category.

We cannot determine with certainty the duration and costs of future clinical trials of any product candidate we may develop or if, when, or to what extent we will generate revenue from the commercialization and sale of any product candidate for which we obtain marketing approval. The duration, costs, and timing of clinical trials and development of any product candidate we may develop will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of clinical trials of product candidates and other research and development activities that we may conduct;
- the actual probability of success for our product candidates, including their safety and efficacy, early clinical data, competition, manufacturing capability, and commercial viability;
- significant and changing government regulation and regulatory guidance;
- the timing and receipt of any marketing approvals;
- the progress of the development efforts of parties with whom we may enter into collaboration agreements;
- our ability to secure manufacturing supply through relationships with third parties;
- the commercialization of our product candidates, if and when approved;
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- the impact of public health emergencies, such as COVID-19, on our ongoing and planned trials.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, business development, and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; professional fees for accounting, auditing, tax and consulting services; investor and public relations costs; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and expenses for rent and maintenance of facilities, and other operating costs that are not specifically attributable to research and development activities.

Interest income

Interest income consists of interest earned on cash equivalents and marketable securities.

Interest expense

Interest expense consists of interest paid on our term loan.

Realized gain (loss) on investments

Realized gain (loss) on investments represents the gain or loss realized on our marketable securities.

Foreign exchange (loss) gain

Foreign exchange (loss) gain represents the loss or gain recorded as a result of remeasuring the financial statements of our foreign subsidiaries.

Other income (expense), net

Other income (expense), net consists of amortization expense and accretion income on investments as well as sublease income.

Income taxes

Since our inception in 2014, we have generated cumulative federal and state net operating loss and research and development credit carryforwards for which we have not recorded any net tax benefit due to uncertainty around utilizing these tax attributes within the respective carryforward periods.

As of December 31, 2022, we had federal net operating loss carryforwards of approximately $174.1 million and Massachusetts net state operating loss carryforwards of approximately $141.3 million which may be available to offset future taxable income. The U.S. federal net operating loss carryforwards include $22.4 million available to reduce future taxable income through 2037 and approximately $151.7 million which do not expire and are available to reduce future taxable income indefinitely. The state net operating loss carryforwards are available to offset future taxable income through 2042. As of December 31, 2022, we also had federal and Massachusetts research and development tax credit carryforwards of $8.2 million and $3.6 million, respectively, which are available to offset federal and state tax liabilities through 2042 and 2037, respectively. Realization of future tax benefits is dependent on many factors, including our ability to generate taxable income within the net operating loss carryforward period. 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 provided under Sections 382 and 383 of the Code, respectively, as well as similar state provisions. These ownership changes may limit the number of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382 of the Code, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50% over a rolling three-year period. We have completed several financings and have conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception and have determined that an ownership change did occur in March 2017. Accordingly, utilization of $12.4 million of the U.S. net operating loss carryforwards which were incurred prior to March 2017 (pre-ownership change) is limited under Section 382 of the Code. After the limitations under Section 382 of the Code, we may utilize approximately $10.8 million of its pre-ownership change net operating loss carryforwards based upon an annual usage of approximately $1.6 million for each of the next five years after the ownership change and approximately $0.2 million for each of the 15 years thereafter. The remaining pre-March 2017 ownership change net operating losses of approximately $1.6 million were written off due to expiration under limitation. The limitation has been determined by first multiplying the value of our stock at the time of the ownership change by the applicable long-term tax-exempt rate. These carryforwards may be subject to further annual limitations under Section 382 of the Code in the event of future changes in ownership. Additionally, we have determined an ownership changed occurred in October of 2019 as a result of the IPO. Accordingly, utilization of approximately $46.1 million of the U.S. net operating loss carryforwards incurred prior to October 2019 is also limited under Section 382 of the Code. We have determined it will be able to utilize the entire $46.1 million of our pre-ownership change net operating loss carryforwards based upon the limitations calculated from the October 2019 ownership change. These carryforwards may be subject to further annual limitations under Section 382 of the Code in the event of future changes in ownership.

Results of operations

Comparison of years ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021:

	Years ended December 31,	
	2022	2021
Revenue	$ —	$ 14,068
Operating expenses:		
Research and development	49,418	60,923
General and administrative	33,584	37,176
Total operating expenses	83,002	98,099
Loss from operations	(83,002)	(84,031)
Interest income	1,327	397
Interest expense	(961)	(764)
Realized gain (loss) on investments	3	(23)
Foreign exchange (loss) gain	(5)	16
Other income (expense), net	1,056	(266)
Loss before income taxes	(81,582)	(84,671)
Tax benefit (provision)	2	(15)
Net loss	$ (81,580)	$ (84,686)

Revenue

No revenue was recognized for the year ended December 31, 2022 compared to $14.1 million for the year ended December 31, 2021. In July 2019, we entered into the Astellas Agreement and received an upfront license fee payment of $80.0 million. In accordance with ASC 606, we recognized the $80.0 million as revenue over the period that research and development services were provided and the Phase 2a clinical study for FX-322 was carried out using the input method. These research and development services concluded in June 2021.

Research and development expenses

	Years ended December 31,		Increase (Decrease)
	2022	2021	(in thousands)
Direct research and development expenses by therapeutic area and product candidate:			
FX-322	$ 10,855	$ 10,334	$ 521
FX-345	4,217	5,471	(1,254)
Multiple Sclerosis	4,782	6,627	(1,845)
Platform development, early-stage research and unallocated expenses:			
Employee-related	20,015	25,557	(5,542)
Laboratory supplies	272	716	(444)
Outsourced research and development	403	2,305	(1,902)
Facility-related	6,403	6,898	(495)
Depreciation and amortization	1,618	1,599	19
Other research and development	853	1,416	(563)
Platform development, early-stage research and unallocated expenses total	29,564	38,491	(8,927)
Total research and development expenses	$ 49,418	$ 60,923	$ (11,505)

The $10.9 million of costs related to FX-322 incurred for the year ended December 31, 2022 consisted primarily of $10.0 million of clinical costs associated with ongoing trials, including the recently completed Phase 2b clinical trial (FX-322-208), and $0.6 million of drug development and manufacturing costs. The $10.3 million of costs related to FX-322 incurred for the year ended December 31, 2021 consisted primarily of $8.4 million of clinical costs associated with ongoing trials and $1.9 million of drug development and manufacturing costs. The overall increase from the year ended December 31, 2021 is due primarily to the FX-322-208 clinical trial activity in the year ended December 31, 2022.

The $4.2 million of costs related to FX-345 incurred for the year ended December 31, 2022 consisted primarily of $2.6 million of drug development and manufacturing costs, $1.2 million in clinical costs associated with the FX-345-101 trial, which we initiated in 2022, and $0.4 million in preclinical safety costs. The $5.5 million of costs related to FX-345 incurred for the year ended December 31, 2021 consisted of $3.1 million in preclinical safety costs and $2.3 million in drug development and manufacturing costs. The overall decrease from the year ended December 31, 2021 is due primarily to the conclusion of preclinical safety work partially offset by costs related to the initiation of the FX-345-101 trial in the year ended December 31, 2022.

The $4.8 million of costs related to MS incurred for the year ended December 31, 2022 consisted primarily of $2.6 million of chemistry and compound characterization costs, $0.7 million in drug development and manufacturing costs, $0.6 million in preclinical safety costs, and $0.4 million in *in vitro* and *in vivo* testing costs. The $6.6 million of costs related to MS incurred for the year ended December 31, 2021 consisted of $3.0 million in preclinical safety costs, $1.6 million in chemistry and compound characterization costs, $0.9 million in *in vitro* and *in vivo* testing costs, and $0.8 million in drug development and manufacturing costs. The overall decrease from the year ended December 31, 2021 is due primarily to a reduction in development and testing costs as we progressed from exploratory activities to identification of specific proprietary compounds that act as our novel target for remyelination in MS.

The $29.6 million of platform development, early-stage research and unallocated expenses incurred for the year ended December 31, 2022 consisted primarily of $20.0 million in employee related costs, including $7.7 million in stock-based compensation expense, $6.4 million of facility-related costs, and $1.6 million of depreciation expense. The decrease from the year ended December 31, 2021 is primarily attributable to a $5.5 million decrease in employee-related expenses due predominantly to our April 2022 reduction in force, a $1.9 million decrease in outsourced research and development expenses as we decreased sponsored research, and a $0.6 million decrease in other research and development expenses as we reduced our reliance on third-party consulting.

General and administrative expenses

The $33.6 million of general and administrative expenses for the year ended December 31, 2022 consisted primarily of $20.6 million of employee-related costs, including $12.1 million in stock-based compensation expense, $5.6 million of professional services costs, $2.7 million in directors' and officers' insurance costs, $1.6 million in rent expense, including utilities and common area maintenance, or CAM, charges, and $1.1 million in depreciation expense. General and administrative expenses decreased $3.6 million from December 31, 2021 due to a $2.1 million decrease in professional services costs as we reduced our reliance on third-party consulting and public relations vendors, a $0.6 million decrease in directors' and officers' insurance costs, and a $0.5 million decrease in employee-related costs due primarily to the April 2022 reduction in force.

Interest income

Interest income was $1.3 million for the year ended December 31, 2022 compared to $0.4 million for the year ended December 31, 2021, due to increases in interest rates from the previous year.

Interest expense

Interest expense was $1.0 million for the year ended December 31, 2022 compared to $0.8 million for the year ended December 31, 2021, due to increases in the interest rate on our term loan.

Realized gain (loss) on investments

Realized gain on investments was $3 thousand for the year ended December 31, 2022 compared to a loss of $23 thousand for the year ended December 31, 2021 due to changes in the composition of investments year over year.

Foreign exchange (loss) gain

Foreign exchange loss was $5 thousand for the year ended December 31, 2022 compared to a gain of $16 thousand for the year ended December 31, 2021. The decrease was due to differences in foreign exchange remeasurement of the financial statements of our foreign subsidiaries.

Other income (expense), net

Other income, net was $1.1 million for the year ended December 31, 2022 compared to expense of $0.3 million for the year ended December 31, 2021. The change from the prior year is due to the inclusion of sublease income beginning in the third quarter of 2022.

Income taxes

Income tax benefit was $2 thousand for the year ended December 31, 2022 compared to expense of $15 thousand for the year ended December 31, 2021.

Liquidity and capital resources

Since our inception, we have incurred significant operating losses. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance the preclinical and clinical development of our product candidates. We expect that our research and development and general and administrative costs will continue to fluctuate, in connection with conducting preclinical studies and clinical trials for our product candidates, contracting with contract manufacturing organizations, or CMOs, to support preclinical studies and clinical trials, expanding our intellectual property portfolio, and providing general and administrative support for our operations. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements or other sources.

We do not currently have any approved products and have never generated any revenue from product sales. We have financed our operations primarily through proceeds from private and public securities financings, a term loan, and amounts received under a collaboration agreement. To date, we have raised approximately $378.3 million, including from grants and option exercises. Our cash, cash equivalents and marketable securities totaled $83.1 million as of December 31, 2022. As of December 31, 2022, we had $10.0 million of current debt and $4.2 million of non-current debt related to our term loan.

In December 2020, we entered into a Loan and Security Agreement with a commercial bank for a term loan with a principal balance of $15.0 million. We made monthly interest only payments through November 30, 2022. The principal balance and interest will be repaid in equal monthly installments through May 1, 2024. Advances under the Loan Agreement will bear an interest rate equal to the greater of either (i) 1.50% plus the Prime Rate (as reported in *The Wall Street Journal*, subject to an interest rate floor of zero) or (ii) 4.75%.

In December 2021, we entered into an Equity Distribution Agreement with Oppenheimer & Co. Inc., or Oppenheimer, to sell shares of our common stock, having an aggregate offering price of up to $125.0 million, from time to time, through an “at the market” equity offering program under which Oppenheimer will act as sales agent and/or principal, or the ATM Program. During the year ended December 31, 2022, we sold 12,767 shares of common stock under the ATM Program for net proceeds of approximately $50 thousand and paid $2 thousand to Oppenheimer in sales agent fees.

On April 8, 2022, we announced a reduction in force of approximately 30% of our workforce to better align our workforce with the needs of our business and focus more of our capital resources on our research and development programs. The total costs related to this reduction in force are approximately $1.0 million in research and development expense and $0.2 million in general and administrative expense, primarily related to severance costs and related expenses.

On February 13, 2023, we announced a restructuring that included downsizing personnel by approximately 55%. These changes are expected to preserve capital, ensuring that we are appropriately resourced to complete a first clinical trial of our MS Program in the second half of 2024. The total costs related to this downsizing are approximately $2.3 million in research and development expense and $1.7 million in general and administrative expense, primarily related to severance costs and related expenses.

Cash flows

The following table summarizes our sources and uses of cash for the periods presented:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Net cash used in operating activities	$ (58,237)	$ (76,059)
Net cash provided by (used in) investing activities	31,133	(66,126)
Net cash (used in) provided by financing activities	(577)	1,358
Net decrease in cash and cash equivalents	$ (27,681)	$ (140,827)

Cash flows for the year ended December 31, 2022

Operating activities

Net cash used in operating activities for the year ended December 31, 2022 was $58.2 million, consisting of a net loss of $81.6 million. The net loss was partially offset by non-cash items related to normal business operations including stock-based compensation expense of $19.8 million, depreciation expense of $2.8 million, non-cash lease expense of $2.4 million and non-cash interest expense of $0.4 million. Net cash used in operating activities was also impacted by a net $2.0 million decrease in operating assets and liabilities, primarily the result of the continued reduction of lease liabilities over the term of the our leased office space.

The decrease in net cash used in operating activities for the year ended December 31, 2022 compared to the year ended December 31, 2021 is primarily due to changes in operating assets and liabilities year over year. Specifically, deferred revenue decreased $14.1 million in the year ended December 31, 2021 due to the recognition of revenue related to the Astellas Agreement. No such decrease occurred in the year ended December 31, 2022. The decrease from December 31, 2021 is also partially due to a $3.1 million decrease in net loss.

Investing activities

Net cash provided by investing activities for the year ended December 31, 2022 was $31.1 million, which was attributable to $85.3 million in redemptions of marketable securities and $17 thousand in sales of property and equipment partially offset by $54.2 million of purchases of marketable securities.

The increase in net cash provided by investing activities for the year ended December 31, 2022 compared to the year ended December 31, 2021 is primarily due to a $56.1 million increase in the redemption of marketable securities and a $38.2 million decrease in the purchase of marketable securities. The increase is also due to a $2.9 million decrease in purchases of property and equipment from the year ended December 31, 2021 as we furnished our new office and laboratory space in 2021 and did not incur such expenditures in 2022.

Financing activities

Net cash used in financing activities for the year ended December 31, 2022 was $0.6 million, primarily attributable to $0.8 million in term loan repayments partially offset by $0.2 million in proceeds from the Employee Stock Purchase Plan and $60 thousand in proceeds from the issuance of common stock under the ATM and exercises of common stock.

The increase in net cash used in financing activities for the year ended December 31, 2022 compared to December 31, 2021 is primarily attributable to the $1.2 million decrease in proceeds from the issuance of common stock. Additionally, we began making principle repayments on our term loan in the year ended December 31, 2022.

Cash flows for the year ended December 31, 2021

Operating activities

Net cash used in operating activities for the year ended December 31, 2021 was $76.1 million, consisting of a net loss of $84.7 million. The net loss was partially offset by non-cash items related to normal business operations including stock-based compensation expense of $21.8 million, depreciation expense of $2.8 million, non-cash lease expense of $1.1 million and non-cash interest expense of $0.4 million. Net cash used in operating activities was also impacted by a net $17.3 million decrease in operating assets and liabilities, primarily due to the $14.1 million reduction in deferred revenue as all remaining

revenue related to the Astellas Agreement was recognized in the year ended December 31, 2021 as well as a $2.3 million decrease in accounts payable due to the timing of invoice receipt and payment.

Investing activities

Net cash used in investing activities for the year ended December 31, 2021 was $66.1 million, which was attributable to $92.4 million of purchases of marketable securities and $2.9 million of purchases of property and equipment, partially offset by $29.2 million in redemptions of marketable securities.

Financing activities

Net cash provided by financing activities for the year ended December 31, 2021 was $1.4 million, primarily attributable to $1.3 million in proceeds from the exercise of stock options and $60 thousand in proceeds from the Employee Stock Purchase Plan.

Funding requirements

We expect our future operating expenses to reflect our ongoing research and development for our MS Program, preclinical activities, studies for INDs, and initiation of clinical trials. In addition, we expect to maintain general and administrative costs to manage the requirements of operating as a public company.

Specifically, our costs and expenses will increase as we:

- pursue the preclinical and clinical development of a candidate for remyelination in MS and any other product candidates using our PCA approach; and
- maintain, expand, and protect our intellectual property portfolio.

We believe that our existing cash, cash equivalents, and marketable securities, will enable us to fund our operating expenses and capital expenditure requirements into 2025. We have based this estimate on assumptions that may prove to be incorrect, and we could utilize our available capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with the research, development, and commercialization of therapeutics, it is difficult to estimate with certainty the amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the progress, costs, and results of our research and preclinical development program for remyelination in MS;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA and comparable foreign regulatory authorities, if applicable, for our product candidates;
- business and operations interruptions resulting from public health emergencies, such as the COVID-19 global pandemic;
- the costs and timing of internal process development, manufacturing activities, and clinical trial management associated with product candidates we advance through preclinical and clinical development;
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements;
- the scope, progress, results, and costs of any product candidates that we may derive from our PCA approach or any other product candidates we may develop alone or with collaborators;
- the extent to which we in-license or acquire rights to other products, product candidates, or technologies;
- additions or departures of key scientific or management personnel;
- the costs and timing of preparing, filing, and prosecuting patent applications, maintaining and protecting our intellectual property rights, and defending against any intellectual property-related claims; and
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales, and distribution for any product candidates for which we or our collaborators obtain marketing approval.

Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our cash needs through a combination of public or private equity or debt financings and other sources, which may include current and new collaborations with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. 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. If we raise additional funds through other sources, such as collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, product development, and 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 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 products or product candidates that we would otherwise prefer to develop and market ourselves.

Contractual obligations and commitments

We are party to an operating lease of approximately 61,307 square feet of office and laboratory space in Lexington, Massachusetts with a term through May 31, 2031. Pursuant to this lease, we have provided a security deposit of $1.7 million which is classified as restricted cash as of December 31, 2022. As of December 31, 2022, our operating lease obligations under this lease are $40.2 million. See Note 14, "*Leases",* for additional information regarding this lease.

Payment obligations for future milestone payments under our collaboration and license agreements are contingent upon future events, such as the achievement of specified product development milestones or generating product sales, and we are unable to estimate the timing or likelihood of achieving these milestones or generating future product sales. We were also required to use diligent efforts to develop and commercialize the MIT licensed products or processes, and to make such products or processes reasonably available to the public under the MIT License. See "—License and collaboration agreements" for more information regarding our payment obligations under these agreements.

We also enter into contracts in the normal course of business with CROs, CMOs, universities, and other third parties for preclinical research studies, clinical trials and testing and manufacturing services. These contracts generally do not contain minimum purchase commitments and are cancelable by us upon prior written notice although, purchase orders for clinical materials are generally non-cancelable. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including non-cancelable obligations of our service providers, up to the date of cancellation or upon completion of a manufacturing run. The amount and timing of such payments are not known or are not material.

Critical accounting policies and use of estimates

Our management's discussion and analysis of financial condition and results of operations is based on our audited consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, revenue, costs and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events, and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

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

Revenue recognition

We account for contracts with customers in accordance with Accounting Standards Codification (ASC), Topic 606, *Revenue from Contracts with Customers* (ASC 606), including all amendments thereto. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as collaborative arrangements and leases. Our disclosure in the accompanying consolidated financial statements reflects the Company's accounting policies in compliance with this standard.

Under ASC 606, an entity recognizes revenue when or as its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To recognize revenue for arrangements that an entity determines are within the scope of ASC 606, the entity performs the

following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies its performance obligations. We only apply the five-step model to contracts when it is probable that the entity will collect substantially all of the consideration to which it will be entitled in exchange for the goods or services it transfers to the customer. Once a contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and identifies as a performance obligation each promise to transfer to the customer either (a) a good or service (or bundle of goods and services) that is distinct, or (b) a series of distinct goods and services that are substantially the same and have been the same pattern of transfer to the customer.

We assess whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner (the "customer" in this type of arrangement) and the availability of the associated expertise in the general marketplace. We also consider the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, an entity is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct. For each arrangement that results in revenues, we identify all performance obligations, which may include, for example, a license to IP and know-how, research and development activities, and/or manufacturing services.

In addition to any upfront payment, if the consideration promised in a contract includes a variable amount, we estimate the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. We determine the amount of variable consideration by using the expected value method or the most likely amount method. We include the estimated variable consideration in the transaction price to the extent it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. If it is probable that a significant revenue reversal will not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or of the licensee such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

For contracts that include sales-based royalties (including milestone payments based on the level of sales) promised in the exchange for licenses of intellectual property, and the license is deemed to be the predominant item to which the royalties relate, we recognize royalty revenue and sales-based milestone payments at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied. In determining the transaction price, we adjust the promised amount of consideration for the effects of the time value of money if the timing of payments provides the Company or the Company's customer with a significant benefit of financing the transfer of goods and services. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. We assess each of its revenue generating arrangements in order to determine whether a significant financing component exists. We recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied, either at a point in time or over time. For performance obligations satisfied over time, we measure progress toward completion of its performance obligations using an input method based on our efforts and inputs to satisfy its performance obligations relative to total expected inputs to the satisfaction of that performance obligation.

Amounts received from a customer prior to revenue recognition are recorded as deferred revenue. Amounts received from a customer that are expected to be recognized as revenue within the 12 months following the balance sheet date are classified as a current liability in the consolidated balance sheets.

Our only revenue recognized since inception is related to the Astellas Agreement. At commencement of the Astellas Agreement, we estimated the performance obligation, the completion of the Phase 2a clinical trial of (FX-322-202), would be satisfied by June 30, 2021. Consistent with our estimate, the performance obligation was satisfied in June 2021.

Accrued research and development expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. 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. Most 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 of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to the following:

- CROs and other third parties in connection with performing research and development activities and conducting preclinical studies and clinical trials on our behalf;
- Vendors in connection with preclinical development activities; and
- CMOs and other vendors in connection with product manufacturing and development and distribution of preclinical supplies.

We base our expenses related to preclinical studies on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs that conduct and manage preclinical studies and clinical trials and CMOs that manufacture product for our research and development activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. 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 cause us to report amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Stock-based compensation

We measure stock options and other stock-based awards granted to our employees, directors, consultants, advisors based on the fair value on the date of the grant, awards, net of actual forfeitures, over the requisite service period, which is generally the vesting period of the respective award. For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed.

We estimate the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options, and our expected dividend yield. Although we do not expect our estimates to be materially different from amounts actually incurred, our option pricing model may cause us to report amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of stock-based compensation expense.

Recent accounting pronouncements

A description of recent accounting pronouncements that may potentially impact our financial position, results of operations, or cash flows is disclosed below:

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses* (Topic 326): Measurement of Credit Losses on Financial Instruments. The FASB has subsequently issued amendments to ASU 2016-13, which have the same effective date and transition date. These standards require that credit losses be reported using an expected losses model rather than the incurred losses model that was previously used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, this standard now requires allowances to be recorded instead of reducing the amortized cost of the investment. These standards limit the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and requires the reversal of previously recognized credit losses if fair value increases. We adopted this standard on January 1, 2023 and it did not have a material impact on the consolidated financial statements.

There are no other recent accounting pronouncements that we believe will have a material impact on our consolidated financial statements.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. Our interest-earning assets consist of cash, cash equivalents and marketable securities, which are denominated in U.S. dollars. We had cash, cash equivalents and marketable securities of $83.1 million, or 69% of our total assets, at December 31, 2022. Interest income earned on these assets was $1.3 million for the year ended December 31, 2022. We also had interest expense of $1.0 million on our term loan for the year ended December 31, 2022. Our interest income and interest expense are sensitive to changes in the general level of interest rates, primarily U.S. interest rates. Such instruments carry a degree of interest rate risk; however, if a change by 10% in interest rates were to have immediately occurred on December 31, 2022, such change would not have had a material impact on our financial position or results of operations. We had $10.0 million of current debt and $4.2 million non-current debt outstanding as of December 31, 2022.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the reports of our independent registered public accounting firms, appear at pages F-1 through F-29 of this Annual Report on Form 10-K for the year ended December 31, 2022. An index of those financial statements is found in Item 15 of Part IV of this Annual Report on Form 10-K.

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

None

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer and Vice President, Finance and Operations (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our Chief Executive Officer and Vice President, Finance and Operations concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. 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 policies or procedures may deteriorate. Our internal control over financial reporting is a process designed under the supervision of our principal executive officer and principal financial officer to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles.

Our management, with the participation of Chief Executive Officer and Vice President, Finance and Operations (our principal executive officer and principal financial officer, respectively), conducted an evaluation of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control –Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2022.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the period covered by this Annual Report on Form 10-K that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

On March 7, 2023, Christopher Loose, Ph.D., notified the Board of Directors of the Company of his resignation as the Company's Interim Chief Executive Officer, effective immediately. David Lucchino, the Company's President and Chief Executive Officer, has returned from a temporary medical leave of absence and resumed his position in full as Chief Executive Officer. Dr. Loose will continue to serve in his position as the Company's Chief Scientific Officer.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The following table sets forth information regarding our executive officers and directors as of the date of this Annual Report on Form 10-K.

Name	Age	Position
Executive Officers		
David L. Lucchino	54	President, Chief Executive Officer, Director, and Co-Founder
Christopher R. Loose, PhD.	42	Chief Scientific Officer and Co-Founder
Carl P. LeBel, Ph.D.	64	Chief Development Officer
Quentin McCubbin	53	Chief Manufacturing Officer
Wendy S. Arnold	51	Chief People Officer
Non-Employee Directors		
Timothy J. Barberich	75	Vice Chairperson and Director
Cynthia L. Feldmann	70	Director
Michael Huang	49	Director
Robert S. Langer, Sc.D.	74	Director
Joel S. Marcus	75	Director

Executive officers

David L. Lucchino has served as our President and Chief Executive Officer and a member of our board of directors since November 2014 and was a co-founder of our Company with Dr. Robert S. Langer and Dr. Christopher R. Loose. From December 2014 until June 2016, Mr. Lucchino served as the President of Entrega Bio, a biotechnology company focused on oral drug delivery technology. Prior to that, Mr. Lucchino co-founded Semprus BioSciences, or Semprus, a biotechnology company, and served as its President and Chief Executive Officer from June 2007 to June 2012. Mr. Lucchino oversaw the development of the company's lead medical product, which received FDA clearance in 2012. Semprus was acquired by Teleflex, Inc., or Teleflex, in June 2012. Prior to Semprus, Mr. Lucchino worked at the investment firm Polaris Partners. He started his biotech career by Co-Founding LaunchCyte, an investment firm where he was also a Managing Director. Mr. Lucchino is the past chairman of the board of directors of MassBio, a nonprofit organization that represents over 1500 life science firms and provides services and support for the biotechnology industry in Massachusetts. He is a member of the College of Fellows of the American Institute for Medical and Biological Engineering and was appointed by Massachusetts' Governor Charlie Baker as a member of the Commonwealth's STEM Advisory Council. Mr. Lucchino also served as a trustee of Mt. Auburn Hospital, a Harvard Medical School facility for fifteen years, a trustee of the Multiple Myeloma Research Foundation, and a member of the Board of NOLS (The National Outdoor Leadership School). Mr. Lucchino holds an MBA from the Massachusetts Institute of Technology's Sloan School of Management, an M.S. from the Newhouse School of Journalism at Syracuse University, and a B.A. in Philosophy and Religious Studies from Denison University. We believe Mr. Lucchino's extensive management experience in the biotechnology and pharmaceutical industry qualifies him to serve on our board of directors.

Christopher R. Loose, Ph.D. co-founded our company and has served as our Chief Scientific Officer since January 2016. Prior to our company, Dr. Loose co-founded Semprus with Mr. Lucchino and Dr. Langer and served as its Chief Technology Officer from June 2007 until its acquisition by Teleflex in June 2012. At Semprus, he led the technology team in the development through regulatory clearance of medical products designed to reduce infection and clotting. Prior to Semprus, Dr. Loose worked as a chemical engineer at Merck Research Labs. In 2011, Dr. Loose was awarded the inaugural

Peter Strauss Entrepreneurial Award from the Hertz Foundation. From 2014 to 2021, Dr. Loose served as an Associate Professor Adjunct of Urology at the Yale School of Medicine and Executive Director of Yale University's Center for Biomedical Innovation and Technology, and he continues to serve as a Lecturer in Yale School of Management. Dr. Loose holds a Ph.D. in Chemical Engineering from MIT and a BSE in Chemical Engineering summa cum laude from Princeton University.

Carl P. LeBel, Ph.D. has served as our Chief Development Officer since March 2018. In 2017, Dr. LeBel founded LeBel Consulting, LLC, a biopharmaceutical consulting company. From February 2009 until November 2016, Dr. LeBel served as the Chief Scientific Officer of Otonomy, Inc., or Otonomy, a biopharmaceutical company where he was responsible for all research and development activities. From 2008 to 2009, he served as the President and Chief Executive Officer of Akesis Pharmaceuticals, Inc., or Akesis, a virtual metabolic disorders company. Prior to Akesis, Dr. LeBel served as an Executive Director in a variety of research and development management positions for Amgen, Inc., or Amgen, a biopharmaceutical company. Before joining Amgen, Dr. LeBel served as a Research Scientist at Alkermes, Inc. Dr. LeBel is a scientific fellow of the American Academy of Otolaryngology and a full member of the Association for Research in Otolaryngology, the American Association for the Advancement of Science and the Society of Toxicology. Dr. LeBel is a co-inventor on numerous patents in the field of drug delivery and treatment for otology-related disorders. He was a National Institute of Environmental Health Sciences post-doctoral fellow in Molecular Neurotoxicology at the University of California Irvine. Dr. LeBel holds a Ph.D. in Biomedical Sciences and Toxicology from Northeastern University and a B.S. in Chemistry from the University of Detroit. As a result of our restructuring announced in February 2023, Dr. LeBel will be leaving the Company effective March 31, 2023.

Quentin McCubbin, Ph.D. has served as our Chief Manufacturing Officer since January 2021. He joined our company from Cerevel Therapeutics, Inc., or Cerevel, a clinical-stage biotechnology company, where he served as Head of Technical Operations for two years. Prior to Cerevel, he spent 19 years at Takeda/Millennium Pharmaceuticals in a variety of roles including six years as Vice President of Pharmaceutical Sciences and Global Head of Process Chemistry. He began his career as a chemist, completing a post-doctoral fellowship at Imperial College in London. He earned his B.S. and Ph.D. in Chemistry from Monash University in Australia.

Wendy S. Arnold has served as our Chief People Officer since February 2020. Ms. Arnold previously served as Senior Vice President, Human Resources at Kaleido Biosciences, Inc., or Kaleido, a healthcare company, where she helped to establish the HR infrastructure, compensation, performance and development programs. Prior to Kaleido, she was the head of the HR business partnership function at Moderna, a biotechnology company, where she helped to lead the HR organization during a period of significant growth, including implementing talent development and engagement initiatives. Prior to that, she was at Celgene Avilomics Research (formerly Avila Therapeutics), where she was responsible for building and developing the HR infrastructure for the company's early research and development division. She also held senior HR positions at Inotek Pharmaceuticals and Amylin Pharmaceuticals. Ms. Arnold received her B.S. from Colorado State University. As a result of our restructuring announced in February 2023, Ms. Arnold will be leaving the Company effective March 31, 2023.

Non-Employee Directors

Timothy J. Barberich has served as a member of our board of directors since September 2016 and as Vice Chairperson of our board of directors since March 2022. Mr. Barberich has served on the board of directors of Verastem, Inc. since 2014, and TScan Therapeutics, Inc. since 2019. Mr. Barberich previously served on the boards of directors for GI Dynamics, Inc. from 2011 to 2021, for Tokai Pharmaceuticals, Inc. from 2009 to 2017, for HeartWare International, Inc. from 2008 to 2016, for Inotek Pharmaceuticals Corporation from 2016 to 2017, and for Neurovance, Inc. from 2010 to 2016. Mr. Barberich is co-founder, and served as the CEO and Chairman of Sepracor Inc. from 1984 to 2009. He holds a B.S. in Chemistry from Kings College. We believe Mr. Barberich's extensive experience in the life sciences industry qualifies him to serve on our board of directors.

Cynthia L. Feldmann has served as a member of our board of directors since September 2020 and is the Chair of our Audit Committee. In March 2022, Ms. Feldmann joined the board of Alexandria Real Estate Equities, Inc., or Alexandria, an urban office real estate investing trust focused on collaborative life science, agtech and technology campuses in AAA innovation cluster locations. She serves on Alexandria's Sciences & Technology Board Committee. Ms. Feldmann has served as a member of the board of directors of UFP Technologies, Inc., or UFPT, since June 2017. She chairs the UFPT Audit Committee and serves on the Nominating & Governance Committee. Since 2005, Ms. Feldmann has served on the board of directors of STERIS PLC, or STERIS, a provider of infection prevention, decontamination, and health science technologies, products and services. She is the Chair of STERIS' Nominating & Governance Committee and previously chaired and is a

current member of the Audit Committee. Ms. Feldmann also served from 2003 to January 2018 on the board of directors of Hanger Inc., or Hanger, a provider of orthotic and prosthetic services and products, and the largest orthotic and prosthetic managed care network in the U.S. Ms. Feldmann served on the Audit Committee, including as Chair of the Audit Committee, the Compensation Committee and the Quality and Technology Committee of Hanger. Ms. Feldmann currently serves on the board of trustees and as a member of the Finance Committee of Falmouth Academy, an academically rigorous, co-ed college preparatory day school for grades 7 to 12. Ms. Feldmann previously served as a director and chair of the Audit Committee and as a member of the Nominating & Governance, Compensation, and Quality and Technology Committees of Heartware International, Inc., a medical device company, from 2012 until its acquisition by Medtronic PLC in August 2016. Previously, Ms. Feldmann had a 27-year career in public accounting; she was Partner at KPMG LLP, holding various leadership roles in the firm's Medical Technology and Health Care & Life Sciences industry groups and was National Partner-in-Charge of the Life Sciences practice for Coopers & Lybrand (now PricewaterhouseCoopersLLP) among other leadership positions she held during her career there. Ms. Feldmann was a founding board member of Mass Medic, a Massachusetts trade association for medical technology companies, where she also served as treasurer and as a member of the board's Executive Committee during her tenure from 1997 to 2001. Ms. Feldmann is a retired CPA and holds a Masters Professional Director Certification from the American College of Corporate Directors. We believe Ms. Feldmann's extensive expertise in auditing and accounting, particularly her experience in the life sciences industry, qualifies her to serve on our board of directors.

Michael Huang has served as a member of our board of directors since October 2018. Since 2021, Mr. Huang has served as a member of the board of directors of Windgap Medical, Inc. Mr. Huang has served as a member of the board of directors of Viracta Therapeutics since 2019. Mr. Huang serves as Managing Partner at Taiwania Capital Management Corporation, a venture capital firm. From 2014 to 2017, Mr. Huang served as Chief Executive Officer of NeuroVive Pharmaceutical Asia, Inc., a biopharmaceutical company. Mr. Huang holds an MBA from Rice University, a M.A. in Chemistry from the University of Texas, Arlington, and a B.S. from the University of Texas, Austin. We believe Mr. Huang's extensive investment experience in the life sciences industry qualifies him to serve on our board of directors.

Robert S. Langer, Sc.D., has served as a member of our board of directors since September 2016. Dr. Langer has served as a David H. Koch Institute Professor at the Massachusetts Institute of Technology since 2005. Dr. Langer currently serves on the board of directors of Moderna, Inc., Seer, Abpro bio and Puretech Health plc, and previously served on the board of directors of Momenta Pharmaceuticals, Inc., Kala Pharmaceuticals, Inc., Fibrocell Science, Inc. and Millipore Corp. Dr. Langer holds a Sc.D. in Chemical Engineering from MIT and a B.S. in Chemical Engineering from Cornell University. We believe Dr. Langer's pioneering academic work, extensive medical and scientific knowledge, and experience serving on public company boards of directors qualify him to serve on our board of directors.

Joel S. Marcus, J.D., CPA has served on our board of directors since December 2018. Mr. Marcus is Executive Chairman and Founder of Alexandria Real Estate Equities, Inc. (NYSE: ARE) or Alexandria, a best-in-class, mission-driven life science REIT that pioneered life science real estate from a specialty niche to a mainstream asset class and today is the preeminent and longest-tenured owner, operator, and developer uniquely focused on collaborative life science, agtech, and technology campuses in AAA innovation cluster locations. Since co-founding the company in 1994 as a garage startup with $19 million in Series A capital and a mission to advance human health, he has led the remarkable growth of Alexandria into an S&P 500 company that as of December 31, 2022 has a total market capitalization of $35.0 billion and a total equity capitalization of $24.9 billion that ranks it in the top 10% among all publicly traded U.S. REITs. Alexandria, which celebrated its 25th anniversary as a New York Stock Exchange listed company in May 2022, has a total shareholder return exceeding 1,670% as of December 31, 2022. Mr. Marcus also founded and continues to lead Alexandria Venture Investments, the company's strategic venture capital platform. Since the platform's inception in 1996, it has actively invested in disruptive life science companies as well as promising agrifoodtech, climate innovation, and technology companies that are advancing new, transformative therapeutic modalities and platforms to meaningfully improve human health. Alexandria Venture Investments has been recognized by Silicon Valley Bank as the #1 most active corporate investor in biopharma by new deal volume for six consecutive years and by AgFunder as one of the top five most active U.S. agtech investors for two consecutive years. Mr. Marcus also currently serves on the boards of directors of Applied Therapeutics, Inc. and Intra-Cellular Therapies, Inc.. He earned his undergraduate and Juris Doctor degrees from the University of California, Los Angeles. We believe that Mr. Marcus' extensive experience in the life sciences industry and as a chief executive officer and attorney qualifies him to serve on our board of directors.

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 2023 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 2023 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 2023 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 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) Financial Statements

The following documents are included on pages F-1 through F-29 attached hereto and are filed as part of this Annual Report on Form 10-K.

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the Consolidated Financial Statements or the Notes thereto set forth below beginning on page F-1.

(3) Exhibits.

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

		Incorporated by Reference				
Exhibit Number	**Exhibit Description**	**Form**	**File No.**	**Exhibit**	**Filing Date**	**Filed/ Furnished Herewith**
3.1	Restated Certificate of Incorporation of Frequency Therapeutics, Inc.	8-K	001-39062	3.1	10/7/19	
3.2	Amended and Restated Bylaws of Frequency Therapeutics, Inc.	8-K	001-39062	3.1	9/25/20	
4.1	Form of Specimen Common Stock Certificate	S-1/A	333-233652	4.1	9/23/19	
4.2	Second Amended and Restated Investors' Rights Agreement, dated as of July 17, 2019	S-1	333-233652	4.2	9/6/19	
4.3	Description of Frequency Therapeutics, Inc. Securities	10-K	001-39062	4.3	3/26/20	
10.1#	2014 Stock Incentive Plan, as amended and form of option agreements thereunder	S-1	333-233652	10.1	9/6/19	
10.2#	2019 Incentive Award Plan and form of award agreements thereunder	S-1/A	333-233652	10.2	9/23/19	
10.3#	Non-Employee Director Compensation Program	S-1/A	333-233652	10.3	9/23/19	
10.4	Form of Indemnification Agreement for Directors and Officers	S-1/A	333-233652	10.5	9/23/19	

10.6	Second Amended and Restated Executive Employment Agreement, dated as of September 20, 2019, between David L. Lucchino and Frequency Therapeutics, Inc.	S-1/A	333-233652	10.7	9/23/19	
10.7†	Exclusive Patent License Agreement, dated as of December 13, 2016, as amended, between Massachusetts Institute of Technology and Frequency Therapeutics, Inc.	10-K	333-233652	10.7	3/15/22	
10.8†	Non-Exclusive Patent License Agreement, dated as of February 7, 2019, between Massachusetts Eye and Ear Infirmary and Frequency Therapeutics, Inc.	S-1	333-233652	10.11	9/6/19	
10.9†	License and Collaboration Agreement, dated as of July 16, 2019, between Astellas Pharma, Inc. and Frequency Therapeutics, Inc.	S-1	333-233652	10.12	9/6/19	
10.10#	2019 Employee Stock Purchase Plan	S-1/A	333-233652	10.13	9/23/19	
10.11	Indenture of Lease, effective as of January 7, 2020 between HCP/KING 75 Hayden LLC and Frequency Therapeutics, Inc.	10-K	001-39062	10.13	3/26/20	
10.12	Sublease Agreement, dated July 8, 2022, by and between Frequency Therapeutics, Inc. and SalioGen Therapeutics, Inc.	8-K	001-39062	10.1	7/12/22	
10.13	Registration Rights Agreement, dated July 17, 2020, by and among Frequency Therapeutics, Inc. and the Investors named therein.	8-K	001-39062	10.2	7/21/20	
10.14	Loan and Security Agreement, dated December 11, 2020, by and between Frequency Therapeutics, Inc. and Silicon Valley Bank.	8-K	001-39062	10.1	12/15/20	
10.15#	Separation Agreement, dated as of March 31, 2022, by and between Frequency Therapeutics, Inc. and Peter P. Pfreundschuh	8-K	001-39062	10.1	3/31/22	
10.16#	Employment Agreement, effective February 3, 2020, by and between Frequency Therapeutics, Inc. and Wendy S. Arnold.	10-K	001-39062	10.16	3/26/21	
21.1	Subsidiaries of Frequency Therapeutics, Inc.					*
23.1	Consent of RSM US, LLP, Independent Registered Public Accounting Firm					*
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					*
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a)					*

	under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	**
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	**
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 Extension Definition Linkbase Document	***
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	***
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	***
104	The cover page for the Company's Annual Report on Form 10-K has been formatted in Inline XBRL and contained in Exhibit 101.	

* Filed herewith
** Furnished herewith
*** Submitted electronically herewith
† Portions of this exhibit have been omitted pursuant to Item 601 of Regulation S-K promulgated under the Securities Act because the information is not material and would be competitively harmful if publicly disclosed.
# A management contract or compensatory plan or arrangement required to be filed as an exhibit pursuant to Item 15(a)(3) of Form 10-K.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

FREQUENCY THERAPEUTICS, INC.

Date: March 10, 2023

By: /s/ David L. Lucchino
David L. Lucchino
President, Chief Executive Officer and Director
(Principal Executive Officer)

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints David L. Lucchino and Richard Mitrano, 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, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ David L. Lucchino **David L. Lucchino**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 10, 2023
/s/ Richard Mitrano **Richard Mitrano**	Vice President, Finance and Operations (Principal Financial and Accounting Officer)	March 10, 2023
/s/ Timothy J. Barberich **Timothy J. Barberich**	Vice Chairperson and Director	March 10, 2023
/s/ Cynthia L. Feldmann **Cynthia L. Feldmann**	Director	March 10, 2023
/s/ Michael Huang **Michael Huang**	Director	March 10, 2023
/s/ Robert S. Langer **Robert S. Langer, Sc.D.**	Director	March 10, 2023
/s/ Joel S. Marcus **Joel S. Marcus**	Director	March 10, 2023

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Frequency Therapeutics, Inc.

Opinion on the Financial Statements
We have audited the accompanying consolidated balance sheets of Frequency Therapeutics, Inc. and its subsidiaries (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for the years then ended, and the related notes to the consolidated financial statements (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

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

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

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

We have served as the Company's auditor since 2017.

/s/ RSM US LLP
Boston, Massachusetts
March 10, 2023

Frequency Therapeutics, Inc.

Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 51,954	$ 79,635
Short-term marketable securities	31,143	51,072
Prepaid expenses and other current assets	4,396	4,041
Total current assets	87,493	134,748
Long-term marketable securities	—	11,719
Property and equipment, net	2,739	5,522
Right of use assets	28,980	31,350
Restricted cash	1,699	1,699
Other long-term assets	327	320
Total assets	$ 121,238	$ 185,358
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,114	$ 2,748
Accrued expenses	5,891	6,101
Lease liabilities, current portion	2,021	1,747
Term loan, current portion	10,000	833
Total current liabilities	21,026	11,429
Lease liabilities, net of current portion	26,761	28,851
Term loan, net of current portion	4,167	14,167
Other long-term liabilities	89	87
Total liabilities	52,043	54,534
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized, no shares issued or outstanding at December 31, 2022 and December 31, 2021, respectively	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized, 35,262,083 and 34,611,213 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	35	35
Additional paid-in capital	331,023	310,936
Accumulated other comprehensive loss	(198)	(62)
Accumulated deficit	(261,665)	(180,085)
Total stockholders' equity	69,195	130,824
Total liabilities and stockholders' equity	$ 121,238	$ 185,358

See accompanying notes.

Frequency Therapeutics, Inc.

Consolidated Statements of Operations
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2022	2021
Revenue	$ -	$ 14,068
Operating expenses:		
Research and development	49,418	60,923
General and administrative	33,584	37,176
Total operating expenses	83,002	98,099
Loss from operations	(83,002)	(84,031)
Interest income	1,327	397
Interest expense	(961)	(764)
Realized gain (loss) on investments	3	(23)
Foreign exchange (loss) gain	(5)	16
Other income (expense), net	1,056	(266)
Loss before income taxes	(81,582)	(84,671)
Tax benefit (provision)	2	(15)
Net loss	$ (81,580)	$ (84,686)
Net loss per share-basic and diluted	$ (2.33)	$ (2.47)
Weighted-average shares of common stock outstanding-basic and diluted	35,075,924	34,351,274

See accompanying notes.

Frequency Therapeutics, Inc.

Consolidated Statements of Comprehensive Loss
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2022	2021
Net loss	$ (81,580)	$ (84,686)
Other comprehensive loss:		
Unrealized loss on marketable securities	(136)	(89)
Total comprehensive loss	(136)	(89)
Comprehensive loss	$ (81,716)	$ (84,775)

See accompanying notes.

Frequency Therapeutics, Inc.

Consolidated Statement of Stockholders' Equity
(in thousands, except share and per share amounts)

	Common shares issued	Common par value	Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' equity
Balance, December 31, 2020	**33,964,000**	**$ 34**	**$ 287,829**	**$ 27**	**$ (95,399)**	**$ 192,491**
Stock-based compensation expense	—	—	21,750	—	—	21,750
Purchases under Employee Stock Purchase Plan	7,064	—	60	—	—	60
Issuance of common stock upon exercise of stock options	642,314	1	1,297	—	—	1,298
Forfeiture of restricted stock	(2,165)	—	—	—	—	—
Other comprehensive loss	—	—	—	(89)	—	(89)
Net loss	—	—	—	—	(84,686)	(84,686)
Balance, December 31, 2021	**34,611,213**	**$ 35**	**$ 310,936**	**$ (62)**	**$ (180,085)**	**$ 130,824**
Stock-based compensation expense	—	—	19,831	—	—	19,831
Purchases under Employee Stock Purchase Plan	76,606	—	196	—	—	196
Issuance of common stock upon exercise of stock options	10,047	—	11	—	—	11
Issuance of common stock under equity offering	12,767	—	50	—	—	50
Issuance of common stock pursuant to restricted stock units	551,450	—	(1)	—	—	(1)
Other comprehensive loss	—	—	—	(136)	—	(136)
Net loss	—	—	—	—	(81,580)	(81,580)
Balance, December 31, 2022	**35,262,083**	**$ 35**	**$ 331,023**	**$ (198)**	**$ (261,665)**	**$ 69,195**

See accompanying notes

Frequency Therapeutics, Inc.

Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (81,580)	$ (84,686)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	19,831	21,750
Depreciation expense	2,766	2,775
Non-cash lease expense	2,370	1,066
Non-cash interest expense	396	347
Loss on disposal of assets	—	16
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	681	(173)
Accounts payable	(677)	(2,292)
Deferred revenue	—	(14,068)
Lease liabilities	(1,816)	(396)
Accrued expenses	(208)	(398)
Net cash used in operating activities	(58,237)	(76,059)
Cash flows from investing activities:		
Sale of property and equipment	17	—
Purchase of property and equipment	—	(2,914)
Purchase of marketable securities	(54,222)	(92,445)
Redemption of marketable securities	85,338	29,233
Net cash provided by (used in) investing activities	31,133	(66,126)
Cash flows from financing activities:		
Proceeds from issuance of common stock	60	1,298
Proceeds from Employee Stock Purchase Plan	196	60
Repayment of term loan	(833)	—
Net cash (used in) provided by financing activities	(577)	1,358
Net decrease in cash, cash equivalents, and restricted cash	(27,681)	(140,827)
Cash, cash equivalents, and restricted cash at beginning of period	81,334	222,161
Cash, cash equivalents, and restricted cash at end of period	$ 53,653	$ 81,334
Supplemental disclosures:		
Cash paid for interest	$ 914	$ 703

See accompanying notes

1. Organization

Frequency Therapeutics, Inc., together with its wholly owned subsidiaries, Frequency Therapeutics, PTY, LTD, Frequency Therapeutics Securities Corporation and Frequency Therapeutics Japan KK (Frequency Japan) (the Company), headquartered in Lexington, Massachusetts, was incorporated in November 2014 as a Delaware corporation. Frequency Japan was closed down in February 2021. The Company is a preclinical-stage regenerative medicine company focused on developing therapeutics to activate a person's innate regenerative potential to restore function.

Liquidity and capital resources

The Company has funded its operations primarily with proceeds from private and public securities financings, a term loan, and amounts received under a collaboration agreement. The Company has incurred recurring losses since its inception. In addition, as of December 31, 2022, the Company had an accumulated deficit of $261,665. The Company expects to continue to generate operating losses for the foreseeable future. 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 assurances that additional funding will be available on terms acceptable to the Company, or at all. The Company believes that existing resources will be sufficient to fund planned operations for at least 12 months from the date the financial statements were available to be issued.

2. Summary of significant accounting policies

Basis of presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting standards set by the Financial Accounting Standards Board (FASB). The FASB sets generally accepted accounting principles (GAAP) that the Company follows to ensure its financial condition, results of operations, and cash flows are consistently reported. References to GAAP issued by the FASB in these notes to the consolidated financial statements are to the FASB *Accounting Standards* Codification (ASC).

Principles of consolidation

The consolidated financial statements include the accounts of Frequency Therapeutics, Inc. and its wholly owned subsidiaries Frequency Therapeutics Securities Corporation, Frequency Therapeutics PTY, LTD and Frequency Japan through the date of its dissolution. All intercompany transactions and balances have been eliminated.

Use of estimates

The preparation of the Company's consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, expenses and related disclosure of contingent assets and liabilities at the date of the consolidated financial statements and reported amounts of expenses during the reporting period. On an ongoing basis, the Company's management evaluates its estimates, which include but are not limited to management's judgments of accrued expenses, revenue recognition, fair value of common stock, valuation of share-based awards, present value of lease liabilities and income taxes. Actual results could differ from those estimates.

Comprehensive loss

Components of comprehensive loss, including net loss, are reported in the financial statements in the period in which they are recognized. Other comprehensive loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. Net loss and other comprehensive loss are reported net of any related tax effect to arrive at comprehensive loss. Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders which for the years ended December 31, 2022 and 2021 consist of unrealized loss on marketable securities.

Segment information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company and the Company's chief operating decision-maker, the Company's chief executive officer, view the Company's operations and manage its business as a single operating segment, which is in the business of developing therapeutics to activate a person's innate regenerative potential to restore function.

Foreign currency

All periods presented are reported in US dollars. The functional currency for entities outside the United States is the US dollar. Realized and unrealized gains and losses from foreign currency transactions are reflected in the consolidated statements of operations as other expense. During the years ended December 31, 2022 and 2021 the Company recorded $5 of foreign currency exchange loss and $16 of foreign currency exchange gain, respectively.

Cash and cash equivalents

The Company considers all highly liquid investments with an original maturity of six months or less at acquisition to be cash equivalents which are stated at fair market value. Cash and cash equivalents at December 31, 2022 and 2021 consists entirely of cash and money market funds.

Restricted cash

The Company has $1,699 of restricted cash as of December 31, 2022 and December 31, 2021, which represents a security deposit on the Company's Lexington, Massachusetts facility.

Marketable securities

Marketable securities represent holdings of available-for-sale marketable debt securities in accordance with the Company's investment policy. Short-term marketable securities mature within one year from the balance sheet date while long-term marketable securities mature after one year. Investments in marketable securities are recorded at fair value, with any unrealized gains and losses reported within accumulated other comprehensive income as a separate component of stockholders' equity until realized or until a determination is made that an other-than-temporary decline in market value has occurred. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are reflected as a component of other expense. Interest on securities sold is determined based on the specific identification method and reflected as interest income. Any realized gains or losses on the sale of investment are reflected as realized gain (loss) on investments.

Concentration of credit risk and off-balance sheet risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents and marketable securities. The Company maintains its cash, cash equivalents, and restricted cash at several accredited financial institutions, in amounts that exceed federally insured limits. Marketable securities consist of short term and long term investments. Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which its money market accounts are maintained.

The Company has no significant off-balance sheet arrangements such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

Significant suppliers

The Company is dependent on third-party manufacturers to supply products 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 single manufacturer of its product candidates for use in clinical trials. The Company would be adversely affected by a significant interruption in the supply of product for use in clinical programs.

Fair value measurements

Fair value is defined as the price that would be received upon sale of an asset or paid to transfer a liability between market participants at measurement dates. ASC Topic 820, *Fair Value Measurement* (ASC 820), establishes a three-level

valuation hierarchy for instruments measured at fair value. The hierarchy is based on the transparency of inputs to the valuation of an asset or liability as of the measurement date. The hierarchy defines three levels of valuation inputs, 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 Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.

Level 3 Unobservable inputs developed using estimates or assumptions developed by the Company, which reflect those that a market participant would use in pricing the asset or liability.

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

The carrying amounts reflected in the consolidated balance sheet for prepaid expenses and other current assets, accounts payable, accrued expenses, other liabilities, and term loan are shown at their historical values which approximate their fair values.

Property and equipment, net

Property and equipment consist of lab equipment, furniture and office equipment and software recorded at cost. These amounts are depreciated using the straight-line method over the estimated useful lives of the assets as follows:

	Estimated useful life
Lab equipment	3 years
Software	3 years
Furniture and office equipment	3 years

Upon retirement or sale, the cost of the assets disposed of and the related accumulated depreciation are eliminated from the balance sheet and related gains or losses are reflected in the consolidated statements of operations.

Impairment of long-lived assets

The Company continually evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company did not recognize any impairment losses for the years ended December 31, 2022 and 2021.

Research and development costs and accruals

Research and development expenses include salaries and benefits, materials and supplies, preclinical and clinical trial expenses, stock-based compensation expense, depreciation of equipment, contract services and other outside expenses. The Company has entered into various research and development-related contracts with research institutions, contract research organizations, contract manufacturers and other companies. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. Costs of certain development activities, such as manufacturing, preclinical and clinical trial expenses, are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development costs. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. Costs incurred in obtaining technology licenses are charged to research and development expense as acquired in-process research and development if the technology licensed has not reached technological feasibility and has no alternative future use.

Leases

The Company accounts for leases under ASC 842, *Leases*. The Company determines if an arrangement is, or contains, a lease at inception and, if so, records a right-of-use (ROU) asset and a lease liability on the consolidated balance sheet for any lease with a term longer than 12 months.

ROU assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. ROU assets and liabilities are recognized at the lease commencement date based on the present value of lease payments to be made over the lease term. The ROU asset also includes any lease payments made at or before the lease commencement date and excludes lease incentives received. As the Company's lease does not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of lease payments. The lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Operating lease expense is recognized on a straight-line basis over the lease term. The Company has elected to not apply the recognition requirements of ASC 842 for short-term leases, which is defined as a lease that, at the lease commencement date, has a lease term of 12 months or less and does not include an option to purchase the underlying asset that the Company is reasonably certain to exercise.

For real estate lease agreements entered into or modified after the adoption of ASC 842 that include lease and non-lease components, the Company has elected to account for the lease and non-lease components, such as common area maintenance charges, as a single lease component.

Collaborative arrangements

The Company analyzes its collaborative arrangements to assess whether they are within the scope of ASC 808, *Collaborative Arrangements* (ASC 808) to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship (e.g., a licensing arrangement) where the contracted party has obtained goods or services that are an output of the Company's ordinary activities in exchange for a consideration and therefore within the scope of ASC 606, *Revenue from Contracts with Customers* (ASC 606). For those elements of the arrangement that are accounted for pursuant to ASC 606, including those to which ASC 606 is applied by analogy, the Company applies the five-step model described in the Company's revenue recognition policy. For elements of collaborative arrangements that are accounted for pursuant to ASC 808, an appropriate and rational recognition method is determined and applied consistently. Reimbursements from the counterparty that are the result of a collaborative relationship with the counterparty, instead of a customer relationship, such as co-development or clinical activities, are recorded as a reduction to research and development expense as the services are performed. Similarly, amounts that are owed to a collaboration partner related to the co-development clinical activities are recognized as research and development expense.

The Company enters into out-licensing agreements that are within the scope of ASC 606. The terms of such out-license agreements include licenses to functional intellectual property (IP), given the functionality of the intellectual property is not expected to change substantially as a result of the licensor's ongoing activities. Such arrangements typically include payment of one or more of the following: non-refundable up-front license fees; reimbursement of certain costs; development and regulatory milestone payments and milestone payments based on the level of sales; and royalties on net sales of licensed products.

The Company considers the economic and regulatory characteristics of the licensed IP, research, development, manufacturing and commercialization capabilities of the licensee and the availability of the associated expertise in the general marketplace to determine if it has standalone value at the inception of the licensing arrangement, which would make the license distinct. In addition, the Company considers whether the licensee can benefit from a promise for its intended purpose without the receipt of any additional good or services promised in the contract, whether the value of the license is dependent on the remaining goods and services, whether there are other vendors that could provide the remaining promise, and whether the license is separately identifiable from the remaining good and services. For licenses that are combined with other goods and services, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of progress and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research and development and licensing agreement. Such a change could have a material impact on the amount of revenue the Company records in future periods.

Revenue is allocated to the licensed IP on a relative standalone selling price basis and, for functional IP, is recognized at a point when the licensed IP is made available for the customer's use and benefit, which generally occurs at the inception of the arrangement. However, in cases, where the functionality of the IP is expected to substantively change as a result of activities of the Company that do not transfer additional promised goods or services, or in cases, where there is an expectation that the Company will undertake activities to change the standalone functionality of the IP and the customer is contractually or practically required to use the latest version of the IP, revenue for the license to functional IP is recognized over time.

Development and regulatory milestone fees, which are a type of variable consideration, are recognized as revenue to the extent that it is probable that a significant reversal will not occur. The Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

The Company has entered into a collaboration arrangement with Astellas Pharma Inc. (Astellas), as further described in Note 13, "*Collaboration agreement*", of notes to consolidated financial statements.

Revenue recognition

The Company accounts for contracts with customers in accordance with ASC 606, including all amendments thereto. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as collaborative arrangements and leases. The Company's disclosure within the below sections or elsewhere within these consolidated financial statements reflects the Company's accounting policies in compliance with this standard.

Under ASC 606, an entity recognizes revenue when or as its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To recognize revenue for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies its performance obligations. The Company only applies the five-step model to contracts when it is probable that the entity will collect substantially all of the consideration to which it will be entitled in exchange for the goods or services it transfers to the customer. Once a contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and identifies as a performance obligation each promise to transfer to the customer either (a) a good or service (or bundle of goods and services) that is distinct, or (b) a series of distinct goods and services that are substantially the same and have been the same pattern of transfer to the customer.

The Company assesses whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner (the "customer" in this type of arrangement) and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, an entity is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct. For each arrangement that results in revenues, the Company identifies all performance obligations, which may include, for example, a license to IP and know-how, research and development activities, and/or manufacturing services.

In addition to any upfront payment, if the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the estimated variable consideration in the transaction price to the extent it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any

related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. If it is probable that a significant revenue reversal will not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or of the licensee such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

For contracts that include sales-based royalties (including milestone payments based on the level of sales) promised in the exchange for licenses of intellectual property, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestone payments at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied. In determining the transaction price, the Company adjusts the promised amount of consideration for the effects of the time value of money if the timing of payments provides the Company or the Company's customer with a significant benefit of financing the transfer of goods and services. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assesses each of its revenue generating arrangements in order to determine whether a significant financing component exists. The Company recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied, either at a point in time or over time. For performance obligations satisfied over time, the Company measures progress toward completion of its performance obligations using an input method based on the Company's efforts and inputs to satisfy its performance obligations relative to total expected inputs to the satisfaction of that performance obligation.

Amounts received from a customer prior to revenue recognition are recorded as deferred revenue. Amounts received from a customer that are expected to be recognized as revenue within the 12 months following the balance sheet date are classified as a current liability in the accompanying consolidated balance sheets.

Patent costs

The Company expenses patent application and related legal costs as incurred and classifies such costs as general and administrative expenses in the accompanying consolidated statements of operations.

Stock-based compensation

The Company accounts for its stock-based compensation in accordance with ASC Topic 718, *Compensation—Stock Compensation* (ASC 718). ASC 718 requires all share-based payments to employees and directors to be recognized as expense in the consolidated statements of operations and comprehensive loss based on their grant date fair values. The Company adopted FASB Accounting Standards Update (ASU) 2016-09 which identifies areas for simplification of several areas of share-based payment transactions. The Company treats non-employee grants in a manner consistent with employee grants. The Company estimates the fair value of options granted using the Black-Scholes option pricing model for stock option grants to both employees and non-employees. The Company believes the fair value of the stock options granted to non-employees is more reliably determinable than the fair value of the services provided.

The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (a) the expected stock price volatility, (b) the expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the lack of sufficient company-specific historical and implied volatility data, the Company has based its computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to the Company, including stage of product development and life science industry focus. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the share-based payment as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

The Company expenses the fair value of its share-based compensation awards to employees and non-employees on a straight-line basis over the requisite service period, which is generally the vesting period.

Income taxes

The Company accounts for income taxes using the asset and liability method in accordance with ASC Topic 740, *Income Taxes* (ASC 740) which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies. At December 31, 2022 and 2021, the Company has concluded that a full valuation allowance is necessary for its deferred tax assets (see Note 11, *Income taxes*").

Net loss per share

Basic net loss per share is computed by dividing net loss by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is computed using the weighted-average number of shares of common stock outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. Diluted net loss per share is the same as basic net loss per share for the years ended December 31, 2022 and 2021 since all potential shares of common stock instruments are anti-dilutive as a result of the loss for such periods.

Basic and diluted net loss per share attributable to common stockholders was calculated as follows:

	Year Ended December 31,	
	2022	2021
Numerator:		
Net loss	$ (81,580)	$ (84,686)
Denominator:		
Weighted-average shares of common stock outstanding-basic and diluted	35,075,924	34,351,274
Net loss per share-basic and diluted	$ (2.33)	$ (2.47)

Recently issued and adopted accounting pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. The Company is an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (Jobs Act). The Jobs Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. Thus,

an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. The Company elected to avail itself of this extended transition period and, as a result, we will not be required to adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses* (Topic 326): Measurement of Credit Losses on Financial Instruments. The FASB has subsequently issued amendments to ASU 2016-13, which have the same effective date and transition date. These standards require that credit losses be reported using an expected losses model rather than the incurred losses model that was previously used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, this standard now requires allowances to be recorded instead of reducing the amortized cost of the investment. These standards limit the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and requires the reversal of previously recognized credit losses if fair value increases. The Company adopted this standard on January 1, 2023 and it did not have a material impact on the consolidated financial statements.

3. Fair value measurements

The Company's financial assets measures at fair value on a recurring basis by level within the fair value hierarchy at December 31, 2022 and 2021 are summarized as follows:

		December 31, 2022		
	Fair Value Hierarchy	Amortization Cost	Unrealized Gain (Loss)	Fair Market Value
Money market funds	Level 1	$ 30,648	$ 1	$ 30,649
Short-term marketable securities	Level 2	31,280	(137)	31,143
		$ 61,928	$ (136)	$ 61,792

		December 31, 2021		
	Fair Value Hierarchy	Amortization Cost	Unrealized Loss	Fair Market Value
Money market funds	Level 1	$ 48,160	$ -	$ 48,160
Short-term marketable securities	Level 2	51,116	(44)	51,072
Long-term marketable securities	Level 2	11,764	(45)	11,719
		$ 111,040	$ (89)	$ 110,951

At December 31, 2022 and 2021, we held 14 and 18 debt securities, respectively, that were in an unrealized loss position. The unrealized losses at December 31, 2022 and 2021 were attributable to changes in interest rates and do not represent credit losses. The Company does not intend to sell the investments before recovery of their amortized cost bases, which may be at maturity. All investments mature within twelve months from December 31, 2022. The following tables summarize the Company's debt securities in an unrealized loss position, aggregated by length of time in a continuous unrealized loss position.

	December 31, 2022					
	Less than 12 Months		More than 12 Months		Total	
	Fair Market Value	Unrealized Loss	Fair Market Value	Unrealized Loss	Fair Market Value	Unrealized Loss
Short-term marketable securities	$ 17,303	$ (78)	$ 9,927	$ (135)	$ 27,230	$ (213)
	$ 17,303	$ (78)	$ 9,927	$ (135)	$ 27,230	$ (213)

	December 31, 2021					
	Less than 12 Months		More than 12 Months		Total	
	Fair Market Value	Unrealized Loss	Fair Market Value	Unrealized Loss	Fair Market Value	Unrealized Loss
Short-term marketable securities	$ 32,991	$ (29)	$ -	$ -	$ 32,991	$ (29)
Long-term marketable securities	11,719	(45)	-	-	11,719	(45)
	$ 44,710	$ (74)	$ -	$ -	$ 44,710	$ (74)

4. Prepaid expenses and other current assets

Prepaid expenses and other current assets consisted of the following:

	December 31, 2022	December 31, 2021
Rent and deposits	$ -	$ 470
Research and development expenses	2,084	858
Accounts receivable	449	144
Insurance	1,608	2,384
Other	255	185
Total	$ 4,396	$ 4,041

5. Property and equipment

Property and equipment include the following:

	December 31, 2022	December 31, 2021
Lab equipment	$ 5,706	$ 6,177
Furniture and office equipment	3,238	3,238
Software	291	291
Total	9,235	9,706
Accumulated depreciation	(6,496)	(4,184)
Property and equipment, net	$ 2,739	$ 5,522

The Company recognized $2,766 and $2,775 of depreciation expense for the years ended December 31, 2022 and 2021, respectively.

6. Accrued expenses

Accrued expenses consist of the following:

	December 31, 2022	December 31, 2021
Payroll and employee related expenses	$ 4,216	$ 4,375
Professional fees	377	767
Third-party research and development expenses	773	840
Other	525	119
Total	$ 5,891	$ 6,101

7. Debt

On December 11, 2020, the Company entered into a Loan and Security Agreement (Loan Agreement) with a commercial bank for a term loan with a principal balance of $15,000. The Company made monthly interest only payments through November 30, 2022. The principal balance and interest will be repaid in equal monthly installments after the interest only period and continue through May 1, 2024 (Loan Maturity Date). Advances under the Loan Agreement will bear an interest rate equal to the greater of either (i) 1.50% plus the Prime Rate (as reported in *The Wall Street Journal*, subject to an

interest rate floor of zero) or (ii) 4.75%. The interest rate at December 31, 2022 was 9.0%. Interest expense related to the Loan Agreement was $961 for the year ended December 31, 2022 and $764 for the year ended December 31, 2021.

The Company may prepay the advance made under the Loan Agreement in whole, at any time subject to a prepayment premium equal to: (a) 2.0% of the then-outstanding principal amount of the advance, if such prepayment occurs on or prior to the first anniversary of the Closing Date; (b) 1.0% of the then-outstanding principal amount of the advance, if such prepayment occurs after the first anniversary of the Closing Date and on or prior to the second anniversary of the Closing Date; and (c) 0.0% of the then-outstanding principal amount of the advance, if such prepayment occurs after the second anniversary of the Closing Date. The prepayment premium is waived if the term loan is refinanced by the bank (in its sole and absolute discretion) on or prior to the Loan Maturity Date.

The Company will pay a final payment of $150, which will occur on the earliest of: (i) the Loan Maturity Date; (ii) the date that the Company prepays all of the outstanding principal in full; (iii) the date the loan payments are accelerated due to an event of default; or (iv) the termination of the Loan Agreement. The Company is accruing the final payment over the term of the loan. The term loan is secured by substantially all of the Company's assets, excluding intellectual property.

8. Stockholders' equity

Preferred stock

The Company has authorized 10,000,000 shares of $0.001 par value preferred stock of which no shares were issued or outstanding as of December 31, 2022.

Common stock

The Company has authorized 200,000,000 shares of $0.001 par value common stock of which 35,262,083 were issued and outstanding as of December 31, 2022. Common shares are voting, and dividends may be paid when, as and if declared by the Board of Directors.

The Company has reserved the following shares of common stock for future issuance as of December 31, 2022 and 2021:

	December 31, 2022	December 31, 2021
Stock options outstanding	5,742,053	6,830,037
Shares available for future grant under stock option plan	988,216	1,552,630
	6,730,269	8,382,667

Equity Offerings

On December 10, 2021, the Company entered into an Equity Distribution Agreement (Sales Agreement) with Oppenheimer & Co. Inc. (Sales Agent) to sell shares of the Company's common stock, par value $0.001 per share, with aggregate gross sales proceeds of up to $125,000, from time to time, through an "at the market" equity offering program. Subject to the terms and conditions of the Sales Agreement, the Sales Agent may sell the shares by methods deemed to be an "at the market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made through The Nasdaq Global Select Market, on any other existing trading market for the Common Stock, to or through a market maker, or, if expressly authorized by the Company, in privately negotiated transactions. The Company or Sales Agent may terminate the Sales Agreement upon notice to the other party and subject to other conditions. The Company will pay the Sales Agent a commission equal to 3.0% of the gross proceeds of any Common Stock sold through the Sales Agent under the Sales Agreement and has provided the Sales Agent with customary indemnification rights.

Issuance costs incurred related to the Sales Agreement are classified as long-term assets on the balance sheet at December 31, 2022.

9. Stock-based compensation

On November 13, 2014, the Company adopted the 2014 Stock Incentive Plan (2014 Plan). All of the Company's employees, officers, directors, and consultants are eligible to be granted options to purchase common shares and restricted stock under the terms of the 2014 Plan. The Company reserved an aggregate of 8,550,415 shares of common stock for issuance under the 2014 Plan. As of December 31, 2022, there were no shares of common stock available for future grants under the 2014 Plan.

On September 17, 2019, the Company's board of directors and on September 19, 2019, its stockholders approved and adopted the 2019 Incentive Award Plan (2019 Plan). Under the 2019 Plan, the Company may grant stock options, stock appreciation rights, restricted stock, restricted stock units, and other stock and cash-based awards to individuals who are then employees, officers, directors or consultants of the Company, and employees and consultants of the Company's subsidiaries. A total of 3,100,000 shares of common stock were approved to be initially reserved for issuance under the 2019 plan. The number of shares under the 2014 Plan subject to outstanding awards as of the effective date of the 2019 Plan that are subsequently canceled, forfeited or repurchased by the Company will be added to the shares reserved under the 2019 Plan. In addition, the number of shares of common stock available for issuance under the 2019 Plan will be automatically increased on the first day of each calendar year during the ten-year term of the 2019 Plan, beginning with January 1, 2020 and ending with January 1, 2029, by the amount equal to 4% of the outstanding number of shares of the Company's common stock on December 31 of the preceding calendar year or such lesser amount as determined by the Company's board of directors.

All stock option grants are non-statutory stock options except option grants to employees (including officers and directors) intended to qualify as incentive stock options under the Internal Revenue Code of 1986, as amended. Incentive stock options may not be granted at less than the fair market value of the Company's common stock on the date of grant, as determined in good faith by the Board of Directors at its sole discretion. Nonqualified stock options may be granted at an exercise price established by the Board of Directors at its sole discretion (which has not been less than fair market value on the date of grant) and the vesting periods may vary. Vesting periods are generally four years and are determined by the Board of Directors. Stock options become exercisable as they vest. Options granted under the 2014 Plan and the 2019 Plan expire no more than ten years from the date of grant.

Stock options

A summary of the stock option activity under the 2014 Plan and the 2019 Plan are as follows:

	Number of shares	Weighted average exercise price [1]	Weighted average remaining contractual term (in years)	Aggregate intrinsic value
Outstanding as of December 31, 2020	6,816,798	$ 10.11	8.45	$ 171,415
Granted	1,357,426	32.76	8.07	—
Exercised	(642,314)	2.02	—	$ 11,652
Forfeited	(701,873)	16.48	—	—
Outstanding as of December 31, 2021	6,830,037	$ 5.35	7.76	$ 6,987
Granted	221,176	1.78	8.32	—
Exercised	(10,047)	1.24	—	$ 37
Forfeited	(1,299,113)	18.04	—	—
Outstanding as of December 31, 2022	5,742,053	$ 2.35	6.69	$ 9,114
Options exercisable as of December 31, 2022	4,579,486	$ 2.40	6.39	$ 7,071
Options unvested as of December 31, 2022	1,162,567	$ 2.12	7.84	$ 2,043

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock.

[1] On August 17, 2022, the Company's Board of Directors approved the repricing of all options granted under the 2019 Incentive Award Plan that were held by then current employees, executives, directors, and consultants for which the exercise price per share was greater than the closing price per share of the Company's common stock on August 17, 2022 (Underwater Options) by reducing the exercise price of each Underwater Option to $2.14, the closing price per share of the Company's common stock on August 17, 2022. See "Repricing of stock options" section for more information.

Stock option valuation

The assumptions that the Company used to determine the grant-date fair value of stock options granted to employees and directors were as follows, presented on a weighted average basis:

	Year Ended December 31,	
	2022	2021
Risk-free interest rate	3.0%	0.5%
Expected term (in years)	6.0	6.0
Expected volatility	80.0%	79.8%
Expected dividend yield	0.0%	0.0%

The weighted-average grant date fair value of options granted to employees during the years ended December 31, 2022 and 2021 was $1.58 and $22.39 respectively.

The total grant date fair value of options vested during the years ended December 31, 2022 and 2021 was $14,219 and $16,304, respectively.

Repricing of stock options

On August 17, 2022, the Board of Directors approved the repricing of each Underwater Option to $2.14, the closing price per share of the Company's common stock on August 17, 2022. Except for the modification of the exercise price, all other terms and conditions of the Underwater Options remain in effect.

The option repricing resulted in incremental stock-based compensation of $2,505, of which $1,630 was recorded as expense in the year ended December 31, 2022 and $875 will be recognized as expense over the remaining vesting period.

Restricted stock units

The below summary includes restricted stock unit activity within the Company's 2019 Incentive Award Plan for the year ended December 31, 2022.

	Number of shares	Weighted average fair value
Unvested, December 31, 2021	626,300	$ 9.54
Awarded	3,576,650	3.01
Vested	(551,450)	9.54
Forfeited	(549,850)	5.06
Unvested, December 31, 2022	3,101,650	$ 2.80

Stock-based compensation

Stock-based compensation expense of $19,831 and $21,750 for the years ended December 31, 2022 and 2021 respectively, is included in research and development and general and administrative expenses in the Company’s consolidated statements of operations and comprehensive loss.

As of December 31, 2022 and 2021, total unrecognized stock-based compensation expense relating to unvested stock options and restricted stock units was $19,537 and $39,112, respectively. This amount is expected to be recognized over a weighted-average period of 1.55 years and 2.49 years, respectively.

10. Employee stock purchase plan

On September 20, 2019, the Company’s board of directors and stockholders approved and adopted the 2019 Employee Stock Purchase Plan (ESPP) which became effective on the date of the Company’s initial public offering of shares of its common stock. The ESPP permits participants to purchase common stock through payroll deductions of up to 15% of their eligible compensation. The number of shares of common stock available for issuance under the ESPP will be automatically increased on the first day of each calendar year during the first ten years of the term of the ESPP, beginning with January 1,

2020 and ending with January 1, 2029, by an amount equal to 1% of the outstanding number of shares of the Company's common stock on December 31 of the preceding calendar year or such lesser amount as determined by the Company's board of directors.

The Company's first offering period of 2021 concluded on June 30, 2021 with the purchase of 7,064 shares in July 2021 related to this offering period. The Company's second offering period of 2021 concluded on December 31, 2021 with the purchase of 31,832 shares in January 2022. The Company's first offering period of 2022 concluded on June 30, 2022 with the purchase of 44,774 shares in July 2022 related to this offering period. As of December 31, 2022, a total of 1,225,527 shares remain for future offering periods. The Company's second offering period of 2022 concluded on December 31, 2022 with the purchase of 24,754 shares in January 2023 related to this offering.

11. Income taxes

Since inception in 2014, the Company has generated cumulative federal and state net operating loss and research and development credit carryforwards for which the Company has not recorded any net tax benefit due to uncertainty around utilizing these tax attributes within the respective carryforward periods.

As of December 31, 2022, the Company had federal net operating loss carryforwards of approximately $174,107 and Massachusetts state operating loss carryforwards of approximately $141,318 which may be available to offset future taxable income. The U.S. federal net operating loss carryforwards include $22,399 available to reduce future taxable income through 2037 and approximately $151,708 which do not expire and are available to reduce future taxable income indefinitely. The state net operating loss carryforwards are available to offset future taxable income through 2042. As of December 31, 2022, the Company also had federal and Massachusetts research and development tax credit carryforwards of $8,177 and $3,556, respectively, which are available to offset federal and state tax liabilities through 2042 and 2037, respectively.

Realization of future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. 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 provided under Sections 382 and 383 of the Code, respectively, as well as similar state provisions. These ownership changes may limit the number of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382 of the Code, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50% over a rolling three-year period. The Company has completed several financings and has conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception and has determined that an ownership change did occur in March 2017. Accordingly, utilization of $12,400 of the U.S. net operating loss carryforwards which were incurred prior to March 2017 (pre-ownership change) is limited under Section 382 of the Code. After the limitations under Section 382 of the Code, the Company may utilize approximately $10,800 of its pre-ownership change net operating loss carryforwards based upon an annual usage of approximately $1,600 for each of the next five years after the ownership change and approximately $180 for each of the 15 years thereafter. The remaining pre-March 2017 ownership change net operating losses of approximately $1,600 were written off due to expiration under limitation. The limitation has been determined by first multiplying the value of our stock at the time of the ownership change by the applicable long-term tax-exempt rate. These carryforwards may be subject to further annual limitations under Section 382 of the Code in the event of future changes in ownership. Additionally, the Company has determined an ownership changed occurred in October of 2019 as a result of the IPO. Accordingly, utilization of approximately $46,123 of the U.S. net operating loss carryforwards incurred prior to October 2019 is also limited under Section 382 of the Code. The Company has determined it will be able to utilize the entire $46,123 of its pre-ownership change net operating loss carryforwards based upon the limitations calculated from the October 2019 ownership change. These carryforwards may be subject to further annual limitations under Section 382 of the Code in the event of future changes in ownership.

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 the evidence, both positive and negative, the Company has recorded a valuation allowance against its deferred tax assets at December 31, 2022 and 2021 because the Company's 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 cumulative loss position and, as a result, a valuation allowance of approximately $77,288 and $50,931 as of December 31, 2022 and 2021 has been established.

The Company has no unrecognized tax benefits. The Company has not, as yet, conducted a study of its research and development credit carryforwards. Such a 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 were required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheet or consolidated statements of operations if an adjustment were required. The Company has elected to recognize interest and penalties related to income tax matters as a component of income tax expense, of which no interest or penalties were recorded for the years ended December 31, 2022 and 2021.

The Company files income tax returns in the U.S. and Massachusetts. The statute of limitations for assessment by the Internal Revenue Service and Massachusetts tax authorities remains open for all years since 2014. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state authorities to the extent utilized in a future period. No federal or state tax audits are currently in process.

A reconciliation of the Company's pre-tax loss for the years ended December 31, 2022 and 2021 is as follows:

	2022	2021
Domestic	$ (81,586)	$ (84,624)
Foreign	4	(47)
Total	$ (81,582)	$ (84,671)

The Company's provision at December 31, 2022 and 2021 consist of the following:

	2022	2021
Current:		
Federal	$ -	$ -
State	(2)	15
Foreign	-	-
Total current	$ (2)	$ 15
Deferred:		
Federal	-	-
State	-	-
Foreign	-	-
Total deferred	$ -	$ -
Total (benefit) provision	$ (2)	$ 15

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate for the years ended December 31, 2022 and 2021 is as follows:

	2022	2021
U.S federal statutory income tax rate	21.0%	21.0%
Permanent differences	(0.1)	—
State income taxes, net of federal benefit	5.4	2.7
Research and development tax credits	5.1	3.6
State rate changes	3.7	—
Stock compensation deductions	(2.8)	1.6
Other items	—	(0.7)
Change in deferred tax asset valuation allowance	(32.3)	(28.2)
Effective income tax rate	—%	—%

The Company's deferred tax assets at December 31, 2022 and 2021 consist of the following:

	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 45,512	$ 36,590
Research and development tax credits	11,163	7,026
Capitalized research and development costs	10,042	—
Intangibles	478	392
Stock compensation	9,507	6,554
Accrued expenses	—	107
Deferred revenue	—	—
Other	357	176
Fixed assets	282	265
Lease liability	7,735	7,269
Gross deferred tax asset	85,076	58,379
Valuation allowance	(77,288)	(50,931)
Net deferred tax assets	$ 7,788	$ 7,448
Deferred tax liabilities:		
Right of use asset	(7,788)	(7,448)
Net deferred tax asset (liability)	$ -	$ -

12. Research and license agreements

Massachusetts Institute of Technology

In December 2016, the Company entered into an exclusive patent license agreement (MIT License Agreement), with the Massachusetts Institute of Technology (MIT), under which the Company received an exclusive, worldwide, royalty-bearing license to certain patent rights to develop, make, have made, use, sell, offer to sell, lease and import products (Licensed Products) and to develop and perform processes (Licensed Processes) which incorporate the licensed technology for the treatment of disease, including but not limited to the prevention and remediation of hearing loss. The Company also has the right to grant sublicenses of its rights under the MIT License Agreement.

The Company is required to use diligent efforts to develop and commercialize the Licensed Products or Processes, and to make such products or processes reasonably available to the public and to spend certain minimum amounts on research and development of Licensed Products and/or Processes each year until the first commercial sale of a Licensed Product and/or a first commercial performance of a Licensed Process. The Company is also subject to certain development obligations with regards to a first Licensed Product. The Company has satisfied certain obligations related to preclinical studies and the filing of an IND for a first Licensed Product with its development activities related to FX-322. The Company's future development obligations are: (i) to commence a Phase 3 clinical trial for such Product within five years of the IND filing for such product, (ii) to file a New Drug Application or equivalent with the FDA or comparable European regulatory agency for such Product within nine years of the IND filing for such Product, and (iii) to make a first commercial sale of such Product within 11 years of the IND filing for such Product. The Company also has certain development obligations for a second Licensed Product. In the event that the Company has failed to fulfill the development timeline obligation with respect to a second Licensed Product and fails to cure such breach within ninety (90) days of written notice by MIT, MIT may restrict the licensed field to the prevention and remediation of hearing loss in humans and animals. The Company does not have the right to control prosecution of the in-licensed patent applications, and its rights to enforce the in-licensed patents are subject to certain limitations.

Upon entering into the MIT License Agreement, the Company paid a $50 license fee payment and issued to MIT shares of our common stock equal to 5% of total then-outstanding capital stock. The Company is required to pay certain annual license maintenance fees which may be credited to running royalties during the same calendar year, if any, and to make potential milestone payments up to $2,900 on each Licensed Product or Licensed Process. In addition, the Company is required to pay a low single-digit royalty on Licensed Products and Licensed Processes and a low-twenties royalty on sublicense revenues.

The MIT License Agreement will remain in effect until the expiration or abandonment of all issued patents and filed patent applications licensed thereunder remain in effect, unless terminated earlier. The Company has the right to terminate for any reason upon a 3-month prior written notice. MIT shall have the right to terminate if the Company ceases to carry on any business related to the MIT License Agreement. MIT may terminate the MIT License Agreement for the Company's material breach uncured within ninety (90) days (or thirty (30) days in the case of nonpayment). MIT may also terminate the MIT License Agreement if the Company or our affiliates commence any action against MIT to declare or render any claim of the licensed patent rights invalid, unpatentable, unenforceable, or non-infringed (a patent challenge), or if our sublicensee commences such actions and the Company does not terminate such sublicense within thirty (30) days after MIT's demand. MIT has the right to increase all payments due, instead of terminating the MIT License Agreement in the case of a patent challenge.

In May 2019, the Company entered into an amendment with MIT, updating the diligence milestones for a second Licensed Product.

In March 2022, the Company entered into an amendment with MIT, removing a patent and certain patent applications from the MIT License Agreement which were unrelated to the Company's hearing and MS programs and which were not being utilized by the Company.

The patents in-licensed by the Company from MIT pursuant to the MIT License claim inventions created by, among others, Dr. Langer, one of the Company's directors. Pursuant to MIT's policy on the ownership, distribution and commercial development of MIT technology, or the MIT Policy, inventors of intellectual property invented at MIT, including the inventors of patents licensed to the Company under the MIT License, are entitled to a portion of the net royalty income derived by MIT from such inventions, but not amounts received by MIT from the sale of common stock previously issued by the Company to MIT pursuant to the MIT License. Accordingly, pursuant to the MIT Policy, Dr. Langer is entitled to receive a portion of the amounts the Company pays to MIT under the MIT License, including the Astellas Royalty Payment and future milestone payments or royalties, if any, that the Company may receive pursuant to the Astellas Agreement. Accordingly, Dr. Langer has received $11 and $6 from MIT under the MIT Policy during the years ended December 31, 2022 and 2021, respectively. Refer to Note 18, "*Related party transactions*", for all related party disclosures.

The Scripps Research Institute (California Institute for Biomedical Research)

In September 2018, the Company entered into a license agreement (CALIBR License Agreement) with the California Institute for Biomedical Research (CALIBR) under which the Company received an exclusive, worldwide, royalty-bearing license to certain patent rights to make, have made, use, sell, offer to sell, and import products (CALIBR Licensed Products) which incorporate the licensed technology for the treatment of multiple sclerosis. The Company also have the right to grant sublicenses of our rights under the CALIBR License Agreement. CALIBR reserves the right to use for itself and the right to grant non-exclusive licenses to other nonprofit or academic institutions, for any internal research and educational purposes.

The Company is required to use commercially reasonable efforts to develop, manufacture, and sell at least one CALIBR Licensed Product. The Company is also subject to certain milestone timeline obligations, which may be extended in certain circumstances as set forth in the CALIBR License Agreement. In October 2021, the Company entered into an amendment with CALIBR which updated the milestone obligations to: (i) initiate a Phase 2 clinical trial (or equivalent) for a CALIBR Licensed Product by December 31, 2023 and (ii) initiate a Phase 3 clinical trial (or equivalent) for a CALIBR Licensed Product by December 31, 2025. The Company does not have the right to control prosecution of the in-licensed patent applications, and the Company's rights to enforce the in-licensed patents are subject to certain limitations.

Upon entering into the CALIBR License Agreement, the Company made a $1,000 license fee payment and is required to make milestone payments up to $26,000 for each Category of CALIBR Licensed Products (Category 1 is any CALIBR Licensed Products containing a compound that modulates any muscarinic receptor and Category 2 is any CALIBR Licensed Products not included in Category 1 that could differentiate oligodendrocyte precursor cells from *in vitro* studies and/or are active in animal models relevant to MS). The Company is also required to pay a middle single-digit royalty on CALIBR Licensed Products and a royalty on sublicense revenues ranging from low-teen percentage to 50%.

The CALIBR License Agreement shall continue in effect until expiration of all Company obligations to pay royalties. Royalties shall be payable on a country-by-country and CALIBR Licensed Product-by-CALIBR Licensed Product basis upon the later of (1) the expiration or abandonment of all valid claims of the licensed patent rights in such country and (2) ten years from the first commercial sale of each CALIBR Licensed Product. The Company may terminate the CALIBR License Agreement at will upon a 30-day prior written notice. The Company may also elect to terminate its license to one or more

licensed patents in any or all jurisdictions by giving ninety (90) days' prior written notice to CALIBR. CALIBR may terminate the CALIBR License Agreement for material breach uncured within thirty (30) days. CALIBR has the right to terminate or reduce the license to a non-exclusive license if the Company fails to use diligent efforts to develop and commercially exploit CALIBR Licensed Products.

Massachusetts Eye and Ear (Formerly Massachusetts Eye and Ear Infirmary)

In February 2019, the Company entered into an Non-Exclusive Patent License Agreement (MEE License Agreement) with the Massachusetts Eye and Ear (MEE) under which it received a non-exclusive, non-sublicensable, worldwide, royalty-bearing license to certain patent rights to develop, make, have made, use, sell, offer to sell, lease and import products and to develop and perform processes which incorporate the licensed technology for the treatment or prevention of hearing loss (MEE licensed products).

The Company is obligated to use diligent efforts to develop and commercialize the MEE licensed products. The Company met one of its milestone timeline obligations by dosing a first subject in a Phase 2 trial by December 31, 2020. The Company is still subject to a milestone timeline obligation to dose a first subject in a Phase 3 trial by December 31, 2024. The Company does not control the filing, prosecution, enforcement, and defense of any licensed patent rights.

Upon entering the MEE License, the Company made a $20 license fee payment. The Company is obligated to pay certain annual license maintenance fees between $5 and $7.5 per each MEE patent family case number included in the licensed MEE patent rights prior to first commercial sale of an MEE licensed product. The Company is also obligated to pay a minimum annual royalty payment of $15 per each MEE patent family case number included in the licensed MEE patent rights after first commercial sale of an MEE licensed product. The Company is also obligated to make milestone payments up to $350 on each product or process that incorporates the licensed patent rights. In addition, the Company has agreed to pay a low single-digit royalty on products and processes that incorporate the licensed patent rights.

The MEE License Agreement shall remain in effect until all issued patents and filed patent applications within the licensed patent rights have expired or been abandoned, unless terminated earlier. The Company has the right to terminate the MEE License Agreement at will by giving thirty (30) business days advance written notice to MEE. MEE has the right to terminate the MEE License Agreement if the Company fails to make any payment due within thirty (30) business days after MEE notifies the Company of such failure. MEE shall have the right to terminate if the Company fails to maintain the required insurance. MEE shall also have the right to terminate the MEE License Agreement upon forty-five (45) business days written notice if the Company becomes insolvent. MEE has the right to terminate for any other default not cured within sixty (60) business days written notice. MEE also has the right to terminate if the Company or its affiliates challenge the validity of the licensed patent rights.

13. Collaboration agreement

In July 2019, the Company entered into a License and Collaboration Agreement with Astellas (Astellas Agreement), under which the Company granted Astellas an exclusive, royalty-bearing, sub-licensable, nontransferable license to certain patent rights to research, develop, manufacture, have manufactured, use, seek and secure regulatory approval for, commercialize, offer for sale, sell, have sold and import, and otherwise exploit licensed products containing both a GSK-3 inhibitor and an HDAC inhibitor (Astellas Licensed Products), including the product candidate FX-322, outside of the United States. The Company also granted Astellas a right of first negotiation and a right of last refusal if it entered into any negotiation or agreement of any kind (other than an acquisition of all of the stock or assets of the Company) with any third party under which such third party would obtain the right to develop, manufacture, or commercialize Astellas Licensed Products in the United States.

These parties have agreed to use commercially reasonable efforts to carry out development activities assigned to it under an agreed-upon development plan. Astellas has agreed to use commercially reasonable efforts to obtain regulatory approval for at least one Astellas Licensed Product in sensorineural hearing loss and in age-related hearing loss, in each case, in one major Asian country and one major European country. The Company has agreed to use commercially reasonable efforts to obtain regulatory approval for at least one Astellas Licensed Product in the United States. Astellas has the sole right to commercialize the Astellas Licensed Products outside of the United States, and the Company has the sole right to commercialize the Astellas Licensed Products in the United States. Astellas has agreed to use commercially reasonable efforts to commercialize Astellas Licensed Products in a major Asian country and a major European country following receipt of regulatory approval in such countries.

The collaboration is governed by a joint steering committee (JSC) established under the Astellas Agreement and shall

be comprised of three representatives each from the Company and Astellas. The JSC shall oversee and coordinate the overall conduct of the development, manufacture and commercialization of the Astellas Licensed Products. All decisions of JSC shall be taken through a unanimous vote with each party's representatives collectively having one vote. Both the parties shall be responsible for carrying out the development and manufacturing activities in their defined territory in accordance with the plan as reviewed and approved in the JSC.

As consideration for the licensed rights under the Astellas Agreement, Astellas paid the Company an upfront payment of $80,000 in July 2019 and has agreed to pay potential development milestone payments up to $230,000 and commercialization milestones of up to $315,000. Specifically, the Company would receive development milestone payments of $65,000 and $25,000 upon the first dosing of a subject in a Phase 2b clinical trial for SNHL in Europe and Asia, respectively and $100,000 and $40,000 upon the first dosing of a subject in a Phase 3 clinical trial for SNHL in Europe and Asia, respectively. If the Astellas Licensed Products are successfully commercialized, the Company would be eligible for up to $315,000 in potential commercial milestone payments and also tiered royalties at rates ranging from low- to mid-teen percentages. The parties shall share equally, on a 50/50 basis, all out-of-pocket costs and joint study costs for all the joint activities conducted pursuant to the development plans or the joint manufacturing plan.

The Astellas Agreement remains in effect until the expiration of all royalty obligations. Royalties are paid on a licensed product-by-licensed product and country-by-country basis until the latest of (i) the expiration of the last valid claim in the licensed patent rights with respect to such Astellas Licensed Product in such country or (ii) a set number of years from the first commercial sale of such Astellas Licensed Product in such country. Astellas may terminate the Astellas Agreement at will upon 60 days' written notice. Each party has the right to terminate the Astellas Agreement due to the other party's material breach if such breach remains uncured for 90 days (or 45 days in the case of nonpayment) or if the other party becomes bankrupt.

The Astellas Agreement is a collaborative agreement that is within the scope of ASC 808. The Company analyzed the joint research and development activities to assess whether they fall within the scope of ASC 808, and will reassess this throughout the life of the arrangement based on changes in the roles and responsibilities of the parties. Based on the terms of the arrangement as outlined above, both parties are deemed to be active participants in the collaboration. Both parties are performing research and development activities in their defined territory and will be performing joint clinical studies in accordance with the development plan and the study protocol approved by the JSC. Additionally, Astellas and the Company are exposed to significant risks and rewards dependent on the commercial success of any product candidates that may result from the collaboration. As such, the collaboration arrangement is deemed to be within the scope of ASC 808.

The arrangement consists of two components; the license of IP and the research and development activities, including committee participation, to support the co-development and research plan. Under the provisions of ASC 808, the Company has determined that it will apply the guidance in ASC 606 to recognize the revenue related to the license since that component of the arrangement is more reflective of a vendor-customer relationship. The Company determined that the license and the related research and development services associated with the Phase 2a clinical study were not distinct from one another, as the license has limited value to Astellas without the performance of the research and development activities and the Phase 2a study is essential to the use of the license. As such, the Company determined that these activities should be accounted for as a single combined performance obligation.

Revenue associated with this single performance obligation was recognized as the research and development work was performed, using an input method on the basis of research and development costs incurred to date relative to total research and development costs expected to be incurred. The transfer of control occurred over this time period and, in management's judgment, was the best measure of progress towards satisfying the performance obligation. The Company determined that the period of performance of the research and development services began upon the signing of the Astellas Agreement and continued until the completion of the Phase 2a clinical trial of FX-322 (FX-322-202). The transaction price of $80,000 was allocated to the single combined performance obligation and recorded as deferred revenue in July 2019 when it was received. This upfront payment was recognized as revenue over the period from July 2019 until June 30, 2021, the completion date of the Phase 2a clinical trial (FX-322-202), using the input method.

The potential development and regulatory milestone payments are fully constrained until the Company can conclude that achievement of the milestone is probable and that it is probable that recognition of revenue related to the milestone will not result in a significant reversal in the amount of cumulative revenue recognized when the uncertainty associated with the variable consideration is ultimately resolved and as such these have been excluded from the transaction price. As part of its evaluation of the constraint, the Company considers numerous factors, including the fact that achievement of the milestones is outside the control of the Company and contingent upon the future success of clinical trials, the licensee's efforts, and the receipt of regulatory approval. Any consideration related to sales-based milestones (including royalties) will be recognized

when the related sales occur as these amounts have been determined to relate predominantly to the license granted to Astellas and therefore are recognized at the later of when the performance obligation is satisfied, or the related sales of licensed products occur. The Company re-evaluates the transaction price, including its estimated variable consideration included in the transaction price and all constrained amounts, at each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

The Astellas Agreement contains joint research and development activities that are not within the scope of ASC 606. The Company will recognize research and development expense related to the joint study costs for all the joint activities in future periods and reimbursements received from Astellas will be recognized as an offset to research and development expense on the consolidated statements of operations during the development period. In the year ended December 31, 2022 and 2021, the Company invoiced Astellas $392 and $885 for joint costs.

14. Leases

On December 11, 2020, the Company entered into an Agreement for Termination of Lease and Voluntary Surrender of Premises (Lease Termination Agreement) with ARE-MA Region No. 20, LLC (Landlord) for the Company's office and laboratory space in Woburn, Massachusetts. The Lease Termination Agreement provides that the Lease Agreement, dated as of August 14, 2016, by and between the Company and Landlord (as the same may have been amended, the Lease) will terminate on March 31, 2021, unless the Company elects to extend the term of the Lease. The Company exercised the option to extend the lease until May 31, 2021.

On January 7, 2020 the Company entered into an indenture of lease (Lexington Lease) with HCP/KING 75 Hayden LLC, for the lease of approximately 61,307 square feet of rentable area in Lexington, Massachusetts or (Lexington Premises). The Lexington Lease commenced on December 11, 2020. In the second quarter of 2021, the Company began using the Lexington Premises as its principal executive offices and laboratory for research and development. The term of the Lexington Lease is expected to end on May 31, 2031. The Company also has the option to extend the Initial Term for two additional terms of five years each.

The Company's rent expense for the years ended December 31, 2022 and 2021 was $4,802 and $4,960, respectively.

Other information	December 31, 2022
Weighted-average remaining operating lease term	8.4 years
Weighted-average discount rate	8.5%

The table below reconciles the undiscounted cash flows to the operating lease liability recorded on the consolidated balance sheet as of December 31, 2022.

2023	4,273
2024	4,402
2025	4,534
2026	4,670
2027	4,810
Thereafter	17,530
Total minimum lease payments	40,219
Less: amount of lease payments representing interest	(11,437)
Present value of future lease payments	28,782
Less: current lease liabilities	(2,021)
Noncurrent lease liabilities	$ 26,761

Future aggregate minimum payments under the noncancelable operating lease as of December 31, 2022 are as follows:

2023	$ 4,273
2024	4,402
2025	4,534
2026	4,670
2027 and beyond	22,340
Total minimum lease payments	$ 40,219

15. Sublease

On July 8, 2022, the Company entered into a Sublease Agreement with SalioGen Therapeutics, Inc. (SalioGen) to sublease approximately 30,040 rentable square feet of the Company's office space in Lexington, MA for a two-year term. The base sublease rent per month for the first and second year of the sublease is $197 and $203, respectively. In addition to base rent, SalioGen will pay 49% of operating costs and taxes payable under the Company's lease for the Lexington, MA office space.

Since commencement, the Company has accounted for the Lexington, MA office space as an operating lease. In accordance with ASC 842, the Company concluded the sublease is also an operating lease. The Company recognized sublease income of $1,186 for the year ended December 31, 2022. The below table shows the expected future sublease income as of December 31, 2022.

Years Ending December 31,	Sublease Income
2023	$ 2,371
2024	1,383
Total future sublease income	$ 3,754

16. Commitments and contingencies

Contract commitments

The Company enters into contracts in the normal course of business with CROs, CMOs, universities, and other third parties for preclinical research studies, clinical trials and testing and manufacturing services. These contracts generally do not contain minimum purchase commitments and are cancelable by us upon prior written notice although, purchase orders for clinical materials are generally non-cancelable. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including non-cancelable obligations of our service providers, up to the date of cancellation or upon the completion of a manufacturing run.

Guarantees

The Company has identified the guarantees described below as disclosable, in accordance with ASC 460, *Guarantees*.

As permitted under Delaware law, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is, or was, serving at the Company’s request in such capacity. The maximum potential amount of future payments the Company could be required to make is unlimited; however, the Company has directors’ and officers’ insurance coverage that should limit its exposure and enable it to recover a portion of any future amounts paid.

The Company is a party to a number of agreements entered into in the ordinary course of business that contain typical provisions that obligate the Company to indemnify the other parties to such agreements upon the occurrence of certain events. Such indemnification obligations are usually in effect from the date of execution of the applicable agreement for a period equal to the applicable statute of limitations. The aggregate maximum potential future liability of the Company under such indemnification provisions is uncertain.

The Company leases office space in Lexington, Massachusetts under a ten-year noncancelable lease. The $1,699 security deposit for this lease is classified as restricted cash as of December 31, 2022. The Company exited the Woburn, Massachusetts facility in the second quarter of 2021. The Company has standard indemnification arrangements under these

leases that require it to indemnify the landlord against all costs, expenses, fines, suits, claims, demands, liabilities, and actions directly resulting from any breach, violation, or nonperformance of any covenant or condition of the lease.

As of December 31, 2022 and 2021, the Company had not experienced any losses related to these indemnification obligations, and no material claims with respect thereto were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related reserves have been established.

Legal Contingencies

The Company accrues a liability for legal contingencies when it believes that it is both probable that a liability has been incurred and that the Company can reasonably estimate the amount of the loss. The Company reviews these accruals and adjusts them to reflect ongoing negotiations, settlements, rulings, advice of legal counsel and other relevant information. To the extent new information is obtained and the views on the probable outcomes of claims, suits, assessments, investigations or legal proceedings change, changes in the Company's accrued liabilities would be recorded in the period in which such determination is made.

In addition, in accordance with the relevant authoritative guidance, for any matters in which the likelihood of material loss is at least reasonably possible, the Company will provide disclosure of the possible loss or range of loss. If a reasonable estimate cannot be made, however, the Company will provide disclosure to that effect. The Company expenses legal costs as they are incurred.

On June 3, 2021 and June 22, 2021, purported stockholders of the Company filed putative class action lawsuits in the U.S. District Court for the District of Massachusetts against the Company and the Company's Chief Executive Officer, President, and Director, David Lucchino. On March 21, 2022, the two lawsuits were consolidated into a single lawsuit, *Quinones et al. v. Frequency Therapeutics, Inc. et al*. and on May 16, 2022, the Company's Chief Development Officer, Dr. Carl LeBel, was added as a defendant. The plaintiffs allege violations of Sections 10(b), 20(a) and Rule 10b5 of the Securities Exchange Act of 1934, as amended (the Exchange Act), due to allegedly false and misleading statements and omissions about the Company's Phase 2a clinical trial (FX-322-202) for its product candidate FX-322 in the Company's public disclosures between October 29, 2020 and March 22, 2021. The lawsuit seeks, among other things, damages in connection with the Company's allegedly artificially inflated stock price between October 29, 2020 and March 22, 2021 as a result of those allegedly false and misleading statements and omissions, as well as interest, attorneys' fees and costs. The Company intends to vigorously defend against all claims asserted in the lawsuit. The Company filed a motion to dismiss the Amended Complaint on July 15, 2022. This matter is at the very early stages of the legal process, and as a result, the Company is not able to estimate a range of possible loss. Since an estimate of the possible loss or range of loss cannot be made at this time, no accruals have been recorded as of December 31, 2022.

On June 21, 2022, the Delaware Chancery Court dismissed a lawsuit brought by two purported stockholders against the Company and others. For previously reported information on this lawsuit, refer to Part I, Item 3, "Legal Proceedings" of the Company's 2021 Form 10-K. On August 16, 2022, these same two purported stockholders of the Company filed a similar lawsuit in Delaware Superior Court against (i) the Company, (ii) Computershare Inc., and (iii) Computershare Trust Company, N.A., entitled *The Gregory J. Parseghian Revocable Trust*, *et al.* v. *Frequency Therapeutics, Inc., et al.* The lawsuit alleges causes of action against the Company for breach of the statutory duty of care, negligence, conversion, and unjust enrichment, based on allegations that actions were taken to prevent the purported stockholders from selling their shares in the Company. The Company intends to vigorously defend against all claims asserted in the lawsuit. This matter is at the very early stages of the legal process, and as a result, the Company is not able to estimate a range of possible loss. Since an estimate of the possible loss or range of loss cannot be made at this time, no accruals have been recorded as of December 31, 2022.

On June 30, 2022, a purported stockholder of the Company filed a shareholder derivative complaint in the U.S. District Court for the District of Delaware purportedly on the Company's behalf against members of the Company's board of directors and the Company as a nominal defendant, entitled *Dewey v. Cohen et. al.* The complaint alleges (i) violations of Section 10(b) and Rule 10b5 of the Exchange Act, (ii) breach of fiduciary duty, (iii) aiding and abetting breach of fiduciary duty, (iv) unjust enrichment, and (v) waste of corporate assets. The claims are based on the same underlying allegations as the *Quinones* case (described above). The complaint seeks, among other things, monetary damages, interest, attorneys' fees and costs. On September 27, 2022, this lawsuit was stayed pending resolution of the *Quinones* case. This matter is at the very early stages of the legal process, and as a result, the Company is not able to estimate a range of possible loss. The Company's board members are each party to an indemnification agreement with the Company that may require the Company to

reimburse the board members for certain expenses and other costs related to this lawsuit. Since an estimate of the possible loss or range of loss cannot be made at this time, no accruals have been recorded as of December 31, 2022.

17. Employee benefit plan

Employees of the Company are eligible to participate in the Company's 401(k) retirement plan (401(k) Plan). Participants may contribute up to 90% of their annual compensation to the 401(k) Plan, subject to statutory limitations. Under the 401(k) Plan Safe Harbor Match, the Company matches 100% of the first 5% of employee contributions and vests 100% at time of match. For the years ended December 31, 2022 and 2021, the Company made matching contributions of $550 and $723, respectively.

18. Related party transactions

As disclosed in Note 12, "*Research and license agreements*", the Company entered into the MIT License Agreement in December 2016. The patents in-licensed by the Company from MIT pursuant to the MIT License Agreement claim inventions created by, among others, Dr. Langer, one of the Company's directors. Accordingly, Dr. Langer has received $11 and $6 from MIT under the MIT Policy during the years ended December 31, 2022 and 2021, respectively.

The Company's lease for its Woburn, Massachusetts facility, terminated in May 2021 as disclosed in Note 14, "*Leases*", was with an entity affiliated with one of the Company's directors and shareholders.

19. Subsequent events

The Company has evaluated subsequent events for recognition, remeasurement and disclosure purposes through March 10, 2023, the date which the consolidated financial statements were available to be issued. The identified subsequent event is as follows:

On February 13, 2023, the Company announced a restructuring in which its hearing program was discontinued. As a result, the Company reduced its workforce by approximately 55% to better align with the needs of its business. The total personnel costs related to the restructuring are estimated to be approximately $4,000 in future cash outlays primarily related to severance costs and related expenses.

Subsidiaries of Frequency Therapeutics, Inc.

Legal Name of Subsidiary	Jurisdiction of Organization
Frequency Therapeutics Pty Ltd	Australia
Frequency Therapeutics Securities Corporation	Massachusetts

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (No. 333-248474) on Form S-1, the Registration Statement (No. 333-250099) on Form S-3, and the Registration Statement (No. 333-234128) on Form S-8 of Frequency Therapeutics, Inc. of our report dated March 10, 2023, relating to the consolidated financial statements, of Frequency Therapeutics, Inc., appearing in this Annual Report on Form 10-K of Frequency Therapeutics, Inc. for the year ended December 31, 2022.

/s/ RSM US LLP

Boston, Massachusetts
March 10, 2023

Exhibit 31.1

CERTIFICATIONS

I, David L. Lucchino, certify that:

1. I have reviewed this Annual Report on Form 10-K of Frequency Therapeutics, 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: March 10, 2023

By: /s/ David L. Lucchino

David L. Lucchino
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Richard Mitrano, certify that:

1. I have reviewed this Annual Report on Form 10-K of Frequency Therapeutics, 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: March 10, 2023

By: /s/ Richard Mitrano

Richard Mitrano
Vice President, Finance and Operations
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION 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 of Frequency Therapeutics, Inc. (the "Company") on Form 10-K for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, David L. Lucchino, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 10, 2023

By: /s/ David L. Lucchino
David L. Lucchino
President and Chief Executive Officer
(principal executive officer)

Exhibit 32.2

CERTIFICATION 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 of Frequency Therapeutics, Inc. (the "Company") on Form 10-K for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Richard Mitrano, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 10, 2023

By: /s/ Richard Mitrano

Richard Mitrano
Vice President, Finance and Operations
(principal financial officer and principal accounting officer)