Reneo®
Pharmaceuticals

Moving Medicines to Move People

Annual Report 2022

Letter from our President & CEO

Dear Fellow Stockholder,

On behalf of our Board of Directors, I am pleased to invite you to attend the Reneo Pharmaceuticals Annual Stockholder Meeting, which will take place via live webcast on June 6, 2023 at 11:30 am Pacific Time. In advance of this meeting, I wanted to briefly highlight what Reneo accomplished during 2022 and our vision for the years ahead.

In 2022, Reneo moved an additional step closer to bringing a much-needed treatment option to patients with mitochondrial disease. We made significant progress with our mavodelpar (REN001) development programs, as well as brought additional pharmaceutical industry expertise to the company. In the first quarter of 2023, we completed enrollment of the pivotal STRIDE study of mavodelpar in adult patients with primary mitochondrial myopathy (PMM) due to mitochondria DNA (mtDNA) defects. We expect to complete the STRIDE study and announce topline results in the fourth quarter of 2023.

Based on interactions with the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), and several other national regulatory agencies in Europe, we received confirmation that positive results from STRIDE and the long-term safety clinical trial (STRIDE AHEAD) could potentially support registration of mavodelpar for adult patients with PMM due to mtDNA defects in the United States and Europe.

Furthermore, we announced positive results from our Phase 1b clinical trial of mavodelpar in adult patients with long-chain fatty acid oxidation disorder (LC-FAOD) in July of 2022. These results supported the recent request and subsequent granting of Fast Track Designation from the FDA for mavodelpar in a genotype of LC-FAOD. We will continue to collaborate with the FDA to finalize our plans for the LC-FAOD program.

As we move closer towards the potential commercialization of mavodelpar in the United States and Europe, we have strengthened our financial, commercial, and operational expertise by making key changes to the leadership team and Board of Directors. This includes the appointments of Michael P. Cruse to the role of Chief Operating Officer, Jennifer P. Lam to the role of Principal Financial and Accounting Officer, and Paul W. Hoelscher and Roshawn A. Blunt to the Board of Directors.

Finally, we ended the calendar year with over $100 million in cash, cash equivalents and short-term investments, which we believe will enable us to fund our operating expenses and capital expenditure requirements through our planned near-term clinical milestones.

Thank you for your continued support and confidence in Reneo, and your participation in this year's Annual Stockholder Meeting.

Gregory J. Flesher

President and Chief Executive Officer

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: 001-40315

RENEO PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**47-2309515**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
18575 Jamboree Road, Suite 275-S, Irvine CA	**92612**
(Address of principal executive offices)	(Zip code)

Registrant's telephone number, including area code: (858) 283-0280

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 Par Value per Share	**RPHM**	**The Nasdaq Stock Market LLC**

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

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

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

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

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

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

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

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

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

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

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

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

Based on the closing price of $2.65 as reported on the Nasdaq Global Market, the aggregate market value of the registrant’s common stock held by non-affiliates of the registrant on June 30, 2022 (the last business day of the registrant’s most recently completed second fiscal quarter) was approximately $38.7 million. Shares of the registrant’s common stock held by each executive officer and director and by each stockholder affiliated with a director or an executive officer have been excluded from this calculation because such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes. The number of outstanding shares of the registrant's common stock as of March 21, 2023 was 25,107,430 shares.

Documents Incorporated by Reference

Part III of this Annual Report on Form 10-K (the Annual Report) incorporates by reference certain information from the registrant’s definitive proxy statement for its 2023 annual meeting of stockholders (the Proxy Statement), which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant’s fiscal year end of December 31, 2022. Except with respect to information specifically incorporated by reference into this Annual Report, the Proxy Statement is not deemed to be filed as part of this Annual Report.

Auditor Firm Id: 42 Auditor Name: Ernst & Young LLP Auditor Location: San Diego, California, United States

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (the Annual Report) may contain "forward-looking statements" within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under Part I, Item 1A, "Risk Factors" in this Annual Report. Except as required by law, we assume no obligation to update these forward-looking statements, whether as a result of new information, future events or otherwise. These statements, which represent our current expectations or beliefs concerning various future events, may contain words such as "may," "will," "expect," "anticipate," "intend," "plan," "believe," "estimate" or other words indicating future results, though not all forward-looking statements necessarily contain these identifying words. Such statements may include, but are not limited to, statements concerning the following:

- our ability to obtain and maintain regulatory approval for mavodelpar (REN001) in any indication or any of our future product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- the commercialization of mavodelpar, if approved in any indication;
- our ability to develop and maintain sales and marketing capabilities, whether alone or with potential future collaborators;
- our plans to research, develop and commercialize mavodelpar, including the timing of our ongoing clinical trials of mavodelpar;
- our expectations regarding the size of target patient populations for mavodelpar, if approved for commercial use, and any additional product candidates we may develop;
- the size and growth potential of the markets for mavodelpar, and our ability to serve those markets;
- the rate and degree of market acceptance of mavodelpar, as well as third-party payor coverage and reimbursement for mavodelpar;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our expectations regarding our ability to obtain, maintain, enforce and defend our intellectual property protection for our product candidates;
- regulatory and legal developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- our estimates regarding the impact of the ongoing coronavirus (together with its variants, COVID-19) pandemic on our business and operations, the business and operations of our collaborators and on the global economy;
- our ability to obtain funding for our operations; and
- the accuracy of our estimates regarding expenses, capital requirements and needs for additional financing.

Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. You should be aware that the occurrence of any of the events discussed under Part I, Item 1A, “Risk Factors” and elsewhere in this Annual Report could substantially harm our business, results of operations and financial condition and that if any of these events occurs, the trading price of our common stock could decline and you could lose all or a part of the value of your shares of our common stock.

The cautionary statements made in this Annual Report are intended to be applicable to all related forward-looking statements wherever they may appear in this Annual Report. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this Annual Report. Except as required by law, we assume no obligation to update our forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, whether as a result of new information, future events or otherwise.

RISK FACTORS SUMMARY

We face many risks and uncertainties, as more fully described in Part I, Item 1A, under the heading "Risk Factors." Some of these risks and uncertainties are summarized below. The summary below does not contain all of the information that may be important to you, and you should read this summary together with the more detailed discussion of these risks and uncertainties contained in Part I, Item 1A, under the heading "Risk Factors." See also "Cautionary Note Regarding Forward-Looking Statements" in this Annual Report.

Risks Related to Our Business and Industry

- We have incurred significant net losses since our inception in 2014 and anticipate that we will continue to incur significant net losses for the foreseeable future. We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.
- We will need substantial additional capital to develop and commercialize mavodelpar and any future product candidates and implement our operating plan. If we fail to complete additional financings, we may be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- We currently depend entirely on the success of mavodelpar, which is our only product candidate. If we are unable to advance mavodelpar through clinical development, obtain regulatory approvals, and ultimately commercialize mavodelpar, or experience significant delays in doing so, our business will be materially harmed.
- Our clinical trials may fail to adequately demonstrate the safety and efficacy of mavodelpar, which could prevent or delay regulatory approval and commercialization.
- Preclinical and clinical drug development is a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results.
- If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- Any delays in the commencement or completion, or termination or suspension, of our clinical trials could result in increased costs to us, delay or limit our ability to generate revenue, and adversely affect our commercial prospects.
- The regulatory approval process is lengthy, expensive and uncertain, and we may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of our product candidates and adversely impact our ability to generate revenue, our business and our results of operations.
- If the market opportunities for mavodelpar and any future product candidates are smaller than we believe they are, or we face substantial competition in our markets, our future revenue may be adversely affected, and our business may suffer.
- We may not be successful in our efforts to expand our pipeline by identifying additional indications for which to investigate mavodelpar in the future. We may expend our limited resources to pursue a particular indication or formulation for mavodelpar and fail to capitalize on product candidates, indications or formulations that may be more profitable or for which there is a greater likelihood of success.
- We currently have no marketing and sales organization. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell mavodelpar and any future product candidates, we may not be able to generate product revenues.

Risks Related to Our Reliance on Third Parties

- We depend on a license agreement with vTv Therapeutics LLC (vTv Therapeutics), and termination of this license could result in the loss of significant rights, which would harm our business.
- We rely on third parties to conduct, supervise, and monitor our clinical trials. If these third parties do not successfully carry out their contractual duties, meet rigorously enforced regulatory requirements, or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize mavodelpar.
- We rely completely on third parties to manufacture our preclinical and clinical drug supplies and we intend to rely on third parties to produce commercial supplies of mavodelpar and any future product candidates, if approved, and these third parties may fail to obtain and maintain regulatory approval for their facilities, fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.

Risks Related to Our Intellectual Property

- Our success depends on our ability to obtain and maintain sufficient intellectual property protection for mavodelpar, any future product candidates, and other proprietary technologies.
- We cannot ensure that patent rights relating to inventions described and claimed in our pending patent applications will issue or that patents based on our patent applications will not be challenged and rendered invalid and/or unenforceable.
- If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection and/or other market exclusivity, our ability to prevent our competitors from commercializing similar or identical product candidates may be adversely affected.
- We may not be able to protect our intellectual property rights throughout the world.
- If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties, such as our license agreement with vTv Therapeutics, or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.
- We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court, and we may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.

Risks Related to Ownership of Our Common Stock

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

PART I

Item 1. Business

Overview

Reneo is a clinical-stage pharmaceutical company focused on the development and commercialization of therapies for patients with rare genetic mitochondrial diseases, which are often associated with the inability of mitochondria to produce adenosine triphosphate (ATP). Our lead product candidate, mavodelpar, is a potent and selective agonist of the peroxisome proliferator-activated receptor delta (PPARδ). Mavodelpar has been shown to increase transcription of genes involved in mitochondrial function and increase fatty acid oxidation (FAO), and may increase production of new mitochondria.

The PPAR family of nuclear hormone receptors, PPARα, PPARγ, and PPARδ, control the transcription of genes critical for regulating energy metabolism and homeostasis. PPARδ is highly expressed in muscle, kidney, brain, and liver tissue. Activation of PPARδ results in changes in the expression of genes involved with multiple aspects of energy metabolism including uptake of fatty acids, utilization of fatty acids as an energy source, and mitochondrial biogenesis. Increases in PPARδ activity also correlate with a shift in muscle tissue towards oxidative, fat-consuming type I fibers that are associated with endurance as opposed to glycolytic, type II fibers. In preclinical and clinical studies, increased PPARδ activity through transgenic overexpression or pharmacological activation increases muscular strength and endurance across a variety of functional measures.

Mavodelpar was studied in healthy male volunteers with one leg immobilized to produce muscle atrophy. Compared to placebo, administration of mavodelpar resulted in statistically significant increases in expression of genes involved in mitochondrial oxidative phosphorylation (OxPhos), and statistically significant improvements in muscle strength. Mavodelpar was studied in an open-label trial in patients with primary mitochondrial myopathies (PMM). Patients with PMM in this trial exhibited improved function, reduced symptoms, and increased expression of genes involved in mitochondrial function. Mavodelpar was also studied in an open-label trial in patients with long-chain fatty acid oxidation disorder (LC-FAOD). In this trial, patients with LC-FAOD due to certain gene defects exhibited improved function and reduced symptoms.

As a PPARδ agonist, mavodelpar may benefit patients with genetic mitochondrial myopathies who experience weakness, fatigue, or deterioration in muscle due to impaired mitochondrial energy production. Patients with these diseases are unable to perform many everyday activities, can experience cardiomyopathy and other organ dysfunction, and typically have a reduced life expectancy. We are currently developing mavodelpar in rare genetic diseases that typically present with myopathy, including PMM and LC-FAOD.

There are currently no approved therapies for the treatment of PMM, representing a high unmet medical need.

Our Product Pipeline

The following table summarizes our mavodelpar development programs.

We are currently developing mavodelpar in the following rare genetic diseases that are associated with a deficit of energy production by the mitochondria and typically present with myopathy:

- PMM: This rare genetic mitochondrial disease has an estimated prevalence in adults of 23:100,000, representing at least 66,000 patients in the United States and 82,000 in Europe. Patients with PMM are unable to move their muscles efficiently because their ability to generate energy through OxPhos is compromised. We are initially targeting adult patients with PMM due to mitochondrial DNA (mtDNA) defects.
- LC-FAOD: This rare genetic mitochondrial disease has an estimated prevalence of 1.5:100,000, representing at least 5,000 patients in the United States and 6,000 in Europe. The genetic alterations observed in these patients reduce their capacity to metabolize long-chain fatty acids as a source of energy for mitochondria. As patients with LC-FAOD grow older, they suffer from myopathy, lack of endurance, exercise intolerance, and fatigue. Muscle exertion in the absence of an adequate source of energy can result in the breakdown of muscle tissue that can subsequently cause kidney and cardiac damage. We are initially targeting adult patients with LC-FAOD with defects in long-chain 3-hydroxy acyl-CoA dehydrogenase (LCHAD), carnitine palmitoyltransferase 2 (CPT2), and trifunctional protein (TFP).

Our Strategy

Our mission is to bring to market therapies that address high unmet medical needs of patients with genetic mitochondrial diseases. We plan to achieve this goal by developing mavodelpar initially for adult patients with PMM and LC-FAOD and will continue to explore other patient populations where mavodelpar may provide benefit. We intend to establish mavodelpar as the standard of care for multiple rare genetic mitochondrial diseases. The components of our strategy are as follows:

- Complete clinical development and seek regulatory approval of mavodelpar in PMM. Following our interactions with the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), and several other national regulatory agencies in Europe, we believe that positive results from our ongoing global, randomized, double-blind, placebo-controlled pivotal Phase 2b trial of mavodelpar in adult patients with PMM due to mtDNA (STRIDE) along with the open-label, long-term safety trial outside of the United States in adult patients with PMM due to mtDNA (STRIDE AHEAD) could potentially support the registration of mavodelpar for adult patients with PMM due to mtDNA defects in the United States and Europe. We intend to submit the data from STRIDE, together with the long-term safety data from STRIDE AHEAD, to the FDA and the EMA in planned marketing applications in 2024. In addition, we are planning to study mavodelpar in patients with PMM due to nuclear DNA (nDNA) defects.
- Commercialize mavodelpar in the United States and key European markets, and establish mavodelpar as the standard of care for rare genetic mitochondrial diseases around the world. We plan to build a fully integrated rare disease pharmaceutical company with a commercial infrastructure in the United States and key European markets. For regions outside of the United States and key European markets, we plan to explore strategic partnerships to bring mavodelpar to patients.
- Maximize the commercial potential of mavodelpar in additional rare genetic mitochondrial disease indications. We have completed a Phase 1b study of mavodelpar in patients with LC-FAOD and are working with the FDA to map out the development pathway for our LC-FAOD program. Additionally, we aim to identify and pursue development of mavodelpar in other diseases that are defined by the inability of mitochondria to produce cellular energy.

- Expand our rare disease pipeline through acquisitions and/or licensing of complementary programs. We plan to license and/or acquire additional programs targeting rare genetic diseases with high unmet medical need. We will leverage our experience in preclinical and clinical development, commercialization, and strong relationships with clinical investigators and patient advocacy organizations to bring therapeutic options to patients.

Background

How muscle cells generate energy and how that process is deficient in patients with genetic myopathies

Cells generate energy in the form of ATP within intracellular structures called mitochondria. Mitochondria use proteins, carbohydrates, and fatty acids to make ATP, which is then used by the cell to support all cellular processes. Muscle tissue requires a high number of mitochondria to support energy needs.

Muscle cells mainly rely on three sources to generate energy: phosphocreatine (P-Cr), carbohydrates, and fatty acids. Muscle cells initially use readily available P-Cr and glycogen to generate this energy. As these sources become depleted, muscle cells turn to fatty acids to generate cellular energy.

Mitochondria are responsible for generating most of the energy for cells in the form of ATP. Cells have hundreds to thousands of mitochondria, with each mitochondrion containing proteins derived from both nuclear and mitochondrial genes. Patients with PMM can have nuclear or mitochondrial gene defects that result in reduced energy production in the mitochondria. Patients with LC-FAOD have deficiencies in the enzymes that break down long-chain fatty acids, resulting in an energy deficit. Patients with both of these diseases suffer from lack of endurance, fatigue, muscle weakness and they are unable to move their muscles efficiently because their ability to generate energy through OxPhos is compromised. Therapies are very limited for patients with rare genetic mitochondrial diseases and consist mainly of dietary manipulations and nutritional supplements to provide alternate sources of energy, and a carefully controlled exercise regimen. Increasing the capacity of these patients to metabolize fatty acids could potentially reduce their energy deficit and improve their ability to function.

Mitochondrial energy production involves a series of highly regulated metabolic processes that are sequenced based on the availability of nutrients and the length of time cells require energy. In the first minute of exertion, mitochondria utilize readily available P-Cr as a source of fuel to create ATP (Figure 1, step 1). When P-Cr is consumed, muscles turn to carbohydrate metabolism, as the next source of fuel to create ATP (Figure 1, step 2). Finally, after several minutes of exercise when P-Cr and carbohydrates are depleted, mitochondria turn to fatty acids as the source of fuel to create ATP (Figure 1, step 3). FAO becomes the primary pathway to generate energy for muscle and other cells during long periods of exercise.

Figure 1. The energy source used by muscles shifts from P-Cr and carbohydrates to fatty acids as supplies of P-Cr and carbohydrates are depleted

Oxidative phosphorylation

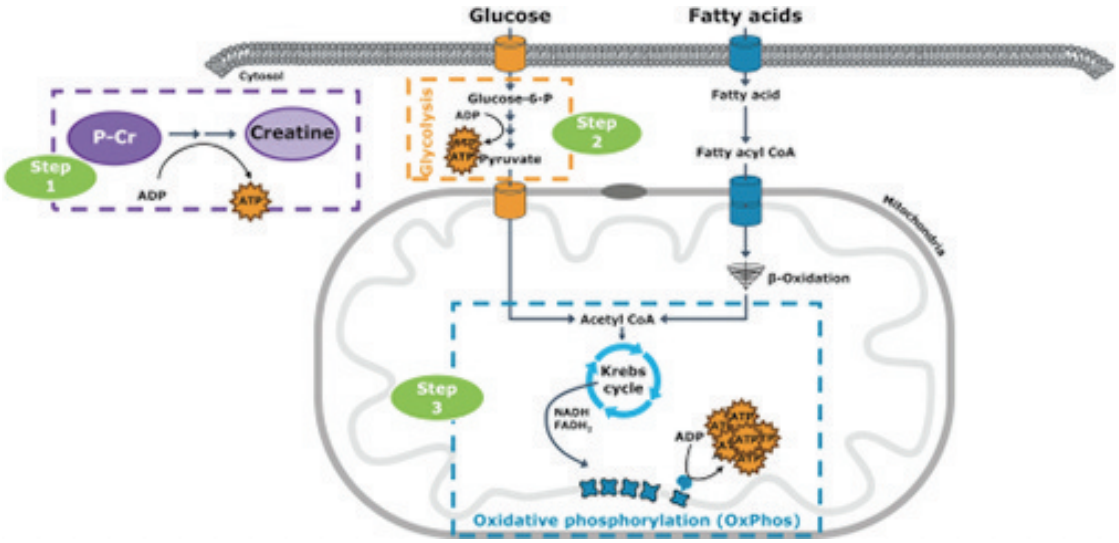
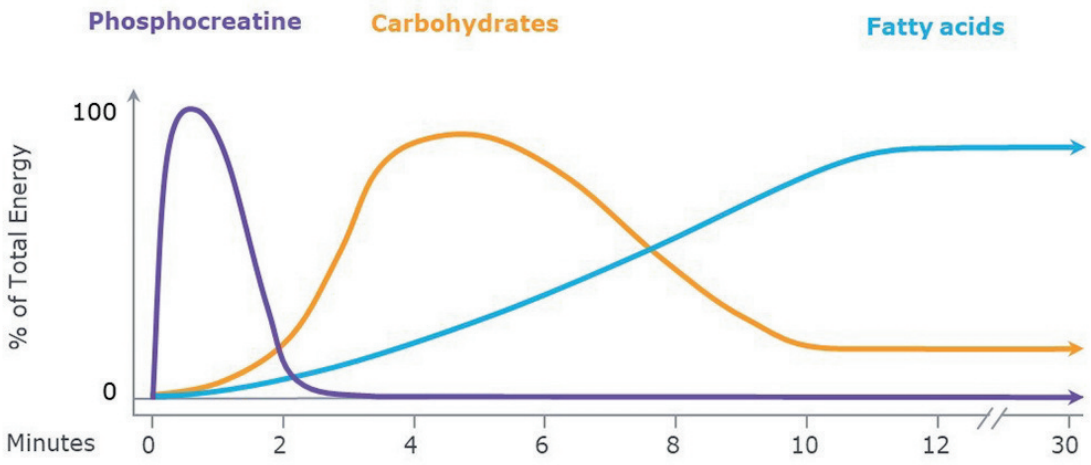


Figure 2. Nutrient utilization by mitochondria



Genetic mitochondrial myopathies are caused by deficiencies in specific steps of mitochondrial energy generation. Patients are unable to sustain normal muscle activity due to deficiencies in ATP production. We believe that enhancing FAO has the potential to provide therapeutic benefit to patients with genetic myopathies.

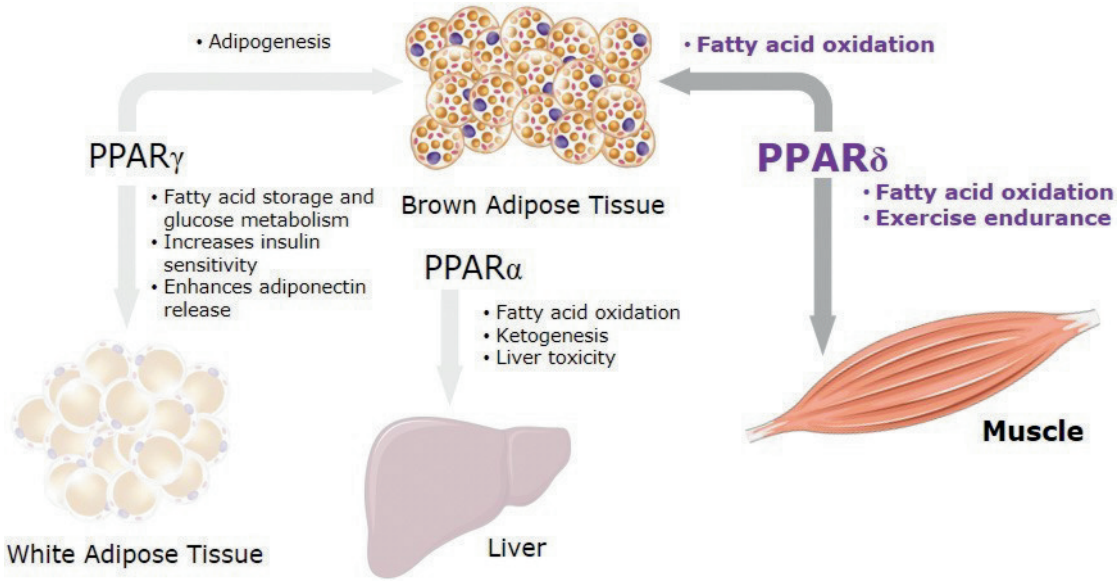
PPARδ, a regulator of FAO

PPARs are members of a family of nuclear receptors that, through their distinct functions and tissue distribution, regulate gene transcription involved in many biological processes, including metabolism and energy production.

There are three PPAR isotypes: alpha (α), gamma (γ) and delta (δ). PPAR α and γ agonists drugs have been approved in cardiovascular and endocrine disorders, respectively.

PPARδ is highly expressed in muscle cells and activation of PPARδ either through genetic manipulation or through small molecule agonists has been shown to increase the ability of muscle cells to use fatty acids and generate energy. Transgenic mice with overexpressed PPARδ were shown to be able to run on a treadmill twice the distance compared to normal mice. Conversely, PPARδ knockout mice were shown to run approximately 30% less distance compared to normal mice. We believe that a selective agonist of PPARδ such as mavodelpar, has potential therapeutic benefits while avoiding some of the adverse events associated with approved PPAR agonists of the PPARα and PPARγ class.

Figure 3. Members of the PPAR family of nuclear receptors have distinct roles in regulating fatty acid metabolism



Disease overview

PMM background

PMM are a group of disorders caused by genetic mutations within the mtDNA or nDNA that affect the activity of enzymes or other proteins in the mitochondria. In PMM these genetic alterations hamper the ability of mitochondria to generate energy from nutrient sources, resulting in energy deficits that are most pronounced in tissues with high energy demand such as muscle, brain, and heart. Energy deficits can affect major muscle groups that are used for walking, climbing, lifting objects, and maintaining posture. Patients with PMM report chronic fatigue and a lack of endurance. Functional muscle impairment is also evident in smaller muscle groups that control, for example, movements of the eyes and eyelids and alterations in other muscles of the face and neck, which can lead to difficulty with swallowing and, more rarely, slurred speech.

Within each mitochondrion there are maternally inherited circular DNA molecules, mtDNA, that is inherited in a unique way such that within each cell there can be variable amounts of both mitochondria with mutated and non-mutated genes. These mtDNA genes code for thirteen proteins critical to cellular energy metabolism. Pathogenic mutations in mtDNA lead to a spectrum of diseases and physiological dysfunctions. This is due to several factors including the variability in prevalence of the mutated versus non-mutated genes within each cell across various tissues in the body. Myopathy is one of the most common clinical manifestations of disease in patients with PMM and can be a debilitating feature because muscle impairment, lack of endurance and exercise intolerance affect mobility and limit the capability of patients with PMM to perform day-to-day activities.

There are currently no approved therapies for the treatment of PMM, representing a high unmet medical need.

LC-FAOD background

LC-FAOD are a type of inherited genetic errors of metabolism resulting in the inability to use dietary long-chain fatty acids as energy sources in the mitochondria. Fatty acids are metabolized in the mitochondria through OxPhos. Mitochondria have specific enzymes that break down each of the fatty acids to produce ATP. Mutations in the genes encoding the enzymes that break down long-chain fatty acids may lead to severe energy deficits. Specific deficiencies include defects in very long-chain acyl-CoA dehydrogenase (VLCAD), LCHAD, mitochondrial TFP, and carnitine palmitoyltransferase (CPT). Patients need at least partial enzyme activity to survive into adulthood. Patients with the most severe defects in these enzymes have a high mortality rate. The most severe cases of LC-FAOD are diagnosed within the first few days or weeks of life. These patients often present with a severe energy deficit that results in lethargy, liver dysfunction, hypoglycemia, encephalopathy, and high risk for sudden death. Older patients usually present with lack of endurance, poor exercise tolerance, muscle aches, rhabdomyolysis or breakdown of muscle tissue and are at risk of developing kidney injury. Patients with LC-FAOD are instructed to avoid fasting, eat frequent meals and, in some cases, supplement with creatinine and medium chain triglycerides (MCT), in order to maintain sources of energy for oxidative metabolism. In June 2020, a new form of MCT called DOJOLVI® (triheptanoin) was approved in the United States as a source of calories for patients with LC-FAOD. However, DOJOLVI® has not demonstrated clear functional benefits on endurance in randomized, controlled clinical trials. We are not aware of any drug interventional studies underway or currently announced for LC-FAOD.

Our Solution, Mavodelpar

Mavodelpar is an oral, small molecule selective PPARδ agonist designed to modulate genes critical to metabolism and generation of energy. Mavodelpar is designed to selectively activate PPARδ receptors found in the nuclear membrane of muscle and other cells. PPARδ is a member of a family of nuclear receptors that regulate cellular energy generation by modulating the expression of genes that control proteins involved in mitochondrial enzyme activity and the formation of new mitochondria (mitochondrial biogenesis). PPARδ is highly expressed in muscle cells and activation of PPARδ either through genetic manipulation or through small molecule agonists has been shown to increase the ability of muscle cells to use fatty acids as well as improve muscle strength and exercise tolerance. We believe these are the mechanisms by which mavodelpar will act to help patients with mitochondrial diseases.

By selectively targeting PPARδ, mavodelpar may address the cellular energy deficit in patients with genetic mitochondrial myopathies such as PMM and LC-FAOD by:

- Increasing OxPhos activity of mitochondria resulting in enhanced production of ATP;
- Increasing the formation of mitochondrial biogenesis and thereby increasing residual OxPhos activity and subsequent ATP production; and
- Increasing the proportion and/or absolute number of functioning mitochondria which may compensate for poorly functioning or non-functional mitochondria.

To date, mavodelpar has been administered to more than 380 subjects across 10 clinical trials.

Experiments in cell lines derived from patients with genetic mitochondrial myopathies have shown that increasing respiratory chain enzyme (complex I, III or IV) levels and activity can compensate the underlying energy deficit. Agonism of PPARδ can increase the activity of these respiratory chain enzymes.

In addition, pharmacological upregulation of mitochondrial biogenesis in patients with PMM may result in improved energy generation. PPAR agonists have been shown to activate genes that play a central role in regulating mitochondrial biogenesis. We believe that activation of these genes may alleviate the ATP deficient state in patients with genetic mitochondrial myopathies by increasing mitochondrial mass through enhanced mitochondrial biogenesis.

In preclinical models, administration of mavodelpar led to a concentration-dependent increase of FAO and an increase in expression of genes involved in mitochondrial biogenesis. Similarly, data from a prior Phase 1 clinical trial of mavodelpar in healthy volunteers who were randomized to receive 4 weeks of treatment with 100 mg mavodelpar orally twice-daily (n=12) or placebo (n=12) showed increased expression of PPARδ regulated genes. Compared to placebo, analysis of muscle biopsies from mavodelpar treated volunteers showed substantial changes in known PPAR regulated target genes involved in fatty acid metabolism and new mitochondria formation.

We have received orphan drug designations for mavodelpar in the United States for PMM and LC-FAOD. Additionally, we have received orphan drug designations for mavodelpar for mitochondrial encephalomyopathy, lactic acidosis, and neurological stroke-like episodes (MELAS), a form of PMM, and LCHAD, a form of LC-FAOD in Europe. As further clinical data becomes available, we plan to apply for additional orphan designations in the United States and Europe.

We have received Fast Track designation for mavodelpar for the treatment of patients with PMM and LC-FAOD due to LCHAD deficiency, one of the predominant LC-FAOD genotypes.

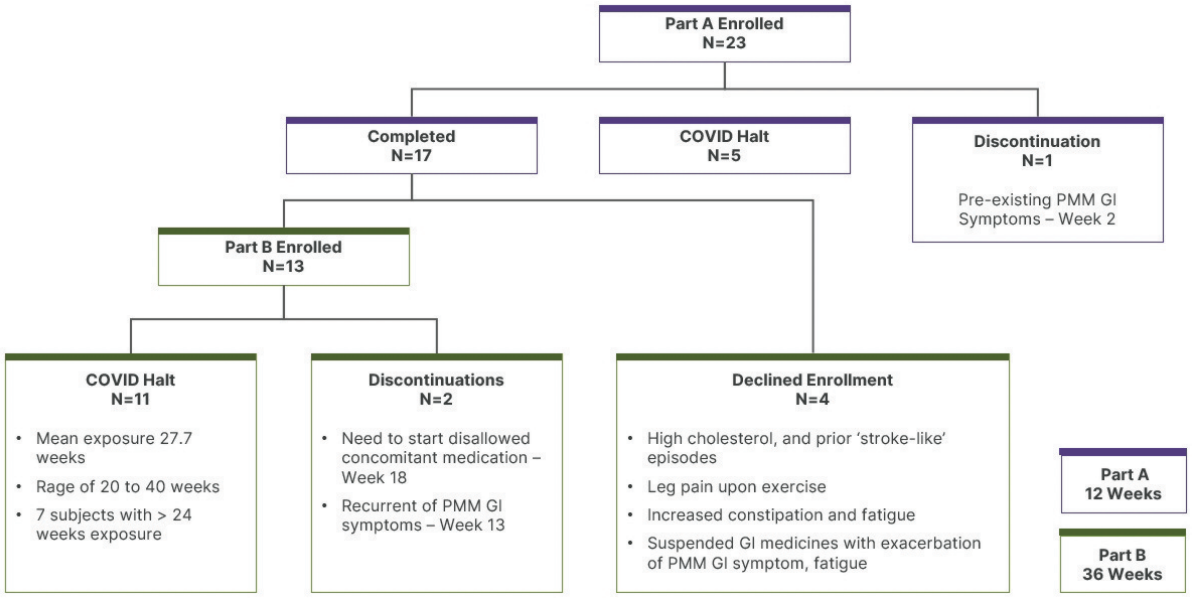
Mavodelpar for the Treatment of PMM

Phase 1b clinical trial in PMM

We completed an open-label Phase 1b trial of mavodelpar in patients with PMM due to mtDNA defects. The primary objective of the trial was to evaluate the safety and tolerability of mavodelpar, and mavodelpar was generally well-tolerated. We selected patients with PMM due to mtDNA defects and excluded patients with PMM due to nDNA defects to reduce heterogeneity in the study. Also, in contrast to patients with PMM due to nDNA defects who have all their mitochondria affected, patients with PMM due to mtDNA defects harbor both normal and mutated mitochondria within their cells (heteroplasmy). In patients with PMM due to mtDNA defects, mavodelpar has the potential to improve the function of affected mitochondria and to increase the overall function of otherwise normal mitochondria. This could potentially happen by impacting mitochondrial biogenesis or by improving mitochondrial function, resulting in improved cellular energy levels for patients with PMM.

The Phase 1b trial was conducted in two parts: Part A (12 weeks dosing) and Part B (optional 36-week treatment extension). All patients were dosed orally with 100 mg mavodelpar once daily. A total of 24 patients were enrolled and 23 patients received mavodelpar in Part A. The planned maximum treatment duration for each patient in both Part A and Part B was 48 weeks. The Phase 1b trial was closed early as a result of the COVID-19 pandemic. At the point of trial closure, a total of 17 patients had completed Part A, 13 patients had entered Part B, and the maximum duration of treatment was approximately 40 weeks. This Phase 1b trial was an open-label study; therefore, was not designed to show statistical significance as compared to a placebo control arm.

Figure 4. Mavodelpar PMM Phase 1b trial enrollment



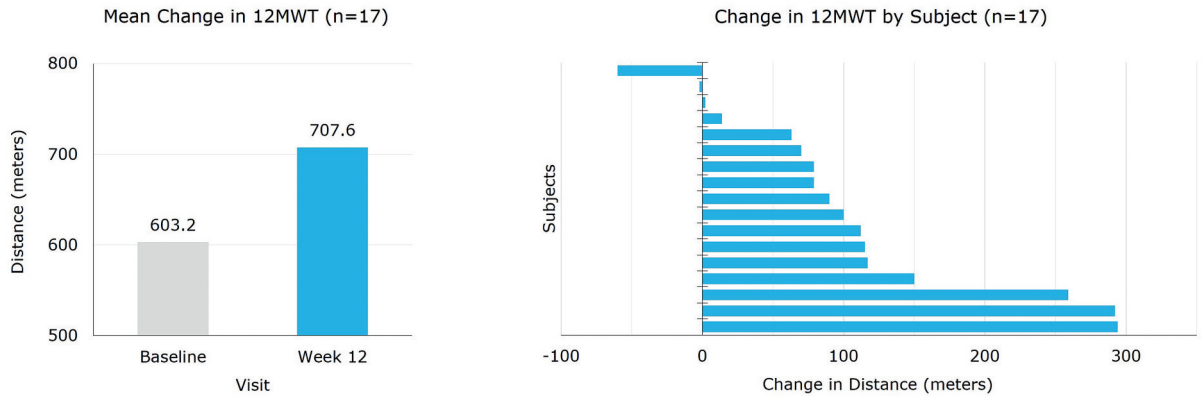
To evaluate changes in patient function, we used a 12-minute walk test (12MWT). We believe that the 12MWT is an ideal assessment of functionality in patients with genetic mitochondrial diseases who commonly lack endurance as the latter half of the exercise period permits the evaluation of patients as they move from P-Cr and carbohydrate metabolism into FAO in the mitochondria.

There were 114 treatment emergent adverse events (TEAE) experienced by 21 out of 23 subjects, with 66 of the 114 TEAEs (57.9%) experienced by 15 subjects which are considered related to study drug. The majority of these TEAEs were mild to moderate in severity. The most commonly reported TEAEs were constipation and headache. Two patients had elevations of creatine phosphokinase of moderate severity that were possibly or probably related to study drug.

Physical performance measures

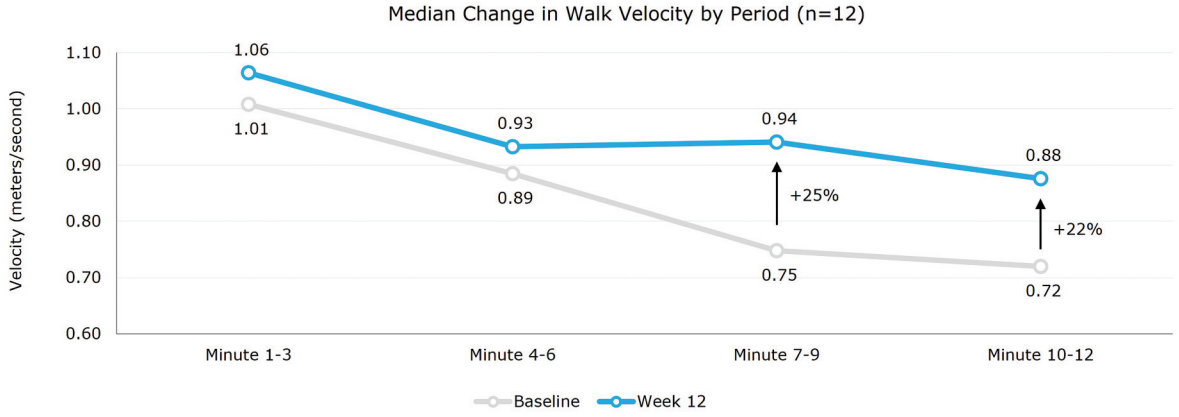
Baseline 12MWT in the Phase 1b trial was 603.2 meters. Following 12 weeks of 100 mg once-daily dosing with mavodelpar, patients achieved an average increase of 104.4 meters (95% CI: 53.1, 155.6) in distance walked during the 12MWT compared to baseline. An increase in distance walked was observed in 15 of 17 patients (88%), with 13 of 17 patients (76%) increasing by 50 meters or greater as illustrated in Figure 5a.

Figure 5a. Mavodelpar-treated patients with PMM had improved 12MWT distances after 12 weeks of treatment



The largest improvement in walk velocity during the 12MWT at week 12 occurred in the second half of the 12-minute period (Figure 5b), which we believe is consistent with mavodelpar's mechanism of action. We expect mavodelpar to improve muscle cell energy by increasing mitochondrial OxPhos, and this process occurs several minutes into exercise (See Figure 1 above).

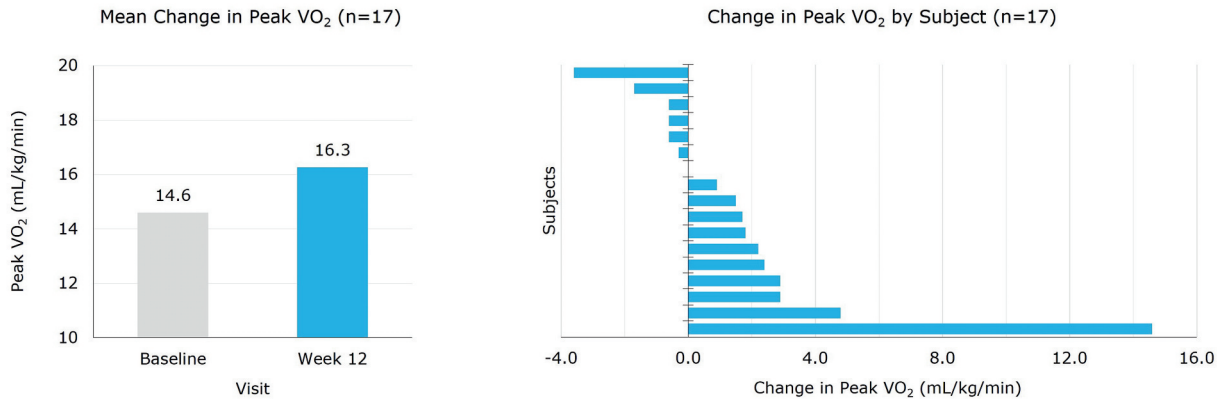
Figure 5b. Mavodelpar-treated patients with PMM had the greatest improvement in walking velocity in the latter half of the 12MWT, consistent with the proposed mechanism of mavodelpar to stimulate fatty acid metabolism



An additional outcome measure in our Phase 1b trial was measurement of peak oxygen consumption (peak VO_2) during maximal exercise. The amount of oxygen used during maximal exercise is a marker of aerobic capacity and is directly correlated with the ability to metabolize fatty acids which require higher amounts of oxygen than other energy sources such as carbohydrates. An average healthy person has a weight-adjusted peak VO_2 of 35 to 40 mL/min/kg for males and 27 to 30 mL/min/kg for females. A weight-adjusted peak VO_2 of 14 mL/min/kg or lower has been determined to predict increased mortality in other patient populations (congestive heart failure).

Baseline weight-adjusted peak VO_2 in the Phase 1b trial was 14.6 mL/min/kg. Following 12 weeks of 100 mg once-daily dosing with mavodelpar, patients achieved an average increase in weighted average peak VO_2 of 1.7 mL/min/kg (95% CI: -0.329, 3.665) compared to baseline (Figure 5c).

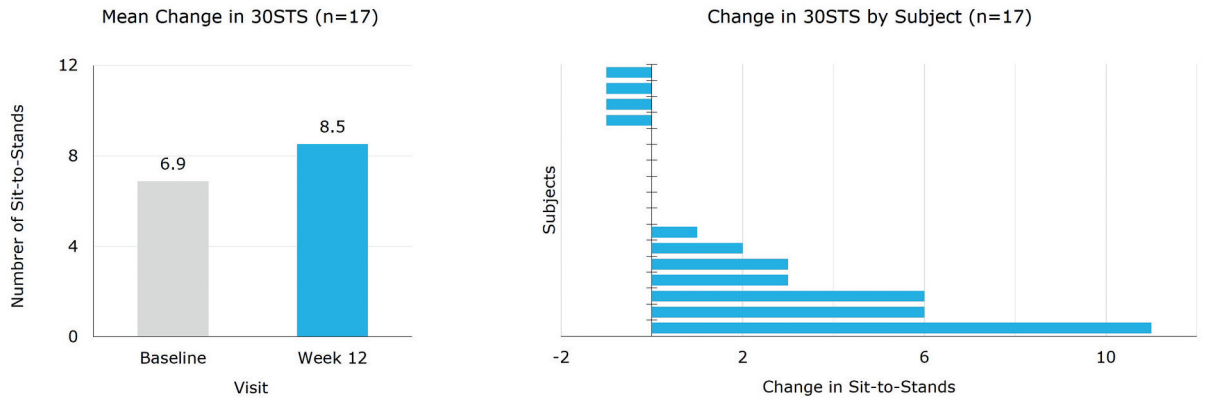
Figure 5c. Peak exercise peak VO_2 increased in patients with PMM after 12 weeks of mavodelpar treatment



Another outcome measure was the sub-maximal exercise test. This test is conducted using a stationary bike for 30 minutes of cycling at 60% of the patient's maximal capacity. At baseline, 7 of the 17 patients (41%) were able to complete the 30-minute test compared to 11 of 17 patients (65%) after 12 weeks of mavodelpar treatment. Overall, a mean improvement of approximately 3 minutes was observed at week 12 compared to baseline, with no increase in heart rate or perceived exertion.

A 30-second sit-to-stand (30STS) test was also performed. The 30STS test measures lower extremity strength and endurance which are needed for daily activities such as climbing stairs, getting out of a chair or bathtub, or rising from a horizontal position. Patients are asked to stand from a sitting position in a chair as many times as possible in 30 seconds and to do so without the use of their arms. At baseline, the patients with PMM in our Phase 1b trial were able to perform this task 6.9 times, which is worse than the typical performance of an elderly person in his or her late 80s. After 12 weeks of treatment with mavodelpar, patients were able to complete the task 8.5 times. Because this test is completed in only 30 seconds, the improvement in performance is more likely due to increased muscle strength rather than improvements in FAO. As shown in Figure 5d below, approximately 40% of patients with PMM showed improvements in lower extremity muscle strength and stamina after 12 weeks of mavodelpar treatment as evaluated with the 30STS test.

Figure 5d. Patients with PMM showed improvements in lower extremity muscle strength and stamina after 12 weeks of mavodelpar treatment as evaluated with the 30STS test



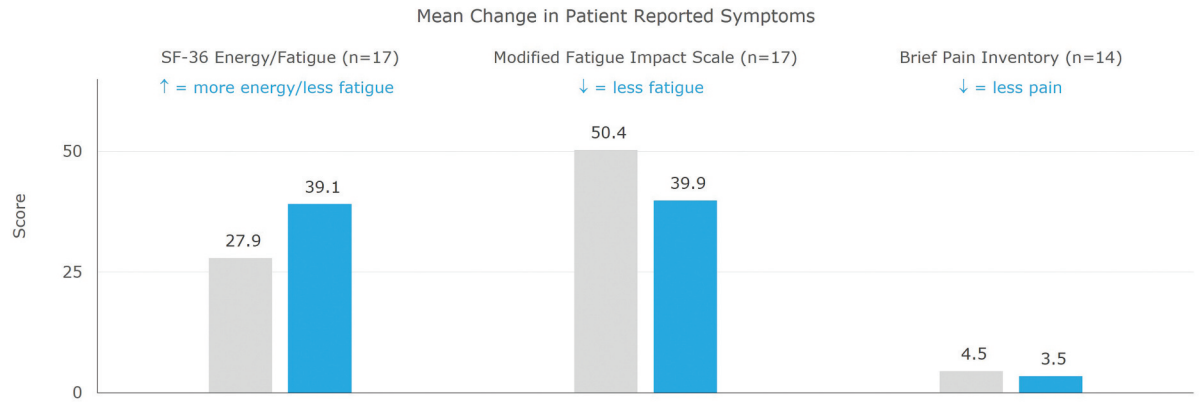
Patient reported outcomes (evaluation of symptoms)

The 36-Item Short Form Health Survey (SF-36) is a 36-item questionnaire that assesses general health including physical activities, mental health, pain, and properties such as energy and fatigue over four weeks. Each domain of the SF-36 can range from 0 to 100, with a higher score representing improvement. As illustrated in the right chart in Figure 5e, after 12 weeks of 100 mg once-daily dosing with mavodelpar, patients (n=17) had a mean improvement in the SF-36 energy/fatigue subscale from 28 at baseline to 39 at 12 weeks.

The Modified Fatigue Impact Scale (MFIS) is a questionnaire that measures both the frequency and impact of fatigue on patients physical, cognitive, and psychosocial functioning over a 4-week period. The total MFIS score scales range from 0 to 84, with a lower score representing less fatigue. As illustrated in the middle chart in Figure 5e, after 12 weeks of 100 mg once-daily dosing with mavodelpar, patients (n=17) had a mean improvement in the MFIS score from 50 at baseline to 40 at 12 weeks.

The Brief Pain Inventory (BPI) measures the patient's perception of pain and the degree that pain interferes with function over the past 24 hours. The BPI scales range from 0 to 10, with a lower score representing less pain. As illustrated in the left chart in Figure 5e, after 12 weeks of 100 mg once-daily dosing with mavodelpar, the patients that reported pain at baseline (n=14), had a mean improvement in the BPI severity scale from 4.5 at baseline to 3.5 at 12 weeks.

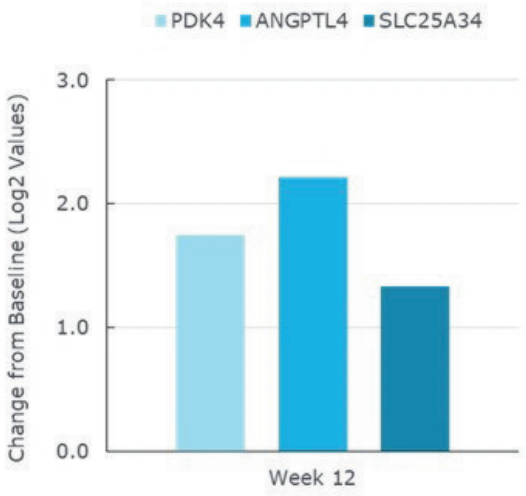
Figure 5e. Mean change from baseline to week 12 in patient reported outcome questionnaires in patients with PMM participating in the Phase 1b trial



Muscle biopsies (evaluation of gene expression)

Muscle biopsies were performed at baseline and after 12 weeks of treatment with mavodelpar to evaluate changes in gene expression (mRNA). Differential gene expression was performed on biopsies from seven subjects that had sufficient sample quantity and quality for analysis at baseline and week 12. As shown in Figure 5f, a statistically significant increase over baseline was observed in the expression of Pyruvate dehydrogenase lipoamide kinase isozyme 4 (PDK4), Angiopoietin-like 4 (ANGPTL4), and Solute carrier family 25 member 34 (SLC25A34).

Figure 5f. Change in PPARδ-regulated gene expression from human muscle following mavodelpar treatment from a Phase 1b clinical trial in patients with PMM



Clinical development plans in PMM

Based on these results, we initiated the STRIDE study, a global, randomized, double-blind, placebo-controlled pivotal Phase 2b trial of mavodelpar in adult patients with PMM due to mtDNA defects. We achieved the target enrollment of 200 patients in the pivotal STRIDE study in March 2023 and anticipate announcement of topline results in the fourth quarter of 2023. STRIDE study is designed to investigate the efficacy and safety of 100 mg mavodelpar administered once-daily over a 24-week period. The primary efficacy endpoint of the trial is the change from baseline in the distance walked during the 12MWT at week 24. Key secondary endpoints include changes from baseline in the MFIS measures and the patient global impression of change scale. Additional secondary endpoints include the 30STS test, step counts, patient global impression of severity scale, BPI, and additional patient-reported outcome measures.

We are also conducting the STRIDE AHEAD study, a 24-month-year, open-label, long-term safety trial outside of the United States in patients with PMM due to mtDNA. STRIDE AHEAD study was recently amended to also allow enrollment of adult patients with PMM due to nDNA defects. Based on interactions with the FDA, EMA, and several other national regulatory agencies in Europe, we believe that positive results from the ongoing pivotal STRIDE and STRIDE AHEAD studies could potentially support registration of mavodelpar for adult patients with PMM due to mtDNA defects in the United States and Europe. We intend to submit the data from STRIDE, together with the long-term safety data from STRIDE AHEAD, to the FDA and the EMA in planned marketing applications in 2024.

Mavodelpar for the Treatment of LC-FAOD

Phase1b clinical trial in LC-FAOD

We completed an open-label Phase 1b study in LC-FAOD adult patients with nDNA defects to assess the safety and tolerability of mavodelpar, and measure changes in functional test such as walk distance, exercise capacity and patient-reported symptoms that could serve as potential endpoints in future clinical studies. The study included patients with defective LCHAD, CPT2, VLCAD, or TFP.

A total of 24 patients were enrolled, including patients with defective LCHAD (n=5), CPT2 (n=8), VLCAD (n=9), or TFP (n=2). We initiated the trial with a dose of 50 mg once-daily in the first three patients followed by 100 mg

once-daily in all subsequent patients. The LCHAD and CPT2 groups had the greatest improvement over baseline in 12MWT (73.7 and 51.9 meters, respectively).

In the LC-FAOD Phase 1b study, mavodelpar was well tolerated. The most common adverse events experienced by patients were rhabdomyolysis (4 patients) and myalgia (4 patients), the majority reported to be mild or moderate in severity. Results of the 12MWT, SF-36 energy/fatigue domain score, and MFIS total score for patients who completed both baseline and week 12 are summarized in Figure 6. Symptom improvement is represented by an increase in SF-36 energy/domain score or a decrease in MFIS total score.

Figure 6. Mean standard error (SE) baseline and week 12 change by genotype[1]

Gene Defect	12MWT [meters]			SF-36 Energy/Fatigue			MFIS Total		
	n	Baseline	Change	n	Baseline	Change	n	Baseline	Change
LCHAD	5	547.7 (133.4)	73.7 (18.0)	5	44.3 (10.4)	19.5 (11.7)	5	32.8 (6.5)	-9.8 (4.2)
CPT2	6	949.6 (119.1)	51.9 (49.4)	6	57.7 (3.2)	0.8 (4.9)	6	23.5 (6.7)	1.0 (3.3)
VLCAD	5	864.3 (65.1)	-36.7 (42.1)	5	57.3 (9.3)	-17.8 (7.8)	5	17.8 (6.8)	15.6 (8.5)

[1] TFP not summarized as only 1 subject completed the study

LC-FAOD Natural History Study

We also completed a 16-week, observational, non-interventional study in patients with LC-FAOD with different nDNA mutations to better understand the natural history of LC-FAOD and changes in patient function and symptoms over time (FORWARD). A total of 58 patients participated in the FORWARD study, including patients with defective LCHAD (n=16), CPT2 (n=30), or VLCAD (n=12).

In the FORWARD study, the most common adverse events experienced by patients were rhabdomyolysis (7 patients) and COVID-19 infection (5 patients), the majority reported to be mild or moderate in severity. Results of the 12MWT, 12-Item Short Form Health Survey (SF-12) vitality domain score, and MFIS total score for patients who completed both baseline and week 16 are summarized in Figure 7. Symptom improvement is represented by an increase in SF-12 vitality score or a decrease in MFIS total score.

Figure 7. Mean (SE) baseline and week 16 change by genotype

Gene Defect	12MWT [meters]			SF-12 Vitality			MFIS Total		
	n	Baseline	Change	n	Baseline	Change	n	Baseline	Change
LCHAD	12	723.0 (63.1)	11.9 (26.7)	13	48.1 (7.7)	-1.9 (6.6)	13	28.1 (4.4)	2.2 (2.9)
CPT2	29	888.6 (31.9)	24.4 (12.9)	30	53.3 (4.9)	-2.5 (4.9)	30	27.7 (2.7)	-2.4 (1.9)
VLCAD	11	818.1 (35.2)	37.9 (17.4)	12	45.8 (6.0)	-6.3 (7.0)	12	33.8 (3.7)	1.8 (3.6)

Based on the results of the LC-FAOD Phase 1b study, in conjunction with the results of the FORWARD study, we intend to continue the development of mavodelpar for certain genotypes of patients with LC-FAOD. Results of the studies were presented at the International Network of Fatty Acid Oxidation Research and Management Conference in August 2022.

We have received Fast Track designation for mavodelpar for the treatment of patients with LC-FAOD due to LCHAD deficiency, one of the predominant genotypes. We are continuing to collaborate with the FDA and European regulatory agencies to advance the LC-FAOD program which will include patients with LCHAD as well as other genotypes. These discussions include obtaining alignment on the study design, patient population, and endpoints for the LC-FAOD program's next clinical trial.

Additional Clinical Trials for mavodelpar

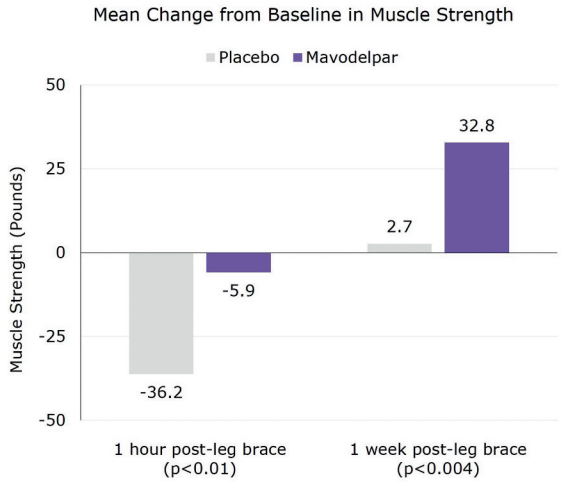
Study	Dose	Duration	Observations
Phase 1 RDBPC† in healthy subjects	25-250 mg	Single-dose	• *Well tolerated*
Phase 1 RDBPC in obese subjects with moderate dyslipidemia	50-200 mg	14 days	• *Well tolerated* • *Decrease in low density lipoprotein (LDL), total cholesterol and triglycerides*
Phase 1 RDBPC in healthy subjects (leg immobilization)	200 mg	28 days	• *Well tolerated* • *Increase in muscle strength* • *Increase in expression of genes involved in fatty acid oxidation and mitochondrial biogenesis*

† randomized double-blind placebo-controlled clinical trial

Limb impairment Phase 1 clinical trial in healthy volunteers

In a prior placebo-controlled Phase 1 clinical trial completed by vTv Therapeutics, 24 healthy volunteers were randomized 1:1 to receive 4 weeks of treatment with either 100 mg mavodelpar orally twice daily (n=12) or placebo (n=12). In the trial, all volunteers had one leg immobilized with a brace for the first 14 days to cause muscle atrophy and weakness. Changes from baseline in muscle strength and gene expression from muscle biopsies were evaluated at various timepoints throughout the clinical trial. Mavodelpar treated volunteers had substantially more leg strength than placebo treated volunteers immediately and one week after the removal of the leg brace. No serious adverse events (SAEs) related to mavodelpar were reported, and TEAEs were similar among subjects who received mavodelpar or placebo.

Figure 8. Results from the muscle strength test from a Phase 1 clinical trial in healthy volunteers



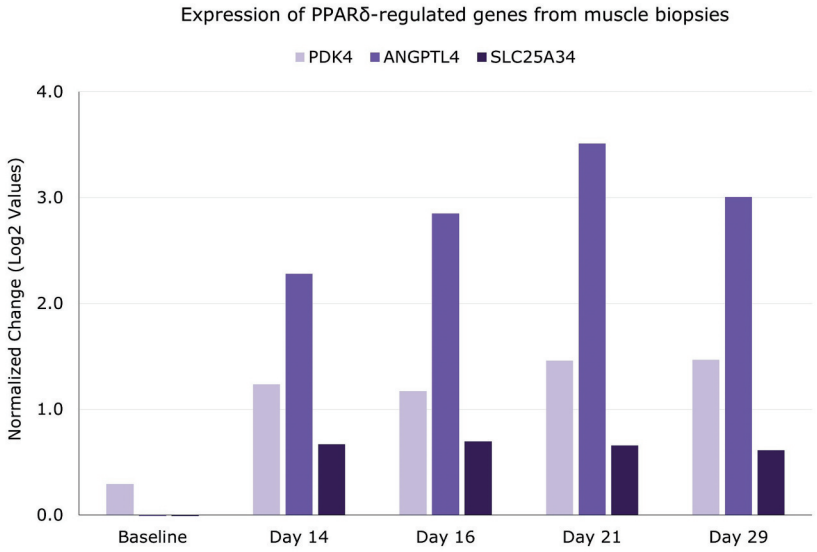
(p-value from a mixed model with baseline value as covariate)

In the description of the Phase 1 clinical results in Figure 8 above, a p-value represents the probability that random chance caused the result. For example, a p-value of 0.001 means that there is a 0.1% probability that the difference between the control group and the treatment group is purely due to random chance. A p-value of less than or equal to 0.05 is a commonly used threshold for identifying statistically significant outcomes. The FDA's evidentiary standard of efficacy when evaluating the results of a clinical trial generally relies on a p-value of less than or equal to 0.05.

Muscle biopsies were collected and analyzed for mRNA of PPARδ-regulated genes involved in mitochondrial biogenesis and function (Figure 9). Muscle biopsies obtained from mavodelpar treated individuals showed substantial increases in the mRNA of the following PPAR-regulated genes compared to placebo-treated controls:

- **PDK4** encodes a mitochondrial protein. This kinase plays a key role in regulation of glucose and fatty acid metabolism.
- **ANGPTL4** is a target of PPARs. The encoded protein is a serum hormone directly involved in regulating lipid metabolism.
- **SLC25A34** belongs to the SLC25 family of mitochondrial carrier proteins. Members of the solute carrier family 25 are known to transport molecules over the mitochondrial membrane.

Figure 9. Change in PPARδ-regulated gene expression from human muscle following mavodelpar treatment from a Phase 1 clinical trial in healthy volunteers



Safety

Overall, mavodelpar has been well tolerated in all clinical trials conducted and there have been no drug related deaths or SAEs reported to date. Most observed TEAEs were mild or moderate in severity. In clinical trials where patients were randomized to mavodelpar or placebo, the incidence and severity of adverse events were similar among individuals who received mavodelpar or placebo.

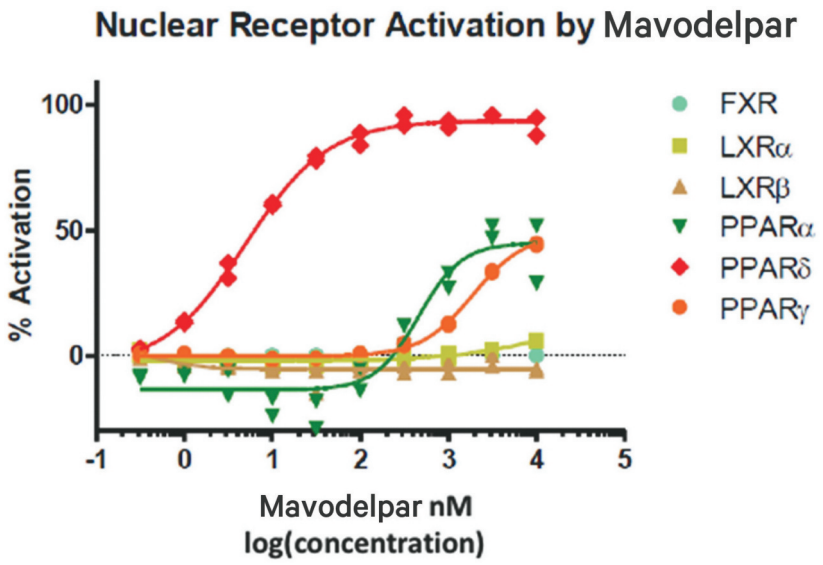
To date, mavodelpar has been administered to more than 380 subjects across 10 clinical trials.

Preclinical Results and Plans

A substantial package of preclinical data along with Phase 1 placebo-controlled clinical data was in-licensed from vTv Therapeutics. This package has been expanded through additional in vitro and in vivo studies to support the future registration of mavodelpar. In these studies, it has been observed that mavodelpar is a potent and

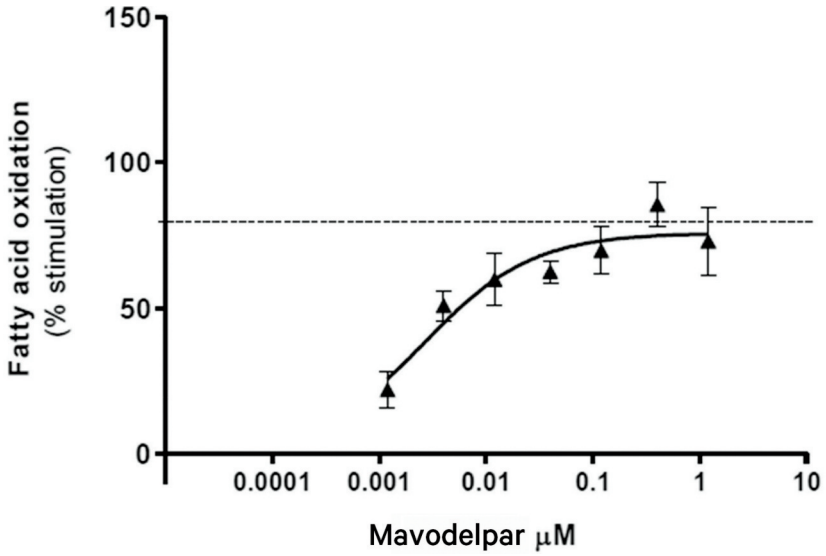
selective agonist of PPARδ with an EC50 value of 31 nM for PPARδ and over 300-fold increased selectivity over PPARα and PPARγ. Mavodelpar has shown minimal or no activity against other ligand-activated nuclear receptors. These other receptors, including the liver X and farnesoid X receptors, were evaluated because they have a role in regulating lipid homeostasis and energy metabolism. Mavodelpar has also been evaluated for these receptors in transcriptional assays with similar findings (Figure 10).

Figure 10. Mavodelpar is a selective agonist of PPARδ



To access effects of mavodelpar on FAO, incubation of mavodelpar on XM5 human muscle cell line with mavodelpar demonstrated a concentration-dependent increase in FAO as shown in Figure 11 below.

Figure 11. Mavodelpar led to a concentration-dependent increase in FAO in XM5 human muscle cell line



In an *in vivo* experiment, administration of mavodelpar to mice led to increased expression of a number of FAO genes and genes involved in mitochondrial biogenesis including PGC1α, a fatty acid transcriptional co-factor;

CPT1B, the rate-limiting enzyme in the transport of fatty acids into the mitochondria; PDK4, a negative regulator of glucose metabolism; and UCP3, a carrier protein involved in regulating metabolic rate in muscle cells (Figure 12).

Figure 12. The transcription of fatty acid metabolism genes was increased after seven days of dosing with mavodelpar in mice

Gene	Name	Description	Fold-change over vehicle (SEM)
PGCα	PPARγ co-activating factor 1α	Mitochondrial Biogenesis	1.65 (0.19)
CPT1B	Carnitine palmitoyltransferase 1B	Fatty acid metabolism	1.35 (0.15)
PDK4	Pyruvate dehydrogenase kinase	Fatty acid metabolism	1.88 (0.17)
UCP3	Mitochondrial uncoupling protein 3	Fatty acid metabolism	2.29 (0.27)

PPARα and PPARγ agonists have been approved for dyslipidemia and glycemic control in diabetes mellitus, respectively. Liver and cardiac toxicity associated with PPAR drugs have been observed. Certain non-selective PPAR agonists have shown carcinogenicity signals in preclinical studies. The FDA requires that two-year carcinogenicity studies be completed in rats and mice for PPAR agonists prior to conducting clinical trials longer than six months in duration due to observations of tumor formation in rodents (FDA Guidance for Industry Diabetes Mellitus: Developing Drugs and Therapeutic Biologics for Treatment and Prevention, February 2008). The purpose of carcinogenicity studies is to identify tumorigenic potential of a new drug candidate in rodents and to assess the relevant risk to humans.

Reneo is conducting a 104-week carcinogenicity study in rats and mice using low, medium and high doses of mavodelpar as well and control groups. These studies are being conducted according to FDA good laboratory practice (GLP) regulations. We expect results from both studies in the fourth quarter of 2023.

We are unaware of any data suggesting that there is a clinical cancer risk with selective PPARδ agonists. CymaBay Therapeutics, Inc. is conducting a Phase 3 clinical trial of up to 52 weeks with seladelpar, a selective PPARδ agonist in patients with primary biliary cholangitis. Astellas Pharma Inc. is conducting a Phase 2/3 clinical trial of up to 52-weeks plus 24-weeks extension with bocidelpar, a selective PPARδ agonist. Collectively, this suggests that both seladelpar and bocidelpar have likely been cleared in two-year carcinogenicity studies and that there is no evidence of a carcinogenicity signal for the selective PPARδ agonist class. We are currently conducting the required two-year carcinogenicity studies with mavodelpar.

We have completed a 6-month toxicology study in rats and a 12-month toxicology study in primates. No adverse effects associated with PPARα or PPARγ agonists were observed with administration of mavodelpar at any dose level.

Sales and Marketing

We currently do not have a commercial organization for the marketing, sales, and distribution of pharmaceutical products. We plan to build a fully integrated rare genetic mitochondrial disease pharmaceutical company and will retain commercial rights to mavodelpar in the United States and key European markets. For other territories, we will seek strategic partnerships to bring mavodelpar to market with the goal of establishing mavodelpar as the standard of care around the world. We may also opportunistically seek strategic collaborations to benefit from the resources of biopharmaceutical companies specialized in either relevant disease areas or geographies.

License Agreement with vTv Therapeutics

In December 2017, we entered into a License Agreement with vTv Therapeutics (vTv License Agreement), under which we obtained an exclusive, worldwide, sublicensable license under vTv Therapeutics intellectual

property relating to vTv Therapeutics' PPARδ agonist program, to develop, manufacture and commercialize PPARδ agonists and products containing such PPARδ agonists, including mavodelpar, or licensed products, for any therapeutic, prophylactic or diagnostic application in humans.

Under the terms of the vTv License Agreement, we made an upfront payment of $3.0 million to vTv Therapeutics and issued to vTv Therapeutics shares of our common stock representing a minority interest in our outstanding equity. Upon the achievement of certain development and regulatory milestones, we are required to pay vTv Therapeutics milestone payments totaling up to $64.5 million. We are also required to pay vTv Therapeutics up to $30 million in total sales-based milestones upon achievement of certain sales thresholds of the licensed product. In addition, we are obligated to make royalty payments to vTv Therapeutics at mid-single digit to low teen percentage royalty rates, based on tiers of annual net sales of licensed products, subject to certain customary reductions. Such royalties will be payable on a licensed product-by-licensed product and country-by-country basis until the latest of (i) expiration of the last-to-expire licensed patents covering a licensed product in a country, which are expected to expire in 2034, absent any patent term adjustments or extension, (ii) expiration of regulatory exclusivity rights for a licensed product in a country, which is expected to be five years of new chemical entity exclusivity upon approval of a licensed product, such as mavodelpar, in the United States, where such exclusivity would run concurrently with seven years of orphan drug exclusivity, if we are the first to receive marketing approval of a licensed product for an orphan disease or condition for which we have received orphan designation, such as approved orphan uses of mavodelpar for the treatment of patients with PMM and LC-FAOD, in the United States, and (iii) the tenth anniversary after the first commercial sale of a licensed product in a country. In July 2021, a milestone under the vTv License Agreement was achieved, and we made a payment of $2.0 million to vTv Therapeutics.

Under the terms of the vTv License Agreement, we have sole authority and responsibility for the worldwide development and commercialization of the licensed products, at our cost, subject to certain diligence obligations to use commercially reasonable efforts with respect to specified development and commercialization efforts, including seeking approval for and commercializing at least one product in two major markets.

The vTv License Agreement, unless terminated earlier, will continue until expiration of the last to expire royalty term. Either party may terminate the vTv License Agreement for the other party's uncured material breach or insolvency. We may terminate the vTv License Agreement at will upon prior written notice. Upon expiration (but not earlier termination) of the vTv License Agreement, the licenses granted to us will survive on a royalty-free basis in perpetuity. Upon termination of the vTv License Agreement, we are required to, upon vTv Therapeutics' request, (i) grant to vTv Therapeutics a non-exclusive, worldwide, royalty-free, fully paid, perpetual, irrevocable, sublicensable license under our intellectual property solely for vTv Therapeutics and its sublicensees to develop, manufacture, and commercialize the licensed products for any therapeutic, prophylactic or diagnostic application in humans or (ii) if vTv Therapeutics agrees to pay us a low single digit percentage royalty on net sales of licensed products by vTv Therapeutics, then such license grant to vTv Therapeutics will be exclusive, and we will assign and transfer to vTv Therapeutics all regulatory materials and approvals related to the licensed product.

Intellectual Property

The proprietary nature of, and protection for, mavodelpar, any future product candidates, and other proprietary technologies are important to our business. We strive to protect our product candidates and other proprietary technologies, processes and know-how through a variety of methods. In regard to our product candidates, we seek and maintain patents intended to cover our products and compositions, their methods of use for treating diseases, the processes for their manufacture, and, as our product candidates proceed through clinical studies, the innovations that arise from these efforts. As a result, we seek to obtain domestic and foreign patent protection and endeavor to promptly file patent applications for new commercially valuable inventions to expand our intellectual property portfolio. Our policy is to pursue, maintain and defend patent rights in strategic areas, whether developed internally or licensed from third parties, and to protect the technology, inventions and improvements that are commercially important to the development of our business. We also rely on trade secrets and other proprietary know-how that may be important to the development of our business.

We have developed and continue to expand our patent portfolio for mavodelpar. We have licensed from vTv Therapeutics eight issued patents in the United States and 19 issued patents in foreign countries covering composition of matter of mavodelpar, among other things, which are expected to expire in 2026, absent any patent term adjustments or extensions. Additionally, we have licensed four issued patents in the United States, six issued patents in foreign countries, one pending application in the United States, and one pending application in Europe, from vTv Therapeutics covering methods of using mavodelpar, which are expected to expire in 2034, absent any patent term adjustments or extensions.

In addition to the licensed vTv Therapeutics patents and applications relating to mavodelpar, we have filed our own patent applications. We co-own one pending application in the United States and five pending applications in foreign countries, and own three pending applications in the United States, one pending international patent application, an issued patent in foreign country, and over 25 pending applications in foreign countries, directed to various methods of use of mavodelpar. These pending patent applications, if issued, would be expected to expire between 2040 and 2043, absent any patent term adjustments or extensions. We also own one issued patent in the United States, one pending application in the United States, one pending international patent applications, and over 15 pending applications in foreign countries directed to methods of manufacturing, and crystalline forms (polymorphs) of mavodelpar. The issued patent, and pending patent applications if issued, are expected to expire in 2041, absent any patent term adjustments or extensions. Patents related to mavodelpar may be eligible for patent term extensions in certain jurisdictions, including up to five years in both the United States and the EU, upon approval of a commercial use of the corresponding product by a regulatory agency in the jurisdiction where the patent was granted.

In addition, we currently have Orphan Drug Designation for mavodelpar for the treatment of LC-FAOD and PMM in the United States and LCHAD deficiency and MELAS in the EU, providing the opportunity to receive seven years of orphan exclusivity in the United States (upon approval of NDA), and ten years of market exclusivity in the EU and Japan (upon receipt of marketing authorization).

As mavodelpar has not previously been approved in the United States for any indication, mavodelpar may be eligible for five years of new chemical entity exclusivity upon approval in the United States, where such exclusivity would run concurrently with its seven years of orphan drug exclusivity, if we obtain orphan drug exclusivity for its approved uses. Further, as mavodelpar has not previously been approved in the EU for any indication, mavodelpar may be eligible for eight years of data exclusivity upon approval in the EU, as well as two years of market exclusivity. In the EU, an additional one year of exclusivity may be obtained if mavodelpar is approved for a new indication that provides a significant clinical benefit.

In addition to patent protection around mavodelpar, we have also licensed from vTv Therapeutics an issued patent in the United States directed to composition of matter around other PPARδ agonists, which is expected to expire in October 2023, absent any patent term adjustments or 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. In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to an approved drug may be extended and only those claims covering the approved drug, a method of using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and some other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We plan to seek patent term extensions from applicable authorities, including the United States Patent and Trademark Office (USPTO) in the United States, to any of our issued patents covering mavodelpar, and any future product candidates, in any jurisdiction where these patent term extensions are available. There is no

guarantee that the applicable authorities, including the USPTO in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property." We also seek to protect our intellectual property in part by entering into confidentiality agreements with companies with whom we share proprietary and confidential information in the course of business discussions, and by having confidentiality terms in our agreements with our employees, consultants, scientific advisors, clinical investigators, and other contractors and also by requiring our employees, commercial contractors, and certain consultants and investigators, to enter into invention assignment agreements that grant us ownership of any discoveries or inventions made by them while in our employ.

In addition to patent protection, we also rely on trademark registration, trade secrets, know how, other proprietary information and continuing technological innovation to develop and maintain our competitive position. We seek to protect and maintain the confidentiality of proprietary information of our business that is not amenable to, or that we do not consider appropriate for, patent protection. We take steps to protect our proprietary information, including trade secrets and unpatented know-how, by entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors. However, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets and unpatented know-how, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

Manufacturing

We do not own or operate manufacturing facilities. We rely on contract manufacturing organizations (CMOs) to produce mavodelpar in accordance with the FDA's current Good Manufacturing Practices (cGMP) regulations for use in our clinical trials. The manufacture of pharmaceuticals for human use is subject to extensive cGMP regulations, which impose various procedural and documentation requirements and govern all areas of record keeping, production processes and controls, personnel training, and quality control. We obtain our supplies from these CMOs on a contract work order basis and do not have long-term supply arrangements in place. We believe there are multiple sources for all the materials required for the manufacture of mavodelpar. As mavodelpar advances through development, we expect to enter into longer-term commercial supply agreements with key suppliers and manufacturers to fulfill and secure our production needs. Our relationships with CMOs are managed by internal personnel with extensive experience in pharmaceutical development and manufacturing.

Competition

The biotechnology and pharmaceutical industries are characterized by rapid technological advancement, significant competition and an emphasis on intellectual property. We face potential competition from many different sources, including major and specialty pharmaceutical and biotechnology companies, academic research institutions, governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with current therapies and new therapies that may become available in the future.

Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces. Mergers and acquisitions in the pharmaceutical, biotechnology and oncology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified

scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or less expensive than any products we may develop. Our competitors also may obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in competitors establishing a strong market position before we are able to enter the market. We believe that the key competitive factors affecting the success of any of our product candidates, if approved, will include efficacy, combinability, safety profile, convenience, cost, level of promotional activity devoted to them and intellectual property protection.

There are no approved therapies indicated for the treatment of PMM in any country. Physicians attempt to treat symptoms in patients with drugs or vitamins and supplements. For example, anti-convulsant drugs are used to prevent or control seizures. CymaBay Therapeutics, Inc. is conducting a Phase 3 clinical trial of up to 52 weeks with seladelpar, a selective PPARδ agonist in patients with primary biliary cholangitis. Astellas Pharma Inc. is conducting a Phase 2/3 clinical trial of up to 52-weeks plus 24-weeks extension with bocidelpar, a selective PPARδ agonist. Other companies are developing therapies for mitochondrial diseases, including, Stealth BioTherapeutics Corp., Abliva AB, Cyclerion Therapeutics, Inc., Khondrion B.V. and Minovia Therapeutics.

There is one product approved in the United States for LC-FAOD. In June 2020, a new form of MCT called DOJOLVI® (triheptanoin) was approved and indicated in the United States as a source of calories for patients with LC-FAOD. However, DOJOLVI® has not demonstrated clear functional benefits on endurance in clinical trials. We are not aware of any drug interventional studies underway or currently announced for LC-FAOD.

Furthermore, it is possible that other companies are also engaged in discovery or nonclinical development of product candidates for PMM or LC-FAOD. These competitors, if successful in clinical development, may achieve regulatory approval and market adoption in advance of our product candidates, constraining our ability to gain significant market share for such product candidates. In addition, our product candidates, if approved, will complete with multiple approved products or products that may be approved for future indications for which we develop such product candidate.

Government Regulation and Product Approval

As a pharmaceutical company we are subject to extensive regulation. Government authorities in the United States (at the federal, state, and local level) and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and export and import of drug products such as those we are developing. Any drug candidates that we develop must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in the EU are addressed in a centralized way, but country-specific regulation remains essential in many respects.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act (FDCA) and implementing regulations. Drugs are also subject to other federal, state, and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. 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 administrative or judicial sanctions. FDA sanctions could

include, among other actions, refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls or withdrawals from the market, 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 extensive preclinical laboratory tests, preclinical animal studies and formulation studies in accordance with applicable regulations, including the FDA's GLP regulations, and other applicable regulations;
- submission to the FDA of an Investigational New Drug (IND) application, which must become effective before human clinical trials may begin;
- approval by an IRB at each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable regulations, including the FDA's current good clinical practices (GCP) regulations to establish the safety and efficacy of the proposed drug for its proposed indication;
- submission to the FDA of a new drug application (NDA) for a new drug;
- a determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA's current cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality, and purity;
- potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of the NDA;
- satisfactory completion of an FDA advisory committee review, if applicable; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Before testing any compounds with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity, and formulation, as well as animal studies, to assess the potential safety and activity of the drug candidate. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLPs. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance.

Clinical trials involve the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be

reviewed and approved by an IRB or ethics committee, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

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

- *Phase 1*. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution, and excretion, the side effects associated with increasing doses and if possible, to gain early evidence of effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase 2*. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases or conditions and to determine dosage tolerance, optimal dosage, and dosing schedule.
- *Phase 3*. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall benefit/risk ratio of the product and provide an adequate basis for product approval. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

In some cases, FDA may require, or sponsors may voluntarily pursue, post-approval studies, or Phase 4 clinical trials, that are conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, such as with accelerated approval drugs, FDA may mandate the performance of Phase 4 trials. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2, and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable 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. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access 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 as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, and purity of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. Data may come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product to the satisfaction of the FDA. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Prescription Drug User Fee Act (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 FDA because the FDA has approximately two months to make a "filing" decision after it the application is submitted The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality, and purity. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the 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 and typically follows the advisory committee's recommendations.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product 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 sites to assure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process, and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or (an) additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies, or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings, or precautions be included in the product labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market

studies or clinical trials. For example, the FDA may require Phase 4 testing, which involves clinical trials designed to further assess a drug safety and effectiveness, and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also determine that a risk evaluation and mitigation strategy (REMS) is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare genetic mitochondrial disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States or, if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare genetic mitochondrial disease or condition.

Expedited Development and Review Programs

The FDA has a number of programs intended to expedite the development or review of products that meet certain criteria. For example, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a Fast Track product has opportunities for more frequent interactions with the review team during product development, and the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Any product submitted to the FDA for approval, including a product with a Fast Track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment,

diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the 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 that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval, which could adversely impact the timing of the commercial launch of the product.

The Food and Drug Administration Safety and Innovation Act established a category of drugs referred to as "breakthrough therapies" that may be eligible to receive breakthrough therapy designation. A sponsor may seek FDA designation of a product candidate as a "breakthrough therapy" if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance. 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. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.

Fast track designation, breakthrough therapy designation, priority review, and accelerated approval do not change the standards for approval, but may expedite the development or approval process. Even if a product 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. We may explore some of these opportunities for our product candidates as appropriate.

Post-Approval Requirements

Any drug products for which we receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, manufacturing, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, and complying with FDA promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval to ensure the long-term stability of the drug product. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP requirements. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA

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

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

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

The FDA also may require post-marketing testing, known as Phase 4 testing, and surveillance to monitor the effects of an approved product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures.

The FDA closely regulates the marketing, labeling, advertising, and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity, and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified

promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

Marketing Exclusivity

Market exclusivity provisions under the FDCA can also 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 (ANDA) or a 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 also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from accepting ANDAs or 505(b)(2) NDAs for drugs referencing the approved application for review. 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.

Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of non-patent market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Other U.S. Healthcare Laws and Compliance Requirements

Although we currently do not have any products on the market, we are and, upon approval and commercialization, will be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. In the United States, such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, price reporting, and healthcare provider sunshine laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting, or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering, or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The 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. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing, or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement

will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. Additionally, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The federal False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-covered, uses. In addition, the Affordable Care Act codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

The Health Insurance Portability and Accountability Act of 1966 (HIPAA) also created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items, or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Additionally, the federal Physician Payments Sunshine Act and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) annually report information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, certain ownership and investment interests held by physicians and their immediate family members.

In order to distribute products commercially, we must also comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers, and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, track, and report gifts, compensation and other remuneration made to physicians and other healthcare providers, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including without

limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we or our collaborators obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we or our collaborators receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such drug products.

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

If we elect to participate in certain governmental programs, we may be required to participate in discount and rebate programs, which may result in prices for our future products that will likely be lower than the prices we might otherwise obtain. For example, drug manufacturers participating under the Medicaid Drug Rebate Program must pay rebates on prescription drugs to state Medicaid programs. Under the Veterans Health Care Act (VHCA) drug companies are required to offer certain drugs at a reduced price to a number of federal agencies, including the U.S. Department of Veterans Affairs and Department of Defense, the Public Health Service and certain private Public Health Service designated entities in order to participate in other federal funding programs, including Medicare and Medicaid. Recent legislative changes require that discounted prices be offered for certain U.S. Department of Defense purchases for its TRICARE program via a rebate system. Participation under the VHCA also requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations. If our products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply.

Different pricing and reimbursement schemes exist in other countries. In Europe, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. EU member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may

require the completion of clinical trials that compare the cost-effectiveness of a particular drug candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

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

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other healthcare funding and applying new payment methodologies. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the Affordable Care Act) was enacted, which affected existing government healthcare programs and resulted in the development of new programs.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the “individual mandate” was repealed by Congress. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (IRA) into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is also unclear how such challenges and the healthcare reform measures of the Biden administration will impact the Affordable Care Act or our business.

Other legislative changes have also been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and due to subsequent legislative amendments to the statute will remain in effect until 2031, unless additional Congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. In addition, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug’s average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

There has also been heightened governmental scrutiny recently over the manner in which pharmaceutical companies set prices for their marketed products, which has resulted in several Congressional inquiries, Presidential executive orders, and proposed federal legislation, as well as state efforts, designed to, among other things, bring more transparency to product pricing, reduce the cost of prescription drugs under Medicare, review

the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the U.S. Department of Health and Human Services (HHS) released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. Further, the IRA, among other things (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. Additionally, the Biden administration released an additional executive order on October 14, 2022, directing HHS to report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We anticipate that certain reform measures will result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. In addition, it is possible that there will be further legislation or regulation that could harm our business, financial condition, and results of operations.

Data Privacy and Security

In the ordinary course of our business, we may process personal or sensitive data. Accordingly, we are, or may become, subject to numerous data privacy and security obligations, including federal, state, local, and foreign laws, regulations, and guidance governing data privacy and security. Such obligations may include, without limitation, the Federal Trade Commission Act, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020 (CPRA) (collectively, the CCPA), the European Union's General Data Protection Regulation 2016/679 (EU GDPR), and the EU GDPR as it forms part of United Kingdom (UK) law (UK GDPR). In addition to the CCPA, several other states within the United States, such as Virginia, Colorado, Utah, and Connecticut have enacted or proposed comprehensive privacy laws and similar laws are being considered in several other states, as well as at the federal and local levels.

The CCPA and EU GDPR are examples of the increasingly stringent and evolving regulatory frameworks related to personal data processing that may increase our compliance obligations and exposure for any actual or perceived noncompliance. For example, the CCPA imposes obligations on covered businesses to provide specific disclosures related to a business's collection, use, and disclosure of personal data and to respond to certain requests from California residents related to their personal data (for example, requests to know of the business's personal data processing activities, to correct or delete the individual's personal data, and to opt out of certain personal data disclosures). Also, the CCPA provides for administrative fines and a private right of action for certain data breaches which may include an award of statutory damages. In addition, the CPRA's recent amendments to the CCPA established a new regulatory agency to implement and enforce the law.

Foreign data privacy and security laws (including, but not limited to, the EU GDPR and UK GDPR) impose significant and complex compliance obligations on entities that are subject to those laws. For example, the EU GDPR applies to any company established in the European Economic Area (EEA) and to companies established outside the EEA that process personal data in connection with the offering of goods or services to data subjects in the EEA or the monitoring of the behavior of data subjects in the EEA. These obligations may include limiting

personal data processing to only what is necessary for specified, explicit, and legitimate purposes; requiring a legal basis for personal data processing; requiring the appointment of a data protection officer in certain circumstances; increasing transparency obligations to data subjects; requiring data protection impact assessments in certain circumstances; limiting the collection and retention of personal data; increasing rights for data subjects; formalizing a heightened and codified standard of data subject consents; requiring the implementation and maintenance of technical and organizational safeguards for personal data; mandating notice of certain personal data breaches to the relevant supervisory authority(ies) and affected individuals; and mandating the appointment of representatives in the UK and/or the EU in certain circumstances. Further, it is unclear how UK data protection laws and regulations will develop in the medium to long term. The UK's Data Protection and Digital Information Bill was laid before the UK Parliament on July 18, 2022, introducing reforms intended to update and simplify the UK's data protection framework, deviating from the EU GDPR. This may impose additional compliance costs on companies that operate in both the UK and the EU.

See the section titled "Risk Factors" for additional information about the laws and regulations to which we are or may become subject and about the risks to our business associated with such laws and regulations.

The U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act of 1977 (FCPA) prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Europe / Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we or our potential collaborators obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. Previously, in the EU, pursuant to the EU Clinical Trials Directive 2001/20/EC, a Clinical Trial Application (CTA) had to be submitted to each country's national regulatory authority in which the clinical trial was to take place, together with an independent ethics committee, much like the FDA and IRB, respectively. Although the Directive had sought to harmonize the EU clinical trials regulatory framework, EU Member States transposed and applied the provisions of the Directive differently, leading to significant variation in the regulatory regimes of the member states. In 2014, a new Clinical Trials Regulation 536/2014, replacing the current Directive, was adopted. The new Regulation is directly applicable in all EU Member States (without national implementation) and entered into application on 31 January 2022. The new Regulation seeks to simplify and streamline the approval of clinical trials in the EU. Pursuant to the Regulation, the sponsor shall submit a single CTA via the EMA's Clinical Trials Information System (CTIS), which will cover all regulatory and ethics assessments from the member states concerned.

Any submissions made from January 31, 2023 onwards must be made through CTIS and all trials authorized pursuant to the Directive that are still ongoing on January 31, 2025 have their details registered on CTIS, in both cases trials registered on CTIS will have to comply with the Regulation. Once the CTA is approved in accordance with a member state's requirements, clinical trial development may proceed. Approval and monitoring of clinical trials in the EU is, as it was under the Directive, the responsibility of individual member states, but compared to the position prior to the applicability of the Clinical Trials Regulation there is likely to be more collaboration, information-sharing, and decision-making between member states. The new Regulation also aims to streamline

and simplify the rules on safety reporting and introduces enhanced transparency requirements, such as mandatory submission of a summary of the clinical trial results to a new EU Database.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Clinical trials of medicinal products in the European Union (EU) must be conducted in accordance with EU and national regulations and the International Conference on Harmonization guidelines on 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.

Prior to commencing a clinical trial, the sponsor must obtain a CTA from the competent authority, and a positive opinion from an independent ethics committee. 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. Any substantial changes to the trial protocol or other information submitted with the CTA must be notified to or approved by the relevant competent authorities and ethics committees. Medicines used in clinical trials must be manufactured in accordance with GMP. Other national and EU-wide regulatory requirements may also apply.

During the development of a medicinal product, the EMA and national regulators provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Scientific Advice Working Party of the Committee for Medicinal Products for Human Use (CHMP). A fee is incurred with each scientific advice procedure. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical trials, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future marketing authorization application (MAA) of the product concerned.

To obtain regulatory approval of an investigational drug or biological product in the EU, we must submit a MAA either under the so-called centralized or national authorization procedures.

Centralized procedure. The centralized procedure provides for the grant of a single marketing authorization (MA), which is issued by the European Commission based on the opinion of the Committee for Medicinal Products for Human Use (CHMP) of the EMA and that is valid in all EU member states, as well as Iceland, Liechtenstein and Norway. The Centralized Procedure is mandatory for certain types of products, medicines that are derived from biotechnology processes, such as genetic engineering, designated orphan medicinal products, and medicines that contain 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, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the Centralized Procedure the maximum timeframe for the evaluation of an MAA is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when the authorization of a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. Under the accelerated procedure the standard 210-day review period is reduced to 150 days.

Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the U.S. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product

developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is however not guaranteed.

The benefits of a PRIME designation include the appointment of a CHMP rapporteur before submission of a MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

- *National authorization procedures*. There are also two other possible routes to authorize medicinal products in several EU countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure.
- *Decentralized procedure*. Using the decentralized procedure, an applicant may apply for simultaneous authorizations in more than one EU country of medicinal products that have not yet been authorized in any EU Member State and that do not fall within the mandatory scope of the centralized procedure.
- *Mutual recognition procedure*. In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national MA.

In the EU, upon receiving MA, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. 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. Once renewed, the MA is valid for an unlimited period unless the European Commission or the national competent authority decides on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. If granted, data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic/biosimilar application. During the additional two-year period of market exclusivity, a generic/biosimilar MA can be submitted, and the innovator's data may be referenced, but no generic/biosimilar product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity and qualify for data exclusivity.

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. The application for orphan drug designation must be submitted before the MAA. Orphan medicinal products are eligible for financial incentives such as free protocol assistance, fee reductions for access to the centralized regulatory procedures and ten years of market exclusivity following drug approval, which can be extended to 12 years if trials are conducted in accordance with an agreed-upon pediatric investigational plan. The exclusivity period may be reduced to six years if, at the end of the fifth year, it is established that the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports (PSURs).

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

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

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

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.

Great Britain (GB) is no longer covered by the EEA's procedures outlined above following the expiry of the Brexit transition period on January 1, 2021 (Northern Ireland will be covered by the centralized authorization procedure and can be covered under the decentralized or mutual recognition procedures). A GB or UK MA will be required to market drugs in GB. However, for three years from January 1, 2021, the Medicines and Healthcare Products Regulatory Agency (MHRA) may adopt decisions taken by the European Commission on the approval of new marketing authorizations through the centralized procedure, and the MHRA will have regard to marketing authorizations approved in a country in the EEA (although in both cases a MA will only be granted if any GB-specific requirements are met). Various national procedures are now available to place a drug on the market in the UK, GB, or Northern Ireland, with the main national procedure having a maximum timeframe of 150 days (excluding time taken to provide any further information or data required). The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation), and after Brexit, new EU laws on clinical trials (including the EU Clinical Trials Regulation, EU CTR) are not applicable in GB. The UK may further diverge from the EU in relation to the regulation of medicinal products which could disrupt cross-border operations between the UK and EU. The Retained EU Law (Revocation and Reform) Bill 2022, which is currently progressing through the United Kingdom Parliament and seeks to allow the UK Government to repeal or replace certain EU Law that was incorporated into UK law effective as of the end of the Brexit transition period, increases the likelihood of such divergence and will need to be closely monitored going forward. Already, as a result of Brexit various benefits of membership no longer apply to the UK, for example, UK sponsored trials that span several EU countries now need to have an individual or organization in the EU to act as a legal representative, or sponsor and the UK does not have access to new EU clinical trial databases such as CTIS pursuant to the Trade and Cooperation Agreement. Additionally, new rules apply to the import of investigational medicinal products from the EU and EEA to GB. The data exclusivity periods in the UK are currently in line with those in the EU, but the Trade and Cooperation Agreement provides that the periods for both data and market exclusivity are to be determined by domestic law, so there could be divergence in the future.

The UK regulatory framework in relation to orphan drug designation is derived from existing EU legislation (as implemented into UK law, through secondary legislation). The European Commission is currently evaluating

new legislation in relation to orphan medicines and these laws will no longer be applicable in GB. Since January 1, 2021, there has been no route to obtain pre-MA orphan designation in GB, however, as a result of the implementation of the Northern Ireland Protocol, EU orphan drug designation and time periods of market exclusivity still remain valid for marketing products in Northern Ireland. Instead, the MHRA now reviews applications for GB orphan designation in parallel with the corresponding MA application. The criteria are essentially the same as under the EU regime, but have been tailored for the GB market, i.e., the prevalence of the condition in GB (rather than the EU) must not be more than 5 in 10,000. For medicinal products that have received orphan status on or after January 1, 2021, a period of 10 years orphan market exclusivity is awarded from the date of MA by the MHRA. An additional two years of exclusivity may be added where pediatric data requirements have been met. Products with an orphan designation in the EU may be considered for a GB orphan MA. However, where centrally authorized MAs have an existing EU orphan designation, these have been converted into GB MAs and shall continue in effect with the remaining period of orphan market exclusivity.

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

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

Employees

As of March 21, 2023, we employed 48 employees, 36 of whom are full-time. At the same date, 29 of our employees were located in the United States and 19 were located in the UK. None of our employees are subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

We expect to continue to add employees in 2023, with a focus on expanding our clinical, research and development and commercialization capabilities. We continually evaluate the business need and opportunity to expand our team and balance in-house expertise and capacity with outsourced expertise and capacity. Currently, we outsource substantial clinic trial work to clinical research organizations and drug manufacturing to contract manufacturers.

Corporate Information

We were incorporated in Delaware in 2014. Our principal executive offices are located at 18575 Jamboree Road, Suite 275-S, Irvine, California 92612, and our telephone number is (858) 283-0280. Our corporate website address is www.reneopharma.com. Information contained on or accessible through our website is not a part of this Annual Report, and the inclusion of our website address in this Annual Report is an inactive textual reference only. Our design logo, “Reneo,” and our other registered and common law trade names, trademarks and service marks are the property of Reneo Pharmaceuticals, Inc.

Emerging Growth Company

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act). We may take advantage of certain exemptions from various public company reporting requirements, including being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure, not being required to have our internal control over financial reporting audited by our independent registered public accounting firm under Section 404 of the Sarbanes-Oxley Act of 2002 (the Sarbanes-Oxley Act), reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a

nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We may take advantage of these exemptions until December 31, 2026 or until we are no longer an "emerging growth company," whichever is earlier. We will cease to be an emerging growth company prior to the end of such period if certain earlier events occur, including if we become a "large accelerated filer" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended (the Exchange Act), our annual gross revenues exceed $1.235 billion or we issue more than $1.0 billion of non-convertible debt in any three-year period.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of accounting standards that have different effective dates for public and private companies until those standards would otherwise apply to private companies. We have elected to use this extended transition period under the JOBS Act until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our consolidated financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

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

Item 1A. Risk Factors

RISK FACTORS

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" before deciding whether to purchase, hold or sell shares of our common stock. The occurrence of any of the risks described below could harm our business, financial condition, results of operations, growth prospects, and/or stock price or cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report and those we may make from time to time. You should consider all of the risk factors described when evaluating our business. Certain statements below are forward-looking statements. See also "Cautionary Note Regarding Forward-Looking Statements" and "Risk Factor Summary" in this Annual Report.

Risks Related to Our Business and Industry

We have incurred significant net losses since our inception in 2014 and anticipate that we will continue to incur significant net losses for the foreseeable future. We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

We are a clinical-stage pharmaceutical company founded in 2014, and our operations to date have focused primarily on raising capital, establishing and protecting our intellectual property portfolio, organizing and staffing our company, business planning, and conducting preclinical and clinical development of, and manufacturing development for, our only product candidate, mavodelpar. Additionally, as an organization, we have not yet demonstrated an ability to successfully complete clinical development, obtain regulatory approvals, manufacture a commercial-scale product, or conduct sales and marketing activities necessary for successful commercialization. As we build our capabilities and expand our organization, we have not yet demonstrated an ability to overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the pharmaceutical area. Consequently, any predictions about our future performance may not be as accurate as they would be if we had a history of successfully developing and commercializing pharmaceutical products.

Investment in pharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effectiveness in the targeted indication or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred significant net losses since our inception. If mavodelpar is not successfully developed and approved in the United States or Europe, we may never generate any revenue. For the years ended December 31, 2022 and 2021, we reported a net loss of $52.0 million and $39.8 million, respectively. As of December 31, 2022, we had an accumulated deficit of $136.7 million.

We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our clinical development of, and seek regulatory approvals for, mavodelpar and any future product candidates. We may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Our prior net losses and expected future net losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of increased expenses, or when, if at all, we will be able to achieve profitability.

The uncertainties around our ability to obtain additional funding raise substantial doubt regarding our ability to continue as a going concern for a period of twelve months following the date that these consolidated financial

statements were issued. See Note 1 of Notes to Consolidated Financial Statements included in this Annual Report for a detailed discussion.

We will need substantial additional capital to develop and commercialize mavodelpar and any future product candidates and implement our operating plan. If we fail to complete additional financings, we may be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Our operations have consumed substantial amounts of cash since our inception. We expect to continue to spend substantial amounts of capital to continue the clinical development of, and seek regulatory approval for, mavodelpar and any future product candidates. We will require significant additional amounts of capital in order to prepare for commercialization, and, if approved, to launch and commercialize mavodelpar.

As of December 31, 2022, we had cash, cash equivalents and short-term investments of $101.2 million. Based on our current operating plan, we believe that our cash, cash equivalents and short-term investments as of December 31, 2022. will enable us to fund our operating expenses and capital expenditure requirements through our planned near-term clinical milestones. However, changing circumstances may cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of clinical trials and preclinical studies for mavodelpar;
- the scope, prioritization and number of our research and indications we pursue;
- the costs and timing of manufacturing for our product candidate, mavodelpar;
- the costs, timing, and outcome of regulatory review of mavodelpar;
- the timing and amount of the milestone or other payments we must make to vTv Therapeutics and any future licensors;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of securing manufacturing arrangements for commercial production;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our product candidate.

In any event, we will require additional capital for the further development and commercialization of mavodelpar and any future product candidates and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Until such time as we can generate significant revenue from sales of our product candidate, if ever, we expect to finance our operations through public or private equity offerings or debt financings, credit or loan facilities, collaborations, strategic alliances, licensing arrangements or a combination of one or more of these funding sources. Additional funds may not be available to us on acceptable terms or at all. In May 2022, we entered into an at-the-market equity offering sales agreement with SVB Securities LLC (ATM facility) under which we may offer and sell, from time to time, at our sole discretion, up to $20.0 million in shares of our common stock.

The remaining capacity under the ATM facility was approximately $18.8 million in shares of common stock as of March 21, 2023.

Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and disruptions to, and volatility in, the credit and financial markets in the United States and worldwide, including those resulting from the ongoing COVID-19 pandemic, bank failures, actual or perceived changes in interest rates and economic inflation. 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 mavodelpar or other research and development initiatives. We also could be required to seek collaborators for mavodelpar and any future product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to mavodelpar and any future product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

We currently depend entirely on the success of mavodelpar, which is our only product candidate. If we are unable to advance mavodelpar through clinical development, obtain regulatory approvals, and ultimately commercialize mavodelpar, or experience significant delays in doing so, our business will be materially harmed.

We currently only have one product candidate, mavodelpar, and our business and future success depends entirely on our ability to develop, obtain regulatory approval for, and then successfully commercialize, mavodelpar, which is currently in clinical development in patients with PMM and patients with LC-FAOD. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development that may be able to better sustain failure of a lead product candidate.

The success of mavodelpar will depend on several factors, including the following:

- successful enrollment in our ongoing and planned clinical trials and completion of such clinical trials with favorable results;
- acceptance by the FDA and EMA of data from our STRIDE, STRIDE AHEAD, or future clinical trials in patients with PMM;
- demonstration of a positive risk/benefit profile for mavodelpar in the relevant patient population, to the satisfaction of applicable regulatory authorities;
- meeting chemistry, manufacturing and controls (CMC) requirements and passing applicable GCP inspections;
- the outcome, timing, and cost of meeting regulatory requirements established by the FDA, EMA, and other comparable foreign regulatory authorities;
- receipt of marketing approvals from applicable regulatory authorities, including one or more NDAs from the FDA and marketing authorizations from the European Commission (based on the opinion of the Committee for Medicinal Products for Human Use (CHMP) of the EMA, and maintaining such approvals);
- establishing commercial manufacturing relationships and receiving/importing commercial supplies approved by the FDA and other regulatory authorities from any future third-party manufacturer;
- establishing sales, marketing, and distribution capabilities and commercializing mavodelpar, if approved, whether alone or in collaboration with others;
- acceptance, if and when approved, by patients, the medical community and third-party payors;
- obtaining and maintaining third-party coverage and adequate reimbursement;
- establishing and maintaining patent and trade secret protection and regulatory exclusivity for mavodelpar;

- maintaining an acceptable risk/benefit safety profile of mavodelpar following approval; and
- maintaining and growing an organization of people who can develop and commercialize mavodelpar.

If we do not achieve one or more of these factors, many of which are beyond our control, in a timely manner or at all, we could experience significant delays or an inability to develop, obtain regulatory approvals or commercialize mavodelpar.

Even if regulatory approvals are obtained, we may never be able to successfully commercialize mavodelpar. In addition, we will need to transition at some point from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition. Accordingly, we may not be able to generate sufficient revenue through the sale of mavodelpar to continue our business.

Our clinical trials may fail to adequately demonstrate the safety and efficacy of mavodelpar, which could prevent or delay regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of a product candidate, we must demonstrate through lengthy, complex, and expensive preclinical testing and clinical trials that a product candidate is both safe and effective for use in each target indication. Clinical trials often fail to demonstrate safety and efficacy of the product candidate studied for the target indication. Most product candidates that commence clinical trials are never approved by regulatory authorities for commercialization. Further, we have used patient reported outcomes in our clinical trials, including our Phase 1b study of mavodelpar in PMM, such as the MFIS, the BPI, and the SF-36 that assesses the general health of patients. Such patient reported outcomes are based on subjective patient feedback and can be inherently difficult to evaluate. Such patient reported outcomes can be influenced by factors outside of our control and can vary widely from day to day for a particular patient, and from patient-to-patient and site-to-site within a clinical trial. It is possible that the FDA or other regulatory agencies will not accept such patient reported outcomes, and any such non-acceptance may require changes to existing trial protocols or the conduct of additional clinical trials. Moreover, our ongoing pivotal STRIDE study and our completed Phase 1b studies in patients with PMM and LC-FAOD utilize a 12MWT as an assessment of endurance and exercise tolerance in patients rather than the six-minute walk test (6MWT) which is more commonly used.

Preclinical and clinical drug development is a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results.

Preclinical and clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. A failure of one or more preclinical or clinical trials can occur at any stage of testing. The results of preclinical studies and early clinical trials of mavodelpar may not be predictive of the results of later-stage clinical trials. In addition, product candidates in later stages of clinical trials may fail to show a positive risk/benefit profile despite having progressed through preclinical studies and initial clinical trials. Also, because there are no approved drugs for PMM and only one approved product, a caloric supplement, for LC-FAOD, there are no regulatory precedents by which we can be guided with respect to regulatory endpoints.

As such, we cannot be certain that our ongoing and planned clinical trials will be successful. Many companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to the inability to enroll patients in rare disease clinical trials and the lack of efficacy or safety profiles, notwithstanding promising results in earlier trials. Moreover, preclinical and clinical data is often susceptible to varying interpretations and analyses. Our completed clinical trials have involved a limited number of patients and clinical trial sites and have been open-label or uncontrolled trials. We may face significant setbacks as we expand the number of patients and clinical sites, potentially affecting the efficiency of trial execution and the consistency of trial data, which may delay or prevent regulatory approval of mavodelpar. Any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of mavodelpar in those and other indications, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Further, if patients drop out of our clinical trials, miss scheduled doses or follow-up visits, or otherwise fail to follow clinical trial protocols, whether as a result of the COVID-19 pandemic, actions taken to slow the spread of COVID-19 or otherwise, the integrity of data from our clinical trials may be compromised or not accepted by the FDA, EMA or other regulatory authorities, which would represent a significant setback for the applicable program.

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

We may not be able to initiate or continue our clinical trials for mavodelpar and any future product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, EMA and comparable foreign regulatory authorities. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the clinical trial, the design of the clinical trial, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

In particular, each clinical indication for which we are evaluating mavodelpar is a rare genetic disease with limited patient populations from which to draw participants in clinical trials. We will be required to identify and enroll a sufficient number of patients with the disease under investigation for our clinical trials of mavodelpar. Potential patients may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our clinical trials. Additionally, other pharmaceutical companies with more resources and greater experience in drug development and commercialization are targeting similar genetic mitochondrial diseases we are targeting and may do so with respect to additional indications we target in the future. Any recruiting of clinical trial patients by competitors from the patient populations we are targeting in our ongoing or future clinical trials may delay or make it more difficult to fully enroll our clinical trials. Our inability to enroll a sufficient number of patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. In addition, we rely on CROs and clinical trial sites to ensure proper and timely conduct of our clinical trials and, while we have agreements governing their services, we will have limited influence over their actual performance.

We are unable to predict with confidence the likelihood or duration of such patient enrollment delays and difficulties, whether related to COVID-19 or otherwise. If patient enrollment is delayed for an extended period of time, our clinical trials could be delayed or otherwise adversely affected.

Any delays in the commencement or completion, or termination or suspension, of our clinical trials could result in increased costs to us, delay or limit our ability to generate revenue, and adversely affect our commercial prospects.

Before we can initiate clinical trials for mavodelpar or any future product candidates, we must submit the results of preclinical studies to the FDA or comparable foreign regulatory authorities, along with other information, including information about CMC, and our proposed clinical trial protocol, as part of an IND application or similar regulatory filing under which we must receive authorization to proceed with clinical development.

Before obtaining marketing approval from regulatory authorities for the sale of mavodelpar or any future product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of mavodelpar and any future product candidates in humans. Clinical testing is expensive, time-consuming, and uncertain as to outcome. In addition, we may rely in part on preclinical, clinical and quality data generated by CROs and other third parties for regulatory submissions for mavodelpar and any future product candidates. While we have or will have agreements governing these third parties' services, we have limited influence over their actual performance. If these third parties do not make data available to us, or, if applicable, do not make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may be significantly delayed, and we may need to conduct additional clinical trials or collect additional data independently. In either case, our development costs would increase.

We do not know whether our current or any future clinical trials will begin on time, need to be redesigned, enroll an adequate number of patients, or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- obtaining regulatory authorizations to commence a clinical trial or reaching a consensus with regulatory authorities on clinical trial design or implementation;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining approval from one or more institutional review boards (IRBs) or Ethics Committees (ECs);
- IRBs or ECs refusing to approve, suspending or terminating the clinical trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the clinical trial;
- changes to clinical trial protocols;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- sites deviating from clinical trial protocol or dropping out of a clinical trial;
- the FDA or comparable foreign regulatory authorities' failure to accept our proposed manufacturing processes and suppliers and/or requirement to provide additional information regarding our manufacturing processes before providing marketing authorization;
- manufacturing sufficient quantities of mavodelpar or any future product candidates or obtaining sufficient quantities of combination therapies for use in clinical trials;
- subjects failing to enroll or remain in our trials at the rate we expect, or failing to return for post-treatment follow-up;
- subjects choosing an alternative treatment for the indications for which we are developing mavodelpar and any future product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- occurrence of SAEs in clinical trials of the same class of agents conducted by other companies;
- inability to establish confirmatory evidence with the regulatory agencies where only a single arm trial is feasible to conduct in certain rare disease populations;
- a facility manufacturing mavodelpar or any of its components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of current good manufacturing practice (cGMP) regulations or other applicable requirements, or infections or cross-contaminations of mavodelpar in the manufacturing process;
- any changes to our manufacturing process, suppliers or formulation that may be necessary or desired;
- third-party vendors not performing manufacturing and distribution services in a timely manner or to sufficient quality standards;
- supply chain disruptions such as scarcity of raw materials used to manufacture mavodelpar;
- impact of possible trade disputes with countries where mavodelpar or its ingredients are manufactured;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, GCP or other regulatory requirements;

- third-party contractors not performing data collection or analysis in a timely or accurate manner;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or
- the impacts of the COVID-19 pandemic on our ongoing and planned clinical trials.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting, or completing our planned and ongoing clinical trials. For example, our Phase 1b study of mavodelpar in patients with PMM was closed early as a result of the COVID-19 pandemic. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs or ECs of the institutions in which such trials are being conducted or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Currently, the FDA and other foreign regulatory agencies have placed a class-wide requirement on all PPAR agonists asking sponsors to complete the two-year rat and mouse carcinogenicity studies before conducting studies longer than six-months in duration. As a result, it may take longer to enroll patients in the long-term safety trial, which could adversely affect the timing of our regulatory submissions for marketing approval. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing, or successful completion of a clinical trial.

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

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

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

Use of mavodelpar or any future product candidates could be associated with side effects, adverse events or other properties that could delay or prevent regulatory approval or result in significant negative consequences following marketing approval, if any.

As is the case with pharmaceuticals generally, it is likely that there may be side effects and adverse events associated with the use of mavodelpar and any future product candidates. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by mavodelpar and any future product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. If drug-related SAEs are observed, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval for mavodelpar for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition, results of operations and prospects significantly.

Additionally, if mavodelpar and any future product candidates receive marketing approval, and we or others later identify undesirable side effects caused by such product candidate, a number of potentially significant negative consequences could result, including:

- we may be forced to suspend marketing of that product, or decide to remove the product from the marketplace;
- regulatory authorities may withdraw approvals or change their approvals of such product;
- regulatory authorities may require additional warnings on the label or limit access of that product to selective specialized centers with additional safety reporting and with requirements that patients be geographically close to these centers for all or part of their treatment;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way the product is administered;
- we could be subject to fines, injunctions, or the imposition of criminal or civil penalties, or sued and held liable for harm caused to subjects or patients; and
- 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 mavodelpar and any future product candidates, if approved, and could significantly harm our business, results of operations, and prospects.

The regulatory approval process is lengthy, expensive and uncertain, and we may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of our product candidates and adversely impact our ability to generate revenue, our business and our results of operations.

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

in clinical development of product candidates, regulatory approval is never guaranteed. Neither we nor any future collaborator is permitted to market mavodelpar and any future product candidates in the United States until we receive approval of an NDA from the FDA. We have not previously submitted an NDA to the FDA, or similar drug approval filings to comparable foreign authorities.

Prior to obtaining approval to commercialize a product candidate in the United States or in foreign markets, we must demonstrate with substantial evidence from adequate and well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for mavodelpar are promising, such data may not be sufficient to support approval by the FDA and comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities, as the case may be, may also require us to conduct additional preclinical studies or clinical trials for mavodelpar and any future product candidates either prior to or post-approval, or may object to elements of our clinical development program.

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

- serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by people using drugs similar to mavodelpar and any future product candidates;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- the FDA or comparable foreign regulatory authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;
- 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 any of its proposed indications;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- 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 mavodelpar, and any future product candidates may not be sufficient to satisfy the FDA or comparable foreign regulatory authorities to support the submission of an NDA or other comparable submissions in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Any of the above events could prevent us from achieving market approval of mavodelpar or any future product candidates and could substantially increase the costs of commercializing mavodelpar or any future product candidates. The demand for mavodelpar or any future product candidates could also be negatively impacted by any adverse effects of a competitor's product or treatment.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market mavodelpar and any future product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Even if we eventually complete clinical trials and receive approval of an NDA or foreign marketing application for mavodelpar and any future product candidates, the FDA or comparable foreign regulatory authority may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, and/or the implementation of a REMS which may be required to ensure safe use of the drug after approval. The FDA or the comparable 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 comparable foreign regulatory authority may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

Our business has been and could continue to be adversely affected by the evolving and ongoing COVID-19 global pandemic in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. The COVID-19 pandemic could adversely affect our operations, as well as the business or operations of our manufacturers, CROs, or other third parties with whom we conduct business.

Our business has been and could continue to be adversely affected by the evolving COVID-19 pandemic, which was declared by the World Health Organization as a global pandemic. As COVID-19 continues to spread, we may experience ongoing disruptions that could severely impact our business and clinical trials.

Our clinical trials have been, and may in the future be, affected by the COVID-19 pandemic. For example, as a result of the COVID-19 pandemic, our Phase 1b study of mavodelpar in patients with PMM was closed early and we temporarily paused enrollment in our other Phase 1b studies. Additionally, the COVID-19 pandemic may impact patient enrollment in all of our ongoing clinical trials. In particular, some sites may pause enrollment to focus on, and direct resources to, COVID-19, while at other sites, patients may choose not to enroll or continue participating in the clinical trial as a result of the pandemic. In addition, patient visits to our clinical trial sites in the United States, Europe, Australia, New Zealand, and Canada at some point in the past or currently have slowed as a result of the COVID-19 pandemic. Further, according to the Centers for Disease Control and Prevention and the National Health Service in the UK, people who have serious chronic medical conditions, including those such as genetic mitochondrial diseases, are at higher risk of getting very sick from COVID-19. As a result, current or potential patients in our ongoing and planned clinical trials may choose to not enroll, not participate in follow-up clinical visits, or drop out of the trial as a precaution against contracting COVID-19. Further, some patients may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services.

If patient enrollment is delayed for an extended period of time, our ongoing and planned clinical trials could be delayed or otherwise adversely affected. Similarly, our ability to recruit and retain principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, may be adversely impacted.

In addition, we may encounter a shortage in supplies of, or in delays in shipping, our study drug or other components of the clinical trial vital for successful conduct of the trial. Further, the successful conduct of our clinical trials depends on retrieving laboratory data from patients. Any failure by the laboratories with which we work to send us such data could impair the progress of such clinical trials. These events could delay our clinical trials, increase the cost of completing our clinical trials, and negatively impact the integrity, reliability, or robustness of the data from our clinical trials.

We are actively monitoring and managing our response and evaluating the actual and potential impacts to our business operations, including on our ongoing and planned clinical trials. We will continue to work closely with

our third-party vendors, collaborators, and other parties in order to seek to advance our programs and pipeline of product candidates, while keeping the health and safety of our employees and their families, partners, third-party vendors, healthcare providers, patients and communities a top priority.

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

From time to time, we may publicly disclose interim, topline, or preliminary data from our clinical trials, including from our studies of mavodelpar in patients with PMM and LC-FAOD, 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 interim, topline, or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Interim, topline, and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, such data should be viewed with caution until the final data are available. Adverse differences between preliminary, interim, or topline data and final data could significantly harm our business prospects.

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 the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate, or our business. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, mavodelpar and any future product candidates may be harmed, which could harm our business, operating results, prospects, or financial condition.

If the market opportunities for mavodelpar and any future product candidates are smaller than we believe they are, or we face substantial competition in our markets, our future revenue may be adversely affected, and our business may suffer.

If the size of the market opportunities in each of our target indications for mavodelpar and any future product candidates is smaller than we anticipate, we may not be able to achieve profitability and growth. We focus our clinical development of mavodelpar on therapies for adult patients with genetic mitochondrial diseases with relatively small patient populations. Given the relatively small number of patients who have the diseases that we are targeting and intend to target with mavodelpar, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare genetic mitochondrial diseases. In addition, our estimates of the patient populations for our target indications have been derived from a variety of sources, including the scientific literature, payor claims data, surveys of clinics, patient foundations, and market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. In addition, the potentially addressable patient population for PMM and LC-FAOD may be limited or may not be amenable to treatment with mavodelpar, if approved. Further, even if we obtain significant market share for mavodelpar in PMM or LC-FAOD, we may never achieve profitability despite obtaining such significant market share, as other pharmaceutical companies with more resources and greater experience in drug development and commercialization are or may be targeting this same genetic mitochondrial disease.

We may not be successful in our efforts to expand our pipeline by identifying additional indications for which to investigate mavodelpar in the future. We may expend our limited resources to pursue a particular indication or formulation for mavodelpar and fail to capitalize on product candidates, indications or formulations that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we are focused on specific indications for mavodelpar. As a result, we may fail to generate additional clinical development opportunities for mavodelpar for a number of reasons, including, mavodelpar may in certain indications, on further study, be shown to have harmful side effects, limited to no efficacy, or other characteristics that suggest it is unlikely to receive marketing approval and achieve market acceptance in such additional indications.

While our initial focus is to advance mavodelpar for PMM to regulatory approval, we may plan to conduct several clinical trials for mavodelpar in parallel over the next several years, including multiple clinical trials in PMM and LC-FAOD, which may make our decision as to which additional indications to focus on more difficult. As a result, we may forego or delay pursuit of opportunities with other indications that could have had greater commercial potential or likelihood of success. However, we may focus on or pursue one or more of our target indications over other potential indications and such development efforts may not be successful, which would cause us to delay the clinical development and approval of mavodelpar. Furthermore, research programs to identify additional indications for mavodelpar require substantial technical, financial, and human resources. We are pursuing a tablet formulation for mavodelpar and may pursue additional formulations. However, we may not successfully develop these additional formulations for chemistry-related, stability-related, or other reasons. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for specific indications may not yield any commercially viable products.

Additionally, we may pursue additional in-licenses or acquisitions of development-stage assets or programs, which entails additional risk to us. Identifying, selecting and acquiring promising product candidates requires substantial technical, financial, and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a particular product candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. For example, if we are unable to identify programs that ultimately result in approved products, we may spend material amounts of our capital and other resources evaluating, acquiring and developing products that ultimately do not provide a return on our investment.

Obtaining and maintaining regulatory approval for a product candidate in one jurisdiction does not mean that we will be successful in obtaining regulatory approval for that product candidate in other jurisdictions.

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

We expect to submit a MAA to the EMA for approval of mavodelpar in the EU for the treatment of PMM and other clinical indications if data support registration. As with the FDA, obtaining an MAA, issued by the European Commission, based on the opinion of the CHMP of the EMA, is a similarly lengthy and expensive process. Regulatory authorities in jurisdictions outside of the United States and the EU also have requirements for approval for product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign

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

We currently have no marketing and sales organization. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell mavodelpar and any future product candidates, we may not be able to generate product revenues.

We currently do not have a commercial organization for the marketing, sales, and distribution of pharmaceutical products. To commercialize mavodelpar and any future product candidates, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We intend to build a highly specialized commercial organization to support the commercialization of mavodelpar, if approved, in the United States and the EU.

The establishment and development of our own sales force or the establishment of a contract sales force to market mavodelpar and any future product candidates will be expensive and time-consuming and could delay any commercial launch. Moreover, we may not be able to successfully develop this capability. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of mavodelpar. To the extent we rely on third parties to commercialize mavodelpar, if approved, we may have little or no control over the marketing and sales efforts of such third parties and our revenues from product sales may be lower than if we had commercialized mavodelpar and any future product candidates ourselves. In the event we are unable to develop our own marketing and sales force or collaborate with a third-party marketing and sales organization, we would not be able to commercialize mavodelpar or any future product candidates.

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

Any regulatory approvals that we receive may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including post-market studies or clinical trials, and surveillance to monitor safety and effectiveness. The FDA may also require us to adopt a REMS to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may include, among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. We or our collaborators may also be required to adopt a REMS or engage in similar actions, such as patient education, certification of health care professionals, or specific monitoring, if we or others later identify undesirable side effects caused by any product that we develop alone or with collaborators.

In addition, if the FDA or a comparable foreign regulatory authority approves a product candidate, the manufacturing, quality control, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export, and recordkeeping for the approved product will be subject to extensive and ongoing regulatory requirements. The FDA and comparable foreign regulatory authorities also require submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP requirements and GCP for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product candidate, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- issue warning letters or untitled letters;

- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners, or require other restrictions on the labeling or marketing of such products;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend, withdraw or modify regulatory approval;
- suspend or modify any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require us to initiate a product recall.

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

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the U.S. Federal Trade Commission, the Department of Justice (the DOJ) the Office of Inspector General of the U.S. Department of Health and Human Services (HHS) state attorneys general, members of the U.S. Congress, and the public. Additionally, advertising and promotion of any product candidate that obtains approval outside of the United States will be heavily scrutinized by comparable foreign entities and stakeholders. Violations, including actual or alleged promotion of our products for unapproved or off-label uses, are subject to enforcement letters, inquiries, and investigations, and civil and criminal sanctions by the FDA, DOJ, or comparable foreign bodies. Any actual or alleged failure to comply with labeling and promotion requirements may result in fines, warning letters, mandates to corrective information to healthcare practitioners, injunctions, or civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval for mavodelpar and any future product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition, and results of operations.

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

Disruptions at the FDA and other U.S. and foreign agencies such as the EMA, following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the

last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, 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.

Even if we obtain regulatory approval for mavodelpar and any future product candidates, mavodelpar and any future product candidates may not gain market acceptance among physicians, patients, healthcare payors and others in the medical community.

Mavodelpar and any future product candidates may not be commercially successful. The commercial success of mavodelpar or any future product candidates, if approved, will depend significantly on the broad adoption and use of such product by physicians and patients for approved indications. The degree of market acceptance of mavodelpar or any future products, if approved, will depend on a number of factors, including:

- the clinical indications for which such product candidate is approved;
- physicians and patients considering the product as a safe and effective treatment;
- the potential and perceived advantages of the product over alternative treatments;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA or other regulatory authorities;
- the timing of market introduction of the product as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage and adequate reimbursement by third-party payors and government authorities;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies; and
- the effectiveness of our sales and marketing efforts and those of any collaboration or distribution partner on whom we rely for sales in foreign jurisdictions.

If mavodelpar and any future product candidate is approved but fails to achieve market acceptance among physicians, patients, healthcare payors or others in the medical community, we will not be able to generate significant revenues, which would have a material adverse effect on our business, prospects, financial condition, and results of operations. In addition, even if mavodelpar and any future product candidate gains acceptance, the markets for the treatment of patients with our target indications may not be as significant as we estimate.

If mavodelpar and any future product candidate is approved for marketing, and we are found to have improperly promoted off-label uses, we may become subject to prohibitions on the sale or marketing of mavodelpar and any future product candidates, significant fines, penalties, sanctions, or product liability claims, and our image and reputation within the industry and marketplace could be harmed.

The FDA, DOJ, and comparable foreign authorities strictly regulate the marketing and promotional claims that are made about pharmaceutical products, such as mavodelpar, if approved. In particular, a product may not be promoted for uses or indications that are not approved by the FDA or comparable foreign authorities as reflected in the product's approved labeling. However, if we receive marketing approval for mavodelpar and any future product candidates, physicians can prescribe such product to their patients in a manner that is inconsistent

with the approved label in their independent professional judgment. If we are found to have promoted such off-label uses, we may receive warning letters from the FDA and comparable foreign authorities and become subject to significant liability, which would materially harm our business. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. If we become the target of such an investigation or prosecution based on our marketing and promotional practices, we could face similar sanctions, which would materially harm our business. In addition, management's attention could be diverted from our business operations, significant legal expenses could be incurred, and our reputation could be damaged. The FDA and other U.S. and foreign governmental authorities have also required that companies enter into consent decrees or imposed permanent injunctions under which specified promotional conduct is changed or curtailed in order to resolve enforcement actions. If we are deemed by the FDA, DOJ, or other U.S. and foreign governmental authorities to have engaged in the promotion of mavodelpar or any future product candidate for off-label use, we could be subject to certain prohibitions or other restrictions on the sale or marketing and other operations or significant fines and penalties, and the imposition of these sanctions could also affect our reputation and position within the industry.

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

Successful sales of mavodelpar and any future product candidates, if approved, depend on the availability of coverage and adequate reimbursement from third-party payors. Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance, and we may not obtain such coverage or adequate reimbursement. Moreover, we focus our clinical development of mavodelpar on therapies for patients with genetic mitochondrial diseases with relatively small patient populations. As a result, we must rely on obtaining appropriate coverage and reimbursement for these populations.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and the amount of reimbursement they will provide. Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor's determination that use of a product is:

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

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. We may not be able to provide data sufficient to obtain coverage and adequate reimbursement. Assuming we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use mavodelpar or any future product candidate unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost. Additionally, the reimbursement rates and coverage amounts may be affected by the approved label for mavodelpar or any future product candidate. If coverage and reimbursement of our future products are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

In addition, the market for mavodelpar and any future product candidates will depend significantly on access to third-party payors' drug formularies or lists of medications for which third-party payors provide coverage and

reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access through formulary controls or otherwise to a branded drug when a less costly generic equivalent or another alternative is available.

In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of mavodelpar and any future product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained. Coverage policies and third-party payor reimbursement rates may change at any time. Therefore, even if favorable coverage and reimbursement status is attained, less favorable coverage policies and reimbursement rates may be implemented in the future.

We intend to seek approval to market mavodelpar in the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for mavodelpar, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, including those in the EU, the pricing of prescription pharmaceuticals and biologics is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval for a drug candidate and in some countries, products cannot be marketed until after such a price has been agreed. In addition, market acceptance and sales of a product will depend significantly on the availability of coverage and adequate reimbursement from third-party payors for a product and may be affected by existing and future health care reform measures.

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

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

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the Affordable Care Act) was enacted in the United States. Among the provisions of the Affordable Care Act of importance to our potential product candidates, the Affordable Care Act: established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; expands eligibility criteria for Medicaid programs; increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program; created a new Medicare Part D coverage gap discount program; established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare and Medicaid Innovation at the Centers for Medicare & Medicaid Services (CMS) to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

There have been judicial, executive and Congressional challenges to certain aspects of the Affordable Care Act. By way of example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the “individual mandate” was repealed by Congress. Further, on August 16, 2022, President Biden signed the IRA into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Affordable Care Act marketplaces through plan year 2025. The IRA also eliminates the “donut hole” under the Medicare Part D

program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a newly established manufacturer discount program. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the Affordable Care Act and our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the Infrastructure Investments and Jobs Act, will remain in effect until 2031. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. In addition, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Such scrutiny has resulted in several recent congressional inquiries, presidential executive orders and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products.

At the federal level, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain high-cost, single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. Under the IRA, certain categories of drugs are excluded from price negotiations, including drugs that receive orphan drug designation as the only FDA-approved indication. While we have obtained orphan drug designation for mavodelpar, if we seek additional indications, or fail to maintain our orphan drug status, we may become subject to the price negotiation process. This could reduce the ultimate price that we receive for mavodelpar, which could negatively affect our business, results of operations, financial conditions, and prospects. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report within ninety (90) days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future.

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

We cannot predict the likelihood, nature, or extent of health reform initiatives that may arise from future legislation or administrative action. We expect that the Affordable Care Act and other healthcare reform measures, including those that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from third-party payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize mavodelpar, if approved.

A variety of risks associated with marketing mavodelpar and any future product candidates internationally could materially adversely affect our business.

We plan to seek regulatory approval for mavodelpar and any future product candidates internationally and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries, including differing reimbursement, pricing and insurance regimes, including as a result of Brexit;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;
- unexpected changes in tariffs, trade barriers, price and exchange controls, and other regulatory requirements;
- economic weakness, including inflation, bank failures, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling internationally;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the U.S. Foreign Corrupt Practices Act of 1977 (FCPA) or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities internationally; and
- business interruptions resulting from geo-political actions, including war and terrorism.

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

If we fail to develop and commercialize additional product candidates, we may be unable to grow our business.

We may seek to in-license or acquire late preclinical or development-stage product candidates that have the potential to complement our existing portfolio. If we decide to pursue the development and commercialization of

any additional product candidates, we may be required to invest significant resources to acquire or in-license the rights to such product candidates or to conduct drug discovery activities. We do not currently have the necessary drug discovery personnel or expertise adequate to discover and develop an additional product candidate on our own. Any other product candidates will require additional, time-consuming development efforts, and significant financial resources, prior to commercial sale, including preclinical studies, extensive clinical trials, and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we may not be able to acquire, discover, or develop any additional product candidates, and any additional product candidates we may develop may not be approved, manufactured, or produced economically, successfully commercialized or widely accepted in the marketplace, or be more effective than other commercially available alternatives. Research programs to identify new product candidates require substantial technical, financial, and human resources whether or not we ultimately identify any candidates. If we are unable to develop or commercialize any other product candidates, our business and prospects will suffer.

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

The pharmaceutical industry is characterized by intense competition and rapid innovation. Although we believe that we hold a leading position in our focus on rare genetic mitochondrial diseases, our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical companies, established and start-up biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis drug products that are more effective or less costly than mavodelpar. We believe the key competitive factors that will affect the development and commercial success of mavodelpar are efficacy, safety and tolerability profile, reliability, convenience of dosing, price and reimbursement.

There are no approved therapies indicated for the treatment of PMM in any country. Physicians attempt to treat symptoms in patients with drugs or vitamins and supplements. For example, anti-convulsant drugs are used to prevent or control seizures. CymaBay Therapeutics, Inc. is conducting a Phase 3 clinical trial of up to 52 weeks with seladelpar, a selective PPARδ agonist in patients with primary biliary cholangitis. Astellas Pharma Inc. is conducting a Phase 2/3 clinical trial of up to 52-weeks plus 24-weeks extension with bocidelpar, a selective PPARδ agonist. Other companies are developing therapies for mitochondrial diseases, including, Stealth BioTherapeutics Corp., Abliva AB, Cyclerion Therapeutics, Inc., Khondrion B.V. and Minovia Therapeutics.

There is one product approved in the United States for LC-FAOD. In June 2020, a new form of medium chain triglyceride (MCT) oil called DOJOLVI® (triheptanoin) was approved and indicated in the United States as a source of calories for patients with LC-FAOD. We are not aware of any drug interventional studies underway or currently announced for LC-FAOD.

Our commercial potential could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than 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, which could result in our competitors establishing a strong market position before we are able to enter the market or make our development more complicated. We believe the key competitive factors affecting the success of mavodelpar are likely to be efficacy, safety, and convenience.

Even though we have obtained orphan drug designation for mavodelpar for the treatment of PMM and LC-FAOD in the United States and LCHAD and MELAS in the EU, we may not be able to obtain or maintain the benefits associated with orphan drug status, including market exclusivity.

Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare genetic mitochondrial disease or condition, which is generally defined as a patient population of fewer than 200,000 people in the United States, or a patient population of greater than 200,000 people in the United States, but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, the criteria for designating an "orphan medicinal product" are similar in principle to those in the United States. A medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition.

Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug may be entitled to a period of marketing exclusivity, which precludes the FDA or the European Commission from approving another marketing application for the same drug for the same indication for that time period. Another drug may receive marketing approval prior to mavodelpar. The applicable period is seven years in the United States and ten years in the EU, which may be extended by six months and two years, respectively, in the case of product candidates that have complied with the respective regulatory agency's agreed upon pediatric investigation plan. The exclusivity period in the EU can be reduced to six years if, at the end of the fifth year, it is established that a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare genetic mitochondrial disease or condition. In addition, even after a drug is granted orphan exclusivity and approved, the FDA and the European Commission can subsequently approve another drug containing a similar active substance or substances, and which is intended to treat the same condition before the expiration of the seven-year (or ten-year in the EU) exclusivity period if the FDA or European Commission concludes that the later drug is safer, more effective or otherwise clinically superior. In addition, if an orphan designated product receives marketing approval for an indication broader than or different from what is designated, such product may not be entitled to orphan exclusivity. Even though the FDA has granted orphan drug designation to mavodelpar for the treatment of PMM and LC-FAOD in the United States and LCHAD and MELAS in the EU, if we receive approval for mavodelpar for a modified or different indication, our current orphan designations may not provide us with exclusivity.

Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process. Also, regulatory approval for any product candidate may be withdrawn, and other product candidates may obtain approval before us and receive orphan drug exclusivity, which could block us from entering the market.

Even if we obtain orphan drug exclusivity for mavodelpar, that exclusivity may not effectively protect us from competition because different drugs can be approved for the same condition before the expiration of the orphan drug exclusivity period.

A Fast Track designation by the FDA may not actually lead to a faster development or regulatory review or approval process for mavodelpar in any designated indication.

If a product candidate is intended for the treatment of a serious or life-threatening condition and the product candidate demonstrates the potential to address unmet medical needs for this condition, the drug

sponsor may apply for Fast Track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation for other indications, we cannot assure you that the FDA would decide to grant it. Even though we have received Fast Track designation for mavodelpar for the treatment of patients with PMM and LC-FAOD due to LCHAD deficiency, one of the predominant LC-FAOD genotypes, we may not experience a faster development process, review or approval. The FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our development program.

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

We may form or seek strategic alliances, create joint ventures or collaborations or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to mavodelpar and any future product candidates that we may develop. We intend to establish commercial partnerships outside of the United States and key European markets. Any of these relationships may require us to incur non-recurring and other charges, increase our near-and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. If we license products or businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. Following a strategic transaction or license, we may not achieve the revenues or cash flows that justifies such transaction. Any delays in entering into new strategic partnership agreements related to mavodelpar could delay the development and commercialization of mavodelpar in certain geographies for certain indications, which would harm our business prospects, financial condition, and results of operations.

We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific, and medical personnel. We are highly dependent on our management, scientific, and medical personnel. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, prospects, financial condition or results of operations.

We conduct our operations in Irvine, California and Sandwich, United Kingdom as well as remotely as a hybrid office/virtual organization. These regions serve as the headquarters to many other biotechnology and pharmaceutical companies and academic and research institutions. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. The withdrawal of the UK from the EU may also negatively affect our ability to attract and retain employees, particularly those from the EU.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options that vest over time and performance-based restricted stock units that vest upon satisfaction of certain performance-based conditions. The value to employees such stock options and performance-based restricted stock units may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific, and development teams may terminate their employment with us on short notice. Although we have employment agreements and/or offer letters with our key employees, these arrangements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain “key man” insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level, and senior managers as well as junior, mid-level, and senior scientific and medical personnel.

Many of the other biotechnology and pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. They may also provide more diverse opportunities and better chances for career advancement. Some of these characteristics are more appealing to high quality candidates than what we can offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can discover, develop and commercialize product candidates will be limited.

We will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of March 21, 2023, we had 48 employees, 36 of whom were full-time. As our development and commercialization plans and strategies develop, we expect to need additional development, managerial, operational, financial, sales, marketing, and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining, and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and regulatory review process for mavodelpar and any future product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize mavodelpar will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities. To date, we have used the services of outside vendors to perform tasks including clinical trial management, manufacturing, statistics and analysis, regulatory affairs, formulation development, and other drug development functions. Our growth strategy may also entail expanding our group of contractors or consultants to implement these tasks going forward. Because we rely on numerous consultants, effectively outsourcing many key functions of our business, we will need to be able to effectively manage these consultants to ensure that they successfully carry out their contractual obligations and meet expected deadlines. However, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval for mavodelpar and any future product candidates or otherwise advance our business. We may not be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all. If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize mavodelpar and any future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

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

We are exposed to the risk that employees, independent contractors, principal investigators, CROs, consultants, and vendors may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (i) the rules of the FDA and other similar foreign regulatory bodies, including those rules that require the reporting of true, complete, and accurate information to the FDA and other similar foreign regulatory bodies; (ii) manufacturing standards; (iii) healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws or (iv) laws that require the true, complete, and accurate reporting of our financial information or data. These laws may impact, among other things, our current activities with principal investigators and research subjects, as well as proposed and future sales, marketing, and education programs. In particular, the promotion, sales, and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and

regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs, and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials.

If we obtain regulatory approval for mavodelpar and begin commercializing those products in the United States, the EU and other countries or jurisdictions, our potential exposure under the laws of such countries and jurisdictions will increase significantly, and our costs associated with compliance with such laws are also likely to increase. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs and equivalent foreign healthcare programs, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Our relationships with customers, healthcare providers, and third-party payors may be subject, directly or indirectly, to federal, state and comparable foreign healthcare fraud and abuse laws, false claims laws, and other healthcare laws and regulations. If we or our employees, independent contractors, consultants, commercial partners, or vendors violate these laws, we could face substantial penalties.

Our relationships with customers, healthcare providers, and third-party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and other healthcare laws and regulations. These laws may impact, among other things, our clinical research program, as well as our proposed and future sales, marketing, and education programs. In particular, the promotion, sales and marketing of healthcare items and services is subject to extensive laws and regulations designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive, and other business arrangements. The U.S. healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person or entity from knowingly and willfully, offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, the purchasing, leasing, ordering or arranging for the purchase, lease, or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that may be alleged to be intended to induce prescribing, purchases or recommendations, include any payments of more than fair market value, and may be subject to scrutiny if they do not qualify for an exception or safe harbor. In addition, a person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;
- federal civil and criminal false claims laws, including the federal civil False Claims Act, and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal government programs that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government, including federal healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act and the civil monetary penalties statute;

- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) which created new federal civil and criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by any trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, which impose requirements on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, and their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information as well as their covered subcontractors; and
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other transfers of value made to physicians, (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and purse practitioners), and teaching hospitals, as well as ownership and investment interests held by such physicians and their immediate family members.

We may also be subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope. For example, we may be subject to the following: anti-kickback and false claims laws and regulations that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, or that apply regardless of payor; laws and regulations that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; laws and regulations that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures, or drug pricing; and laws and regulations requiring the registration of pharmaceutical sales and medical representatives.

Additionally, we may be subject to consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Because of the breadth of these laws and regulations and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities, or our arrangements with physicians, could be subject to challenge under one or more of such laws and regulations. It is not always possible to identify and deter employee misconduct or business noncompliance, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Efforts to ensure that our business arrangements will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If we or our employees, independent contractors, consultants, commercial partners and vendors violate these laws and regulations, we may be subject to investigations, enforcement actions and/or significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve

allegations of non-compliance with these laws and regulations, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of mavodelpar outside the United States will also likely subject us to foreign equivalents of the healthcare laws and regulations mentioned above, among other foreign laws and regulations.

We are subject to stringent and changing U.S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences.

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

In the United States, federal, state, and local governments have enacted numerous data privacy and security laws and regulations, including data breach notification laws, state and federal health information privacy laws, personal data privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), and other similar laws (e.g., wiretapping laws). In addition, we may obtain health data from third parties (including research institutions from which we obtain clinical trial data) that is subject to privacy and security requirements under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), and their respective implementing regulations. Depending on the facts and circumstances, we could be subject to civil, criminal, and administrative penalties if we knowingly obtain, use, or disclose individually identifiable protected health information in a manner that is not authorized or permitted by HIPAA. In addition, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020, or the CPRA (collectively, the CCPA), applies to personal data of consumers, business representatives, and employees, and requires businesses to provide specific disclosures in privacy notices and honor requests of California residents to exercise certain privacy rights related to their personal data. The CCPA provides for administrative fines for noncompliance (up to $7,500 per violation) and allows private litigants affected by certain data breaches to recover significant statutory damages. Further, the CPRA's recent amendments expand the CCPA's requirements, including by adding a new right for individuals to correct their personal data and establishing a new regulatory agency to implement and enforce the law. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA increases compliance costs and potential liability with respect to other personal data we maintain about California residents. Other states, such as Virginia, Colorado, Utah, and Connecticut have also passed comprehensive privacy laws, and similar laws are being considered in several other states. While these states, like the CCPA, also exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely.

Outside the United States, an increasing number of laws, and regulations may govern data privacy and security. For example, the EU GDPR, the UK GDPR, Canada's Personal Information Protection and Electronic Documents Act (PIPEDA), Australia's Privacy Act, and New Zealand's Privacy Act, impose strict requirements for processing personal data. For example, under the EU GDPR and UK GDPR, companies may face temporary or definitive bans on data processing and other coercive actions, fines of up to 20 million euros or 17.5 million pounds (respectively) or 4% of annual global revenue, whichever is greater, or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

In addition, we may be unable to transfer personal data from Europe and other jurisdictions to the United States or other countries due to data localization requirements or limitations on cross-border data flows. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to

other countries. In particular, the European Economic Area (EEA) and the UK have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws they believe are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA standard contractual clauses and UK's international data transfer agreement, these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA and the UK or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. These challenges and risks concerning cross-border transfers of personal data out of the EEA and UK to recipients in other jurisdictions, notably recipients in the United States, may be of particular significance to us and our operations as the majority of the trials we conduct take place in locations outside the United States, with a large number occurring in the EEA or UK. Furthermore, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activities groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data out of Europe for allegedly violating the GDPR's cross-border data transfer limitations. In addition to data privacy and security laws, we are also bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful.

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

Obligations related to data privacy and security are quickly changing, becoming increasingly stringent, and creating regulatory uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources and may necessitate changes to our information technologies, systems, and practices and to those of any third parties that process sensitive data on our behalf.

We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties upon whom we rely on may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties upon which we rely fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences. These consequences may include, but are not limited to, government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims); additional reporting requirements and/or oversight; bans on processing personal data; and orders to destroy or not use personal data.

Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including clinical trials); inability to process sensitive data or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring of our operations.

The withdrawal of the UK from the EU may adversely impact our ability to obtain regulatory approvals of our product candidates in the UK, result in restrictions or imposition of taxes and duties for importing our product candidates into the EU or UK, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the EU or UK.

Following the result of a referendum in 2016, the UK left the EU on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the UK and the EU, the UK was subject to a transition period until December 31, 2020 (the Transition Period) during which EU rules continued to apply. A trade and cooperation agreement (the Trade and Cooperation Agreement) that outlines the future trading relationship between the UK and the EU was agreed on in December 2020, provisionally applied from January 1, 2021 and became formally effective on May 1, 2021. Since the expiry of the Transition Period, the UK operates under a distinct regulatory regime. EU pharmaceutical laws only apply to the UK in respect of Northern Ireland (as laid out in the Protocol on Ireland and Northern Ireland). Since January 1, 2021, the EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law". As there is no general power to amend these regulations, the UK government passed a new Medicines and Medical Devices Act which seeks to address regulatory gaps through implementing regulations and delegated powers covering the fields of human medicines, clinical trials of human medicines, veterinary medicines and medical devices. The purpose of the Act is to enable the existing UK regulatory frameworks to be updated. Although regulatory authorities in the UK have indicated that new UK rules will be put in place, detailed proposals are yet to be published. Significant political and economic uncertainty therefore remains about how much the relationship between the UK and EU will differ as a result of the UK's withdrawal.

Since a significant proportion of the regulatory framework in the UK applicable to our business and our product candidates is derived from EU directives and regulations, Brexit, has had, and may continue to have, a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the UK or the EU. For example, Great Britain (GB) is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization (MA) from the European Commission (based on the opinion of the CHMP of the EMA), and a separate MA will be required to market our product candidates in GB, including mavodelpar and any future product candidates. Any delay in obtaining, or an inability to obtain, any marketing approvals in GB, as a result of Brexit or otherwise, would prevent us from commercializing mavodelpar in GB and restrict our ability to generate revenue and achieve and sustain profitability. While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the UK and the EU there are additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period, and shipments between the UK and the EU are more likely to be delayed compared to the position prior to Brexit. Further, should the UK further diverge from the EU from a regulatory perspective in relation to medicinal products, this could lead to a more complex and costly regulatory burden on us. In addition, while the Trade and Cooperation Agreement provides for mutual recognition of GMP inspections and certificates, it does not provide for contain wholesale mutual recognition of UK and EU pharmaceutical rules and product standards, for example in relation to batch testing and pharmacovigilance, which remain subject to further bilateral discussions. Therefore, additional batch testing between the EU and UK markets and other divergent or duplicative regulatory obligations may be required, which could result in additional expense and supply chain delays. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK or the EU for mavodelpar and any future product candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. The Retained EU Law (Revocation and Reform) Bill 2022, which is currently progressing through the UK Parliament and seeks to allow the UK Government to repeal or replace certain EU Law that was incorporated into UK law effective as of the end of the Transition Period, increases the likelihood of such divergence between UK and EU law, and the consequences set out above. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the EU and the UK. It is also possible that Brexit may negatively affect our ability to attract and retain employees in the UK, particularly those from the EU.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of mavodelpar and any future product candidates.

We face an inherent risk of product liability as a result of the clinical testing of mavodelpar and any future product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if mavodelpar or any future product candidates causes or is perceived to cause injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing, or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of mavodelpar. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for mavodelpar and any future product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulatory authorities;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing, or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize mavodelpar and any future product candidates; or
- a decline in our share price.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry an aggregate of up to $7 million of product liability insurance covering our clinical trials. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. If we determine that it is prudent to increase our product liability coverage due to the commercial launch of any approved product, we may be unable to obtain such increased coverage on acceptable terms, or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our ability to utilize our net operating loss (NOL) carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire (if at all). See Note 10, *Income Taxes* of Notes to Consolidated Financial Statements included in this Annual Report for further discussion.

Under the Tax Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act (the CARES Act) federal NOL carryforwards generated in tax years beginning after December 31, 2017 may be carried forward

indefinitely but, in the case of tax years beginning after 2020, may only be used to offset 80% of our taxable income annually. Our NOLs and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a rolling three-year period in excess of 50 percentage points (by value), as defined under Section 382 of the Internal Revenue Code of 1986, as amended. Our ability to utilize our NOL carryforwards and other tax attributes to offset future taxable income or tax liabilities may be limited as a result of ownership changes. Similar rules may apply under state tax laws. Such limitations could result in the expiration of our carryforwards before they can be utilized and, if we are profitable, our future cash flows could be adversely affected due to our increased taxable income or tax liability. We may have experienced ownership changes in the past and may experience ownership changes as a result of future offerings and/or subsequent changes in our stock ownership (some of which are outside our control). In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Changes in tax laws or regulations that are applied adversely to us or our customers may have a material and adverse effect on our business, cash flow, financial condition or results of operations.

The Tax Act enacted many significant changes to the U.S. tax laws. Future guidance from the IRS and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. For example, the CARES Act modified certain provisions of the Tax Act. Changes in corporate tax rates, the realization of net deferred tax assets relating to our U.S. operations, the taxation of foreign earnings and the deductibility of expenses under the Tax Act or future tax reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges in the current or future taxable years and could increase our future U.S. tax expense. For example, the recently enacted IRA includes provisions that will impact the U.S. federal income taxation of corporations, including imposing a minimum tax on the book income of certain large corporations and an excise tax on certain corporate stock repurchases that would be imposed on the corporation repurchasing such stock. The foregoing items, as well as any other future changes in tax laws, could have a material adverse effect on our business, cash flow, financial condition or results of operations. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the CARES Act, the IRA, or any newly enacted federal tax legislation.

Tax authorities may disagree with our positions and conclusions regarding certain tax positions, resulting in unanticipated costs, taxes or non-realization of expected benefits.

A tax authority may disagree with tax positions that we have taken, which could result in increased tax liabilities. For example, the U.S. Internal Revenue Service or another tax authority could challenge our allocation of income by tax jurisdiction and the amounts paid between our affiliated companies pursuant to our intercompany arrangements and transfer pricing policies, including amounts paid with respect to our intellectual property development. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable nexus, often referred to as a “permanent establishment” under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. A tax authority may take the position that material income tax liabilities, interest and penalties are payable by us, in which case, we expect that we might contest such assessment. Contesting such an assessment may be lengthy and costly and if we were unsuccessful in disputing the assessment, the implications could increase our anticipated effective tax rate, where applicable.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults or non-performance by financial institutions could adversely affect our current financial condition and projected business operations.

Events involving limitations to liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank (SVB) was closed by the California Department of Financial Protection and Innovation, and the Federal Deposit Insurance Corporation (FDIC) was appointed as receiver. Subsequently, the FDIC announced that all deposits with SVB are fully insured. We maintain operating accounts at SVB from which we pay employees and other third parties for goods and services. Any disruption to SVB operations may result in delays in payments to employees and other third parties.

Risks Related to Our Reliance on Third Parties

We depend on a license agreement with vTv Therapeutics, and termination of this license could result in the loss of significant rights, which would harm our business.

We are dependent on technology, patents, know-how, and proprietary materials, both our own and licensed from others. We entered into a license agreement with vTv Therapeutics in December 2017 pursuant to which we were granted an exclusive, worldwide, sublicensable license under vTv Therapeutics intellectual property relating to vTv Therapeutics' PPARδ agonist program, to develop, manufacture and commercialize PPARδ agonists and products containing such PPARδ agonists, including mavodelpar, or licensed products, for any therapeutic, prophylactic or diagnostic application in humans. Any termination of this license will result in the loss of significant rights and will restrict our ability to develop and commercialize mavodelpar.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below under "Risks Related to Our Intellectual Property." If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer.

We rely on third parties to conduct, supervise, and monitor our clinical trials. If these third parties do not successfully carry out their contractual duties, meet rigorously enforced regulatory requirements, or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize mavodelpar.

We currently rely on, and intend to continue relying on, third-party CROs in connection with our clinical trials for mavodelpar. We control or will control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with applicable protocol, legal, regulatory, and scientific standards, and our reliance on our CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these CROs fail to comply with applicable GCP regulations, 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. Upon inspection, such regulatory authorities may determine that our clinical trials do not comply with the GCP regulations. In addition, our clinical trials must be conducted with drug product produced under cGMP regulations and will require a large number of test subjects. Our failure or any failure by our CROs to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of our CROs violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Our CROs are not our employees and, except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing preclinical, clinical and nonclinical programs. These 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 affect their performance on our behalf. If our CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced 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 other reasons, our clinical trials may be extended, delayed, or terminated and we may not be able to complete development of, obtain regulatory approval for or successfully commercialize mavodelpar and any future product candidates. As a result, our financial results and the commercial prospects for mavodelpar and any future product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding CROs involves substantial cost and requires extensive management 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. Although we carefully manage our relationships with our CROs, we may encounter challenges or delays in the future and these delays or challenges may have a material adverse impact on our business, prospects, financial condition, and results of operations.

In addition, quarantines, shelter-in-place, and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at our CROs, which could disrupt our clinical timelines, which could have a material adverse impact on our business, prospects, financial condition, and results of operations.

We rely completely on third parties to manufacture our preclinical and clinical drug supplies and we intend to rely on third parties to produce commercial supplies of mavodelpar and any future product candidates, if approved, and these third parties may fail to obtain and maintain regulatory approval for their facilities, fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.

We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our clinical drug supplies for use in the conduct of our clinical trials, and we lack the resources and the capability to manufacture mavodelpar and any future product candidates on a clinical or commercial scale. Instead, we rely on contract manufacturers for such production.

We do not currently have any long-term agreement with a manufacturer to produce raw materials, active pharmaceutical ingredients (APIs) and the finished products of mavodelpar used in our current product format and we rely on single-source suppliers for clinical supply of API and drug product of mavodelpar. We intend to enter into agreements for commercial production with third-party suppliers. Our reliance on third-party suppliers and manufacturers, including single-source suppliers, could harm our ability to develop mavodelpar or commercialize it, if approved. Further, any delay in identifying and qualifying a manufacturer for commercial production could delay the potential commercialization of mavodelpar and any future product candidates, and, in the event that we do not have sufficient product to complete our clinical trials, it could delay such trials.

The facilities used by our contract manufacturers to manufacture mavodelpar and any future product candidates must be approved by the applicable regulatory authorities, including the FDA, pursuant to inspections that will be conducted after an NDA or comparable foreign regulatory marketing application is submitted. We currently do not control the manufacturing process of mavodelpar and are completely dependent on our contract manufacturing partners for compliance with the FDA's cGMP requirements for manufacture of both the active drug substances and finished drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the FDA's strict regulatory requirements, they will not be able to secure or maintain FDA approval for the manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authority does not approve these facilities for the manufacture of mavodelpar or any future product candidates or if it withdraws any such approval in the future, or if our suppliers or contract manufacturers decide they no longer want to supply or manufacture for us, we may need to find alternative manufacturing facilities, in which case we might not be able to identify manufacturers for clinical or

commercial supply on acceptable terms, or at all, which would significantly impact our ability to develop, obtain regulatory approval for, or market mavodelpar and any future product candidates.

In addition, the manufacture of pharmaceutical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up and validating initial production and absence of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state, and foreign regulations. Furthermore, if contaminants are discovered in our supply of mavodelpar or any future product candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Any stability or other issues relating to the manufacture of mavodelpar may occur in the future. In addition, quarantines, shelter-in-place, and similar government orders, or the perception that such orders, shutdowns, or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at our third-party manufacturing facilities upon which we rely, or the availability or cost of materials, which could disrupt the supply chain for our product candidates. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to provide our product candidate to patients in clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

If we or our third-party manufacturers use hazardous substances in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances by our third-party manufacturers. Our manufacturers are subject to federal, state, and local laws and regulations in the United States governing the use, manufacture, storage, handling and disposal of medical, radioactive and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development, and production efforts, which could harm our business, prospects, financial condition, or results of operations.

Risks Related to Our Intellectual Property

Our success depends on our ability to obtain and maintain sufficient intellectual property protection for mavodelpar, any future product candidates, and other proprietary technologies.

Our commercial success will depend in part on our ability to obtain and maintain a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to mavodelpar, any future product candidates, and other proprietary technologies we develop. If we are unable to obtain or maintain patent protection with respect to mavodelpar, any future product candidates, and other proprietary technologies we may develop, our business, financial condition, results of operations, and prospects could be materially harmed.

We generally seek to protect our products and product candidates and related inventions and improvements that we consider important to our business. We own a portfolio of U.S. and non-U.S. patent applications for

mavodelpar and have licensed rights to a number of U.S. and non-U.S. patents and patent applications for mavodelpar. Some of our owned and licensed patents and patent applications cover or relate to mavodelpar, including composition of matter, uses to treat particular conditions and methods of manufacturing.

We have developed and continue to expand our patent portfolio for mavodelpar. We have licensed from vTv Therapeutics eight issued patents in the United States and 19 issued patents in foreign countries covering composition of matter of mavodelpar, among other things, which are expected to expire in 2026, absent any patent term adjustments or extensions. Additionally, we have licensed four issued patents in the United States, six issued patents in foreign countries, one pending application in the United States, and one pending application in Europe, from vTv Therapeutics covering methods of using mavodelpar, which are expected to expire in 2034, absent any patent term adjustments or extensions.

In addition to the licensed vTv Therapeutics patents and applications relating to mavodelpar, we have filed our own patent applications. We co-own one pending application in the United States and five pending applications in foreign countries, and own three pending applications in the United States, one pending international patent application, an issued patent in foreign country, and over 25 pending applications in foreign countries, directed to various methods of use of mavodelpar. These pending patent applications, if issued, would be expected to expire between 2040 and 2043, absent any patent term adjustments or extensions. We also own one issued patent in the United States, one pending application in the United States, one pending international patent applications, and over 15 pending applications in foreign countries directed to methods of manufacturing, and crystalline forms (polymorphs) of mavodelpar. The issued patent, and pending patent applications if issued, are expected to expire in 2041, absent any patent term adjustments or extensions. Patents related to mavodelpar may be eligible for patent term extensions in certain jurisdictions, including up to five years in both the United States and the EU, upon approval of a commercial use of the corresponding product by a regulatory agency in the jurisdiction where the patent was granted.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover such technology. There can be no assurance that our patent applications or the patent applications of our future licensors will result in patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties.

Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our and our licensors' proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. These uncertainties and/or limitations in our ability to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

We cannot be certain that the claims in our U.S. pending patent applications, corresponding international patent applications and patent applications in certain foreign territories, or those of our future licensors, will be considered patentable by the USPTO, courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our future issued patents will not be found invalid or unenforceable if challenged.

In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

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 intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. 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 process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on any issued patents and/or applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to foreign patent agencies. While an inadvertent lapse may sometimes be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance (including as a result of the ongoing COVID-19 pandemic) 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, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If such event were to occur, our competitors might be able to enter the market with similar or identical products or technology earlier than should otherwise have been the case, which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

Patent rights are of limited duration. The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. 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 product candidates are commercialized. Even if patents covering our product candidates are obtained, once the patent term has expired for a product, we may be open to competition from generic products. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours. Upon issuance in the United States, the term of a patent can be increased by patent term adjustment, which is based on certain delays caused by the USPTO, but this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. The term of a United States patent may also be shortened if the patent is terminally disclaimed over an earlier-filed patent. Extensions may be available under certain circumstances, but the term of a patent and, correspondingly, the protection it affords is limited. A patent term extension (PTE) based on regulatory delay may be available in the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the PTE does not extend to the full scope of the claim, but instead only to the scope of the claim covering the product as approved. Laws governing analogous PTEs in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain PTE or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to launch their product earlier than might otherwise be the case, which could materially adversely affect our business, financial condition, results of operations and prospects.

Furthermore, our patents covering certain components of our product candidates may expire prior to the commercialization of our product candidates or soon thereafter. As a result, third parties may be able to utilize these components of our products after expiration of these patents.

Even if we or our licensors obtain patents covering our product candidates, when the terms of all patents covering a product expire, our business may become subject to competition from competitive products, including generic products. Given the amount of time required for the development, testing, and regulatory review and approval of new product candidates, patents protecting such candidates may 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. For example, we have licensed patents from vTv Therapeutics that cover composition of matter of mavodelpar, which are set to expire in 2026, absent any patent term adjustments or extensions.

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

Depending upon the timing, duration, and specifics of any FDA marketing approval of mavodelpar, or any future product candidate we may develop, one or more of patents issuing from our U.S. patent applications may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984 (Hatch-Waxman Amendments). The Hatch-Waxman Amendments permit a PTE of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. Similar patent term restoration provisions to compensate for commercialization delay caused by regulatory review are also available in certain foreign jurisdictions, such as in Europe under Supplemental Protection Certificate (SPC). If we encounter delays in our development efforts, including our clinical trials, the period of time during which we could market mavodelpar and any future product candidates under patent protection would be reduced. Additionally, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents, or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue may be materially reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

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

We have pending U.S., international (*i.e.*, PCT), and other foreign patent applications in our portfolio relating to mavodelpar. However, we cannot predict:

- if and when patents may issue based on our patent applications;
- the scope of protection of any patent issuing based on our patent applications;
- whether the claims of any patent issuing based on our patent applications will provide protection against competitors,
- whether or not third parties will find ways to invalidate or circumvent our patent rights;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications;

- whether we will need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- whether the patent applications that we own or in-license will result in issued patents with claims that cover our product candidates or uses thereof; and/or
- whether, as the COVID-19 pandemic continues to spread around the globe, we may experience patent office interruption or delays to our ability to timely secure patent coverage to our product candidates.

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

Derivation proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party.

Derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our future licensors. 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. Our defense of 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 such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our development programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection and/or other market exclusivity, our ability to prevent our competitors from commercializing similar or identical product candidates may be adversely affected.

The patent position of biotechnology and pharmaceutical companies is highly uncertain and involves complex legal, scientific, and factual questions and has been the subject of frequent litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our patent applications may not result in patents being issued which protect mavodelpar, any future product candidates, and other proprietary technologies we may develop or which effectively prevent others from commercializing competitive technologies and products. Further, no consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States and in many jurisdictions outside of the United States. Changes in either the patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in the patents that may be issued from the applications we currently or

may in the future own or license from third parties. Further, if any patents we obtain or license are deemed invalid and unenforceable, our ability to commercialize or license our technology could be adversely affected.

Moreover, 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 patent applications we own or in-license in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-license may be challenged or circumvented by third parties or may be narrowed or invalidated as a result of challenges by third parties. Consequently, we do not know whether our product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents or the patents of our future licensors by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents or the patents of our future licensors may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant review (PGR) and inter partes review (IPR), or other similar proceedings challenging our owned patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, our patents or the patents of our future licensors may become subject to post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our priority of invention or other features of patentability with respect to our patents and patent applications and those of our future licensors. Such challenges may result in loss of patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our patents and patent applications or the patents and patent applications of our future licensors is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators will be successful in protecting mavodelpar, any future product candidates, and other proprietary technologies and their uses by obtaining, defending and enforcing patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable, or may otherwise not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with, or eliminate our ability to make, use and sell our potential product candidates;
- other parties may have designed around our claims or developed technologies that may be related or competitive to our platform, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications, either by claiming the same

composition of matter, methods or formulations or by claiming subject matter that could dominate our patent position;

- any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any products or product candidates that we may develop;
- because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to mavodelpar, any future product candidates, and other proprietary technologies and their uses;
- an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications for any application with an effective filing date before March 16, 2013;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop, and market competing product candidates in those countries.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, or maintain 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. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection for such output. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in any of our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

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

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use mavodelpar, any future product candidates, and other proprietary technologies and erode or negate any competitive advantage we may have, which could have a material adverse effect on our financial condition and results of operations. For example:

- others may be able to make compounds that are similar to mavodelpar and any future product candidates but that are not covered by the claims of our patents;
- we might not have been the first to make the inventions covered by our pending patent applications;
- we might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;

- any patents that we obtain may not provide us with any competitive advantages;
- it is possible that the pending patent applications we own or license will not lead to issued patents;
- issued patents that we own or license may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- we may not develop additional proprietary technologies that are patentable;
- our competitors might conduct research and development activities in countries where we do not have patent rights or where patent protection is weak 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 patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our products;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns;
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates;
- we cannot ensure that we will be able to successfully commercialize our products on a substantial scale, if approved, before the relevant patents that we own or license expire; or
- the patents of others may have an adverse effect on our business.

Others have filed, and in the future are likely to file, patent applications covering products and technologies that are similar, identical or competitive to ours or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference, opposition or invalidity proceedings before U.S. or non-U.S. patent offices.

We cannot be certain that the claims in our issued patents and pending patent applications covering mavodelpar or any future product candidates will be considered patentable by the USPTO, courts in the United States, or by patent offices and courts in foreign countries. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property internationally.

The strength of patents in the biotechnology and pharmaceutical fields involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover mavodelpar and any future product candidates in the United States or in foreign countries. Even if such patents do successfully issue, third parties may challenge the ownership, validity, enforceability, or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful opposition to our patents could deprive us of exclusive rights necessary for the successful commercialization of mavodelpar and any future product candidates. Furthermore, even if they are unchallenged, our patents may not adequately protect our intellectual property, provide exclusivity for mavodelpar or any future product candidates or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents we hold with respect to mavodelpar or any future product candidates is threatened, it could dissuade companies from collaborating with us to develop, or threaten our ability to commercialize, mavodelpar or any future product candidates.

Composition of matter patents for pharmaceutical product candidates, in particular patents with claims covering the molecular structure of the active pharmaceutical ingredient, often provide the strongest form of intellectual property protection for those types of products, as such patents provide protection without regard to any variations in formulation, method of use, or manufacturing process of the product. While we have an exclusive

license to compositions of matter patents covering the molecular structure of mavodelpar, those patents will likely expire, absent patent term adjustment or extension, before the expiration of any regulatory exclusivity period that we may receive for mavodelpar. We also own one issued patent in the United States, that is expected to expire in 2041, absent any patent term adjustments or extensions, one pending application in the United States, and one pending international patent applications in foreign countries directed to polymorphs of mavodelpar. We cannot be certain that the claims in our pending patent applications directed to the polymorph of mavodelpar will be considered patentable by patent offices in foreign countries, or that the claims in any of our issued patents will be considered valid and enforceable by courts in the United States or foreign countries. Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute. Method of synthesis patents protect the method used to manufacture a product. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product so long as it is made in a different way.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications or those of our future licensors and the enforcement or defense of our issued patents or those of our future licensors.

In September 2011, the Leahy-Smith America Invents Act, or America Invents Act, was signed into law. The America Invents Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first inventor to file" system in which, assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we may not be certain that we or our future licensors are the first to either (1) file any patent application related to our product candidates or (2) invent any of the inventions claimed in the patents or patent applications.

The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including PGR, IPR, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

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

For U.S. patent applications in which claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our participation in an interference proceeding may fail and, even if successful, may result in substantial costs and distract our management and other employees.

Changes in U.S. patent law, or patent laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect mavodelpar, any future product candidates, and other proprietary technologies.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly on obtaining and enforcing patents. Obtaining and enforcing patents in the pharmaceutical industry involves a high degree of technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. Therefore, our patent rights may be affected by developments or uncertainty in U.S. or foreign patent statutes, patent case law, USPTO rules and regulations or the rules and regulations of foreign patent offices. In addition, the United States may, at any time, enact changes to U.S. patent law and regulations, including by legislation, by regulatory rulemaking, or by judicial precedent, that adversely affect the scope of patent protection available and weaken the rights of patent owners to obtain patents, enforce patent infringement and obtain injunctions and/or damages. For example, over the past several years the Court of Appeals for the Federal Circuit and the Supreme Court issued various opinions, and the USPTO modified its guidance for practitioners on multiple occasions, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Other countries may likewise enact changes to their patent laws in ways that adversely diminish the scope of patent protection and weaken the rights of patent owners to obtain patents, enforce patent infringement, and obtain injunctions and/or damages. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents, and whether Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us.

Further, the United States and other governments may, at any time, enact changes to law and regulation that create new avenues for challenging the validity of issued patents. For example, the America Invents Act created new administrative post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings that allow third parties to challenge the validity of issued patents. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

After March 2013, under the America Invents Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third-party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before we file an application covering the same invention, could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product

candidates and other proprietary technologies we may develop or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing the claimed invention where the other party can show that they used the invention in commerce before our filing date or the other party benefits from a compulsory license. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Patents are of national or regional effect. Filing, prosecuting, and defending patents on mavodelpar, any future product candidates, and other proprietary technologies we develop in all countries throughout the world would be prohibitively expensive. In addition, the laws of some foreign countries do not protect intellectual property rights in the same manner and to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement of such patent protection 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.

The requirements for patentability may differ in certain countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval for a drug and its patent status. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors.

In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

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 or pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. As an example, European applications will soon have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court (UPC). The option of a Unitary Patent will be a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Further, the standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. As such, we do not know the degree of future protection that we will have on our technologies, products and product candidates. While we will endeavor to try to protect our technologies,

products and product candidates with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time consuming, expensive and unpredictable.

Further, 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 invasion of 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 that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly 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.

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

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

Our current and 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 we in-licensed. If other third parties have ownership rights or other rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

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

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses.

Presently we have intellectual property rights through licenses from third parties, including vTv Therapeutics, related to mavodelpar. Because our program may require the use of additional proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, mavodelpar may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license, on reasonable terms, proprietary rights related to any compositions, formulations, methods of use, processes or other intellectual property rights from third parties that we identify as being necessary for mavodelpar. In such event, we may be required to expend significant time and resources to develop or license replacement technology, which may not be available. Even if we are able to obtain a license to such proprietary rights, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

The patent protection and patent prosecution for some of our product candidates may be dependent on third parties.

While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to our product candidates, there may be times when the filing and prosecution activities for patents and patent applications relating to our product candidates are controlled by our future licensors or collaboration partners. When we obtain licenses from or collaborate with third parties, we may not have the right to control the preparation, filing, and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties, or such activities, if controlled by us, may require the input of such third parties. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business, or in compliance with applicable laws and regulations, including by payment of all applicable fees for patents covering our product candidates, which may affect the validity and enforceability of such patents or any patents that may issue from such application. If any of our future licensors or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering our product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our future licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, including making royalty and milestone payments, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could have a material adverse impact on our business. Our business would suffer if any such licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Furthermore, if any licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical or similar to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

Our rights to develop and commercialize our technology and product candidates may be subject, in part, to the terms and conditions of licenses granted to us by others.

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

The licensing and acquisition of third-party proprietary rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party proprietary rights that we may consider necessary or attractive in order to commercialize mavodelpar. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

It is possible that we may be unable to obtain licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to 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 product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us, either on reasonable terms, or at all. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment, or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights on commercially reasonable terms, our ability to commercialize our products, and our business, financial condition, and prospects for growth, could suffer.

We may enter into license agreements in the future with others to advance our existing or future research or allow commercialization of our existing or future product candidates. These licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future.

For example, we may collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate an exclusive license to any of the institution's proprietary rights in technology resulting from the collaboration. Regardless of such option to negotiate a license, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer, on an exclusive basis, their proprietary rights to other parties, potentially blocking our ability to pursue our program.

In addition, subject to the terms of any such license agreements, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. In such an event, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a

manner consistent with the best interests of our business. If our future licensors fail to prosecute, maintain, enforce, and defend such patents or patent applications, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our future product candidates that are subject of such licensed rights could be adversely affected.

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

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties, such as our license agreement with vTv Therapeutics, or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a license agreement with vTv Therapeutics under which we are granted intellectual property rights that are important to our business and our only product candidate, mavodelpar. If we fail to comply with our obligations under the license agreement, or we are subject to insolvency, the license agreement may be terminated, in which event we would not be able to develop, commercialize or market mavodelpar.

The agreements under which we 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 license in the future prevent or impair our ability to maintain our licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

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

Disputes may arise between us and our licensors regarding intellectual property rights subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property rights of the licensor that are not subject to the license agreement;
- our right to sublicense intellectual property rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of mavodelpar, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own, which are described herein. If we or our licensor fail to adequately protect this intellectual property, our ability to develop, manufacture or commercialize products could suffer.

If disputes over intellectual property rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, our business, results of operations, financial condition, and prospects may be adversely affected. We may enter into additional licenses in the future and if we fail to comply with obligations under those agreements, we could suffer adverse consequences.

In the future, we may need to obtain additional licenses of third-party technology that may not be available to us or are available only on commercially unreasonable terms, and which may cause us to operate our business in a more costly or otherwise adverse manner that was not anticipated.

From time to time, we may be required to license technologies relating to our therapeutic research programs from additional third parties to further develop or commercialize our product candidates. Should we be required to obtain licenses to any third-party technology, including any such patents required to manufacture, use or sell our product candidates, such licenses may not be available to us on commercially reasonable terms, or at all. The inability to obtain any third-party license required to develop or commercialize any of our product candidates could cause us to abandon any related efforts, which could seriously harm our business and operations.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our products.

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

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

- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

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

Our success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe, misappropriate or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including inter partes review, post grant review, interference and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. The implementation of these procedures brings uncertainty to the possibility of challenges to our patents in the future and the outcome of such challenges. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing mavodelpar.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our activities related to mavodelpar may give rise to claims of infringement of the patent rights of others. The biotechnology and pharmaceutical industries have produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. Identification of third-party patent rights that may be relevant to our operations is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to our research and other operations or necessary for the commercialization of our product candidates in any jurisdiction. We also cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, including our research programs, product candidates, their respective methods of use, manufacture and formulations thereof, and could result in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. We cannot assure you that any of our current or future product candidates will not infringe existing or future patents. We may not be aware of patents that have already issued that a third party might assert are infringed by one of our current

or future product candidates. Nevertheless, we are not aware of any issued patents that will prevent us from marketing mavodelpar.

Third parties, including our competitors, in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our products. We do not always conduct independent reviews of pending patent applications and patents issued to third parties. Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of mavodelpar. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be currently pending third-party patent applications which may later result in issued patents that mavodelpar, any future product candidates, and other proprietary technologies may infringe, or which such third parties claim are infringed by the use of our technologies. Parties making claims against us for infringement or misappropriation of their intellectual property rights may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize mavodelpar or future product candidates. Defense of these claims, regardless of their merit, could involve substantial expenses and could be a substantial diversion of management and other employee resources from our business.

If we collaborate with third parties in the development of technology in the future, our collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. In the future, we may agree to indemnify our commercial collaborators against certain intellectual property infringement claims brought by third parties.

Any claims of patent infringement asserted by third parties would be time-consuming and could:

- result in costly litigation;
- cause negative publicity;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing mavodelpar or any future product candidates until the asserted patent expires or is finally held invalid, unenforceable, or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- require us to pay damages to the party whose intellectual property rights we may be found to be infringing, which may include treble damages if we are found to have been willfully infringing such intellectual property;
- require us to pay the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be willfully infringing; and/or
- require us to enter into royalty or license agreements, which may not be available on commercially reasonable terms, or at all, or which might be non-exclusive, which could result in our competitors gaining access to the same technology.

If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do either. Proving invalidity or unenforceability is difficult. For example, in the United States, proving invalidity before federal courts requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may

incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, which may not be available, defend an infringement action or challenge the validity or enforceability of the patents in court. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid or unenforceable, we may incur substantial monetary damages, encounter significant delays in bringing mavodelpar to market and be precluded from developing, manufacturing or selling mavodelpar.

We do not always conduct independent reviews of pending patent applications and patents issued to third parties. We cannot be certain that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction, because:

- some patent applications in the United States may be maintained in secrecy until the patents are issued;
- patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived;
- pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, mavodelpar, and any future product candidates or the use of mavodelpar and any future product candidates;
- identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases, and the difficulty in assessing the meaning of patent claims;
- patent applications in the United States are typically not published until 18 months after the priority date; and
- publications in the scientific literature often lag behind actual discoveries.

Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our interpretation of the relevance or the scope of claims in a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. Further, we may incorrectly determine that our technologies, products, or product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or internationally that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our products or product candidates. Furthermore, we cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours, and others may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import mavodelpar and future approved products or impair our competitive position. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of mavodelpar. Any such patent application may have priority over our patent applications, which could further

require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar invention prior to our own invention, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications and may be entitled to priority over our applications in such jurisdictions.

Some third parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our business, results of operations, financial condition and prospects.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product, we may have to pay substantial damages, including treble damages and attorneys' fees if we are found to be willfully infringing a third party's patents, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure.

We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of mavodelpar. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize mavodelpar, which could harm our business significantly. Even if we were able to obtain a license, the rights may be nonexclusive, which may give our competitors access to the same intellectual property.

Although no third party has asserted a claim of patent infringement against us as of the date of this Annual Report, others may hold proprietary rights that could prevent our product candidates from being marketed. It is possible that a third party may assert a claim of patent infringement directed at any of our product candidates. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidates, treatment indications, or processes could subject us to significant liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product candidates, treatment indications, or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court, and we may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.

Third parties including competitors may infringe, misappropriate or otherwise violate our patents, patents that may issue to us in the future, or the patents of our licensors that are licensed to us. To stop or prevent infringement or unauthorized use, we may need to or choose to file infringement claims, which can be expensive and time-consuming. We may not be able to stop or prevent, alone or with our licensors, infringement, misappropriation, or other violation of our intellectual property, particularly in countries where the laws may not protect those rights as fully as in the United States.

If we choose to go to court to stop another party from using the inventions claimed in our patents, a court may decide that a patent we own or in-license is not valid, is unenforceable and/or is not infringed by that third party for any number of reasons. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements for patentability, including lack of novelty, obviousness, obviousness-type double patenting, lack of written description, indefiniteness, or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution, i.e., committed inequitable conduct. Third parties may also raise similar claims before the USPTO, even outside the context of litigation, including re-examination, PGR, IPR, and derivation proceedings. Similar mechanisms for challenging the validity and enforceability of a patent exist in foreign patent offices and courts and may result in the revocation, cancellation, or amendment of any foreign patents we or our licensors hold now or in the future. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business. There is also a risk that, even if the validity of our patents is upheld, the court will decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover such invention, or decide that the other party's use of our patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1).

With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our future licensors, and the patent examiners are unaware during prosecution. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications or the patents and patent applications of our future licensors, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or platform, or any product candidates that we may develop. Such a loss of patent protection would 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 or those of our licensors. 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 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 or manufacturing partnerships that would help us bring mavodelpar and any future product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Our ability to enforce our patent rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, if the breadth or strength of protection provided by our patents and patent applications or the patents and patent applications of our future licensors is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented product and practicing our own patented technology.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties and we may conclude that even if a third party is infringing our issued patent, any patents that may be issued as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In addition, the uncertainties associated with litigation could compromise our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology or other product candidates, or enter into development partnerships that would help us bring our product candidates to market. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

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

We rely on trade secrets, including unpatented know-how, technology and other proprietary information, to protect our proprietary technologies and maintain our competitive position, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, and other third parties, to protect our trade secrets and other proprietary information. In addition to contractual measures, we try to protect the confidential nature of our trade secrets and other proprietary information using commonly accepted physical and technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and these agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including

information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

In addition, such commonly accepted physical and technological security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, advisor, or other third party with authorized access. Our security measures may not prevent an employee, outside scientific collaborator, CRO, third-party manufacturer, consultant, advisor, potential partner, and other third party from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. Even though we use commonly accepted security measures, the criteria for protection of trade secrets can vary among different jurisdictions. Further, we may need to share our proprietary information, including trade secrets, with our current and future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors.

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 the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced, and our competitive position would be harmed.

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

Elements of our product candidates, including processes for their preparation and manufacture, may involve proprietary know-how, and other proprietary information that is not covered by patents, and thus for these aspects we may consider trade secrets, including unpatented know-how, and other proprietary information to be our primary intellectual property. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

Trade secrets, including unpatented know-how, and other proprietary information, can be difficult to trace, protect and enforce. We require our employees to enter into written employment agreements containing provisions of confidentiality and obligations to assign to us any inventions generated in the course of their employment. We further seek to protect our potential trade secrets, proprietary know-how and information in part, by entering into non-disclosure and confidentiality agreements with parties who are given access to them, such as outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, and other third parties. With our consultants, advisors, contractors and outside scientific collaborators, these agreements typically include invention assignment obligations. Although we have taken steps to protect our trade secrets and unpatented know-how, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets and unpatented know-how, and we may not be able to obtain adequate remedies for such breaches. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective.

Trade secrets may be independently developed by others in a manner that could prevent legal recourse by us. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. Though our agreements with third parties typically restrict the ability of our employees, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, and other third parties, to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of our products and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed and we would have no right to prevent them from using that technology or information to compete with us. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

We may be subject to claims that we or our employees, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, and other third parties have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

We have entered into and may enter in the future into non-disclosure and confidentiality agreements to protect the proprietary positions of third parties, such as outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, and other third parties. We may become subject to litigation where a third party asserts that we or our employees inadvertently or otherwise breached the agreements and used or disclosed trade secrets or other information proprietary to the third parties. We may also be subject to claims that we have wrongfully hired an employee from a competitor. Defense of such matters, regardless of their merit, could involve substantial litigation expense and be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions. Moreover, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology. Failure to defend against any such claim could subject us to significant liability for monetary damages or prevent or delay our developmental and commercialization efforts, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Parties making claims against us may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, operating results, financial condition and prospects.

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

Our current or future trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks, and we may be unable to obtain future trademarks or trade names that we intend to use. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors 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 trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights, or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

Moreover, any name we have proposed to use with mavodelpar in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. Similar requirements exist in Europe. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Risks Related to Ownership of Our Common Stock

An active, liquid and orderly trading market for our common stock may not be sustained.

Prior to the closing of our initial public offering (IPO) in April 2021, there was no public market for shares of our common stock. An active trading market for our shares may not be sustained. You may not be able to sell your shares quickly or at the market price if trading in shares of our common stock is not active. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the price at which they were purchased. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration.

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

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this “Risk Factors” section and elsewhere in this Annual Report, these factors include:

- the commencement, enrollment or results of our ongoing and planned clinical trials of mavodelpar or any future clinical trials we may conduct for any future product candidates, or changes in the development status of mavodelpar or any future product candidates;

- acceptance by the FDA and EMA of data from our ongoing pivotal STRIDE study or any future clinical trials we conduct;
- any delay in our regulatory filings for mavodelpar and any future product candidates;
- adverse results or delays in clinical trials or preclinical studies;
- our decision to initiate a clinical trial, not to initiate a clinical trial, or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval for mavodelpar and any future product candidates;
- changes in laws or regulations applicable to mavodelpar and any future product candidates, including but not limited to clinical trial requirements for approvals;
- our failure to commercialize mavodelpar and any future product candidates;
- the failure to obtain coverage and adequate reimbursement of mavodelpar and any future product candidates, if approved;
- changes in the structure of healthcare payment systems;
- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of mavodelpar and any future product candidates;
- introduction of new products or services offered by us or our competitors, or the release or publication of clinical trial results from competing product candidates;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- the size and growth, if any, of the markets for patients with PMM and LC-FAOD, and other rare genetic mitochondrial diseases that we may target;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- developments with respect to our intellectual property rights;
- our commencement of, or involvement in, litigation; and
- general political and economic conditions, including those resulting from the COVID-19 pandemic and bank failures.

In addition, the stock market in general, and pharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have

experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

Our executive officers and directors, combined with our stockholders who own more than 5% of our outstanding capital stock, beneficially own shares representing a significant percentage of our common stock. Therefore, these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

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

We may seek additional capital through a combination of public or private equity offerings or debt financings, credit or loan facilities, collaborations, strategic alliances, licensing arrangements or a combination of one or more of these funding sources. 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 stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or current or future product candidates, or grant licenses on terms unfavorable to us.

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

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act). For as long as we continue to be an emerging growth company, we may take advantage of certain exemptions from various public company reporting requirements, including being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this Annual Report, not being required to have our internal control over financial reporting audited by our independent registered public accounting firm under Section 404 of the Sarbanes-Oxley Act of 2002 (Sarbanes-Oxley Act), reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We may take advantage of these exemptions until December 31, 2026 or until we are no longer an emerging growth company, whichever is earlier. We will cease to be an emerging growth company prior to the end of such five-year period if certain earlier events occur, including if we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, our annual gross revenues exceed $1.235 billion or we issue more than $1.0 billion of non-convertible debt in any three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to use this extended transition period under the JOBS Act until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company, which would allow us to take advantage of many of the same exemptions available to emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation. We will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than $100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter. Investors may find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of The Nasdaq Stock Market LLC (Nasdaq). The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal controls over financial reporting. Each fiscal year, we are required to provide a report by our management on, among other things, our internal control over financial reporting as discussed in our Annual Report on Form 10-K filing for that year. The reporting on our assessment of the effectiveness of our internal control over financial reporting needs to include disclosure of any material weaknesses identified in our internal control over financial reporting, as well as a statement that our independent registered public accounting firm has audited the effectiveness of our internal control over financial reporting. While we qualify as an emerging growth company under SEC rules for fiscal year 2023 and therefore are not required to obtain such an audit for fiscal year 2023, in the event that we qualify as a large accelerated filer or accelerated filer under SEC rules in future years, our independent registered public accounting firm will be required to audit the effectiveness of our internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act (Section 404(b)). Any mandatory or voluntary compliance with Section 404(b) will result in increased costs, expenses, and management resources. However, for as long as we remain an emerging growth company as defined in the JOBS Act, we intend to take advantage of the exemption permitting us not to comply with the independent registered public accounting firm attestation requirement.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our consolidated financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

We cannot assure you that the measures we have taken to date, and actions we may take in the future, will prevent or avoid potential future material weaknesses. Moreover, our current controls and any new controls that we develop may become inadequate because of changes in conditions in our business. Further, material weaknesses in our disclosure controls and procedures and internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective internal control over financial reporting or any difficulties encountered in their implementation or improvement could harm our operating results or cause us to fail to meet our reporting obligations and may result in a restatement of our financial statements for prior periods, which could cause the price of our common stock to decline. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

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

We are subject to the reporting requirements of the Exchange Act, which requires, among other things, that we file with the SEC annual, quarterly, and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (Dodd-Frank Act) was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Emerging growth companies and smaller reporting companies are exempted from certain of these requirements, but we may be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition, results of operations and prospects. The increased costs will decrease our net income or increase our consolidated net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of December 31, 2022, there were 24,699,553 shares of our common stock outstanding.

In addition, shares of common stock that are either subject to outstanding options or performance-based restricted stock units or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, and Rule 144 and Rule 701 under the Securities Act of 1933, as amended (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.

Further, the holders of 14,588,254 shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that we will need significant additional capital in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities, and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock. As of March 21, 2023, the remaining capacity under the ATM facility was approximately $18.8 million in shares of common stock.

Pursuant to our 2021 Equity Incentive Plan (the 2021 Plan), our management is authorized to grant stock options and other stock awards to our employees, directors and consultants. Additionally, the number of shares of our common stock reserved for issuance under our 2021 Plan will automatically increase on January 1 of each year through and including January 1, 2031, by 5% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by our board of directors. In addition, pursuant to our 2021 Employee Stock Purchase Plan, the number of shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year through and including January 1, 2031, by the lesser of (i) 1% of the total number of shares of our common stock outstanding on the last day of the calendar month before the date of the automatic increase, and (ii) 729,174 shares; provided that before the date of any such increase, our board of directors may determine that such increase will be less than the amount set forth in clauses (i) and (ii). Unless our board of directors elects not to increase the number of shares available for future grant each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

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

We have never declared or paid any cash dividend 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, future debt instruments may materially restrict our ability to pay dividends on our common stock. Any return to stockholders would therefore be limited to the appreciation, if any, of their stock.

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

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

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;

- a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president, or by a majority of the total number of authorized directors;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

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

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers, or other employees to us or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers, or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws; (iv) any action or proceeding to interpret, apply, enforce, or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; (v) any action or proceeding as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and (vi) any action asserting a claim against us or any of our directors, officers, or other employees governed by the internal affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants.

These provisions would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation and our

amended and restated bylaws provide that the federal district courts of the United States of America are the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, including all causes of action asserted against any defendant named in such complaint. While the Delaware courts have determined that such choice of forum provisions are facially valid and several state trial courts have enforced such provisions and required that suits asserting Securities Act claims be filed in federal court, there is no guarantee that courts of appeal will affirm the enforceability of such provisions and a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation and our amended and restated bylaws. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions. If a court were to find either exclusive forum provision in our amended and restated certificate of incorporation and our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with litigating Securities Act claims in state court, or both state and federal court, which could seriously harm our business, financial condition, results of operations, and prospects.

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 lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive forum provision 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 further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

General Risk Factors

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, and anti-corruption and anti-money laundering laws and regulations, including the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, clinical research organizations, contractors and other collaborators and partners from authorizing, promising, offering, providing, soliciting or receiving, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products internationally once we enter a commercialization phase, and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, clinical research organizations, contractors and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Business disruptions could seriously harm our future revenues and financial condition and increase our costs and expenses.

Our operations, and those of our CROs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires,

extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce mavodelpar. Our ability to obtain clinical supplies of mavodelpar and any future product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. Our corporate headquarters is located in California near major earthquake faults and fire zones. The ultimate impact on us, our suppliers and our general infrastructure of being located near major earthquake faults and fire zones and being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural disaster.

If our information technology systems or data, or those of third parties upon which we rely, are or were compromised, we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; loss of customers or sales; and other adverse consequences.

In the ordinary course of business, we and the third parties upon which we rely process sensitive data, and, as a result, we and the third parties upon which we rely face a variety of evolving threats, including but not limited to ransomware attacks, which could cause security incidents.

Cyberattacks, malicious internet-based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive data and information technology systems, and those of the third parties upon which we rely. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer "hackers," threat actors, "hacktivists," organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation-states, and nation-state-supported actors.

Some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties upon which we rely, may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our services. Further, the loss of clinical trial data from completed or ongoing clinical trials could result in delays in, or cancellations of any regulatory approval or clearance efforts and significantly increase our costs to recover or reproduce the data, and subsequently commercialize the product. Additionally, theft of our intellectual property or proprietary business information could require substantial expenditures to remedy.

We and the third-parties upon which we rely are subject to a variety of evolving threats including social-engineering attacks (including through phishing attacks), malicious code (such as computer viruses or bugs), misconduct or error by employees or contractors, malware (including as a result of advanced persistent threat intrusions), ransomware, supply chain attacks, natural disasters, terrorism, war, telecommunication and electrical failure, adware, denial of service attacks (such as credential stuffing), credential harvesting, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fires, floods, and other similar threats.

In particular, ransomware attacks are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, loss of sensitive data, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments.

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

Additionally, future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program.

In addition, our reliance on third-party service providers could introduce new cybersecurity risks and vulnerabilities, including supply-chain attacks, and other threats to our business operations. We rely on third-party service providers and technologies to operate critical business systems to process sensitive data in a variety of contexts, including, without limitation, cloud-based infrastructure, data center facilities, encryption and authentication technology, employee email, and other functions. We also rely on third-party service providers to provide other products, services, parts, or otherwise to operate our business. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been compromised.

Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive data or our information technology systems, or those of the third parties upon whom we rely. A security incident or other interruption could disrupt our ability (and that of third parties upon whom we rely) to provide our products.

We may expend significant resources or modify our business activities to try to protect against security incidents. Additionally, certain data privacy and security obligations may require us to implement and maintain specific security measures or industry-standard or reasonable security measures to protect our information technology systems and sensitive data.

While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We take steps to detect and remediate vulnerabilities, but we may not be able to detect and remediate all vulnerabilities because the threats and techniques used to exploit the vulnerability change frequently and are often sophisticated in nature. Therefore, such vulnerabilities could be exploited but may not be detected until after a security incident has occurred. These vulnerabilities pose material risks to our business. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities.

Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosures or the failure to comply with such requirements could lead to adverse consequences.

If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences such as government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing sensitive data (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may cause customers to stop using our products or services, deter new customers from using our products or services, the development and commercialization of mavodelpar could be delayed, and negatively impact our ability to grow and operate our business. Likewise, we rely on third parties to conduct clinical trials, and similar incidents relating to their information technology systems or data could also have a material adverse effect on our business.

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

In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position.

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

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

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

We lease approximately 5,100 square feet of office space for our headquarters in Irvine, California under a non-cancelable operating lease through November 2026. We also lease approximately 2,600 square feet of space for an office in the UK under an agreement that expires in October 2027. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings

From time to time, we may become involved in legal proceedings relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition or cash flows.

Item 4. Mine Safety Disclosures

None.

PART II

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

Market Information

Our common stock has been listed on the Nasdaq Global Market under the symbol "RPHM" since April 9, 2021. Prior to that date, there was no public market for our common stock.

Holders of Common Stock

As of March 21, 2023, there were 25,107,430 shares of our common stock outstanding held by approximately 25 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.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Securities Authorized for Issuance Under Equity Compensation Plans

See Item 12 of Part III of this Annual Report for information about our equity compensation plans which is incorporated by reference herein.

Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Stock Performance Graph

Not required for smaller reporting companies.

Use of Proceeds

We commenced our IPO pursuant to the registration statement on Form S-1 (File No. 333-254534) that was declared effective on April 8, 2021 and registered an aggregate of 7,187,500 shares of our common stock. On April 13, 2021, we completed our IPO and sold 6,250,000 shares of our common stock at a public offering price of $15.00 per share for aggregate gross proceeds of $93.8 million before deducting underwriters' discounts and commissions and offering-related expenses. Net proceeds, after deducting underwriting discounts and commissions of $6.6 million and offering expenses of approximately $2.6 million, were $84.6 million. Jefferies LLC, SVB Securities LLC and Piper Sandler & Co. acted as joint book-running managers.

As of December 31, 2022, we have not used any of the proceeds from our IPO. We invested the funds received in highly liquid money market funds and short-term investments. The net proceeds from the IPO will be

used, together with our cash, cash equivalents, and short-term investments to fund continued research and development of mavodelpar in patients with PMM and LC-FAOD, other clinical trials and preclinical studies, and commercial readiness preparations, and to provide funds for working capital and other general purposes. None of the offering proceeds were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates.

Item 6. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes included in Item 8 "Financial Statements and Supplementary Data" and included elsewhere in this Annual Report. This discussion and analysis contains forward-looking statements based upon our current beliefs, estimates, plans and expectations that involve risks, uncertainties and assumptions. Our actual results may differ materially from those contained in these forward-looking statements as a result of various factors, including those set forth under "Risk Factors" or in other parts of this Annual Report.

Overview

Reneo is a clinical-stage pharmaceutical company focused on the development and commercialization of therapies for patients with rare genetic mitochondrial diseases, which are often associated with the inability of mitochondria to produce ATP. Our lead product candidate, mavodelpar, is a potent and selective agonist of the PPARδ. Mavodelpar has been shown to increase transcription of genes involved in mitochondrial function and increase FAO, and may increase production of new mitochondria.

The PPAR family of nuclear hormone receptors, PPARα, PPARγ, and PPARδ, control the transcription of genes critical for regulating energy metabolism and homeostasis. PPARδ is highly expressed in muscle, kidney, brain, and liver tissue. Activation of PPARδ results in changes in the expression of genes involved with multiple aspects of energy metabolism including uptake of fatty acids, utilization of fatty acids as an energy source, and mitochondrial biogenesis.

Increases in PPARδ activity also correlate with a shift in muscle tissue towards oxidative, fat-consuming type I fibers that are associated with endurance as opposed to glycolytic, type II fibers. In preclinical and clinical studies, increased PPARδ activity through transgenic overexpression or pharmacological activation increases muscular strength and endurance across a variety of functional measures. Mavodelpar was studied in healthy male volunteers with one leg immobilized to produce muscle atrophy. Compared to placebo, administration of mavodelpar resulted in statistically significant increases in expression of genes involved in mitochondrial OxPhos, and statistically significant improvements in muscle strength. Mavodelpar was studied in an open-label trial in patients with PMM. Patients with PMM in this trial exhibited improved function, reduced symptoms, and increased expression of genes involved in mitochondrial function. Mavodelpar was also studied in an open-label trial in patients with LC-FAOD. In this trial, patients with LC-FAOD due to certain gene defects exhibited improved function and reduced symptoms.

As a PPARδ agonist, mavodelpar may benefit patients with genetic mitochondrial myopathies who experience weakness, fatigue, or deterioration in muscle due to impaired mitochondrial energy production. Patients with these diseases are unable to perform many everyday activities, can experience cardiomyopathy and other organ dysfunction, and typically have a reduced life expectancy. We are currently developing mavodelpar in rare genetic diseases that typically present with myopathy, including PMM and LC-FAOD.

There are currently no approved therapies for the treatment of PMM, representing a high unmet medical need.

We have received orphan drug designations for mavodelpar in the United States for PMM and LC-FAOD. Additionally, we have received orphan drug designations for mavodelpar for MELAS, a form of PMM, and LCHAD, a form of LC-FAOD in Europe.

We have received Fast Track designation for mavodelpar for the treatment of patients with PMM and LC-FAOD due to LCHAD deficiency, one of the predominant LC-FAOD genotypes. We are continuing to collaborate with the FDA and European regulatory agencies to advance the LC-FAOD program which will include patients with LCHAD as well as other genotypes. These discussions include obtaining alignment on the study design, patient population, and endpoints for the LC-FAOD program's next clinical trial.

Mavodelpar for the Treatment of PMM

We completed an open-label Phase 1b study of mavodelpar in patients with PMM due to mtDNA defects to assess the safety and tolerability of mavodelpar, and evaluated changes in patient function using a 12MWT. Mavodelpar was well-tolerated and had an adequate safety profile in this trial. Compared to baseline, patients receiving mavodelpar once-daily for 12 weeks experienced an average increase in distance of 104.4 meters in the 12MWT, an average increase in weight-adjusted peak VO_2 of 1.7 mL/min/kg, a reduction in fatigue and pain, and increased expression of genes involved with transport and metabolism of nutrients in the mitochondria including PDK4, ANGPTL4, and SLC25A34.

Based on these results, we initiated the STRIDE study, a global, randomized, double-blind, placebo-controlled pivotal Phase 2b trial of mavodelpar in adult patients with PMM due to mtDNA defects. We achieved the target enrollment of 200 patients in the pivotal STRIDE study in March 2023 and anticipate announcement of topline results in the fourth quarter of 2023. STRIDE study is designed to investigate the efficacy and safety of 100 mg mavodelpar administered once-daily over a 24-week period. The primary efficacy endpoint of the trial is the change from baseline in the distance walked during the 12MWT at week 24. Key secondary endpoints include changes from baseline in the MFIS measures and the patient global impression of change scale. Additional secondary endpoints include the 30STS test, step counts, patient global impression of severity scale, BPI, and additional patient-reported outcome measures.

We are also conducting the STRIDE AHEAD study, a 24-month, open-label, long-term safety trial outside of the United States in patients with PMM due to mtDNA. STRIDE AHEAD study was recently amended to also allow enrollment of patients with PMM due to nDNA defects and the amendment is undergoing regulatory review. Based on interactions with the FDA, EMA, and several other national regulatory agencies in Europe, and several European regulatory agencies, we believe that positive results from the ongoing pivotal STRIDE and STRIDE AHEAD studies could potentially support registration of mavodelpar for adult patients with PMM in the United States and Europe. We intend to submit the data from STRIDE, together with the long-term safety data from STRIDE AHEAD, to the FDA and the EMA in planned marketing applications in 2024.

Mavodelpar for the Treatment of LC-FAOD

We completed an open-label Phase 1b study in LC-FAOD adult patients with nDNA defects to assess the safety and tolerability of mavodelpar, and measure changes in functional test such as walk distance, exercise capacity and patient-reported symptoms that could serve as potential endpoints in future clinical studies. The study included patients with defective LCHAD, CPT2, VLCAD, or TFP.

A total of 24 patients were enrolled, including patients with defective LCHAD (n=5), CPT2 (n=8), VLCAD (n=9), or TFP (n=2). We initiated the trial with a dose of 50 mg once-daily in the first three patients followed by 100 mg once-daily in all subsequent patients. The LCHAD and CPT2 groups had the greatest improvement over baseline in 12MWT (73.7 and 51.9 meters, respectively).

In the LC-FAOD Phase 1b study, mavodelpar was well tolerated. The most common adverse events experienced by patients were rhabdomyolysis (4 patients) and myalgia (4 patients), the majority reported to be

mild or moderate in severity. The LCHAD and CPT2 groups had the greatest improvement over baseline in 12MWT (73.7 and 51.9 meters, respectively).

We also completed the FORWARD study, a 16-week, observational, non-interventional study in patients with LC-FAOD with different nDNA mutations to better understand the natural history of LC-FAOD and changes in patient function and symptoms over time. A total of 58 patients participated in the FORWARD study, including patients with defective LCHAD (n=16), CPT2 (n=30), or VLCAD (n=12).

Based on the results of the LC-FAOD Phase 1b study, in conjunction with the results of the FORWARD study, we intend to continue the development of mavodelpar for certain genotypes of patients with LC-FAOD. Results of the studies were presented at the International Network of Fatty Acid Oxidation Research and Management Conference in August 2022.

Financial Overview

Since our inception in 2014, our operations have primarily focused on raising capital, establishing and protecting our intellectual property portfolio, organizing and staffing our company, business planning, and conducting preclinical and clinical development of and manufacturing development for mavodelpar. We do not have any product candidates approved for sale, have not generated any revenue from product sales, and do not expect to generate revenues from the commercial sale of our product candidate for several years, if ever. Since inception, we have incurred significant operating losses. Our net losses were $52.0 million and $39.8 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $136.7 million, and cash, cash equivalents and short-term investments of $101.2 million. We have funded our operations primarily through the issuance and sale of equity securities.

We expect to continue to incur net operating losses for at least the next several years, and we expect our research and development expenses, general and administrative expenses, and capital expenditures will continue to increase as we conduct our ongoing and planned clinical trials and preclinical studies, engage in other research and development activities, seek regulatory approvals for any product candidates that successfully complete clinical trials, incur development milestone payments related to our research and development activities, prepare for commercialization, hire additional personnel, and protect our intellectual property.

Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development and commercialization activities. As a result, we will need to raise additional capital. Until such time as we can generate significant revenue from sales of our product candidate, if ever, we expect to finance our operations through public or private equity offerings or debt financings, credit or loan facilities, collaborations, strategic alliances, licensing arrangements or a combination of one or more of these funding sources. Additional funds may not be available to us on acceptable terms or at all. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and disruptions to, and volatility in, the credit and financial markets in the United States and worldwide, including those resulting from the ongoing COVID-19 pandemic, bank failures, as well as actual or perceived changes in interest rates and economic inflation. If we fail to obtain necessary capital when needed on acceptable terms, or at all, it could force us to delay, limit, reduce or terminate our product development programs, commercialization efforts or other operations. Based upon our current operating plan, we believe that our cash, cash equivalents, and short-term investments as of December 31, 2022 will enable us to fund our operating expenses and capital expenditure requirements through our planned near-term clinical milestones.

License Agreement

In December 2017, we entered into the vTv License Agreement, under which we obtained an exclusive, worldwide, sublicensable license under certain vTv Therapeutics intellectual property to develop, manufacture and commercialize PPARδ agonists and products containing such PPARδ agonists, including mavodelpar, for any therapeutic, prophylactic or diagnostic application in humans. Under the terms of the vTv License Agreement, we

paid vTv Therapeutics an initial upfront license fee of $3.0 million and $2.0 million of milestone payments and issued an aggregate of 576,443 shares of our common stock to vTv Therapeutics.

Upon the achievement of certain pre-specified development and regulatory milestones, we are also required to pay vTv Therapeutics milestone payments totaling up to $64.5 million. We are also required to pay vTv Therapeutics up to $30.0 million in total sales-based milestones upon achievement of certain sales thresholds of the licensed product. In addition, we are obligated to make tiered royalty payments to vTv Therapeutics at mid-single digit to low teen percentage royalty rates, based on tiers of annual net sales of licensed products, subject to certain customary reductions. A milestone payment of $2.0 million was achieved and recorded for the year ended December 31, 2021. There were no milestone payments achieved or recorded for the year ended December 31, 2022.

Components of Our Results of Operations

Operating Expenses

Research and Development Expenses

Research and development expenses primarily relate to preclinical and clinical development of mavodelpar. Research and development expenses include:

- personnel expenses, including salaries, benefits, and stock-based compensation expense;
- external expenses incurred under agreements with CROs, investigative sites and consultants to conduct and support our preclinical studies and clinical trials;
- raw materials related to manufacturing of our product candidate for clinical trials and preclinical studies, including fees paid to third-party manufacturers;
- expenses related to regulatory activities, including filing fees paid to regulatory agencies;
- facility costs including rent, depreciation, and maintenance expenses; and
- fees for maintaining licenses under our third-party licensing agreements.

Research and development expenses are recognized as incurred and payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received. Costs for certain activities, such as manufacturing and preclinical studies and clinical trials, are generally recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and collaborators. We expense amounts paid to acquire licenses associated with products under development when the ultimate recoverability of the amounts paid is uncertain and the technology has no alternative future use when acquired.

The following table summarizes our research and development expenses for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,	
	2022	2021
Clinical and regulatory	$ 19,919	$ 14,863
Contract manufacturing cost	8,915	6,450
Nonclinical	3,931	2,339
Research and development-other expense	4,940	4,517
Total	$ 37,705	$ 28,169

We expect our research and development expenses to increase substantially for the foreseeable future as we advance our product candidate into and through clinical trials, continue to conduct preclinical studies and pursue regulatory approval of our product candidate. The process of conducting the necessary clinical research to

obtain regulatory approval is costly and time-consuming. The actual probability of success for our product candidate may be affected by a variety of factors including: the safety and efficacy of our product candidate, early clinical data, investment in our clinical program, competition, manufacturing capability and commercial viability. We may never succeed in achieving regulatory approval for our product candidate. As a result of the uncertainties discussed above, at this time we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of and obtain regulatory approval for our product candidate. Our research and development costs may vary significantly based on factors such as:

- the scope, rate of progress, expense and results of clinical trials and preclinical studies;
- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the number of patients that participate in the trials;
- uncertainties in patient enrollment or drop out or discontinuation rates, particularly in light of the current COVID-19 pandemic environment;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the safety and efficacy of our product candidate;
- the cost and timing of manufacturing our product candidates; and
- the extent to which we establish strategic collaborations or other arrangements.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel expenses, including salaries, benefits, and stock-based compensation expense, for personnel in executive, finance, accounting, and human resource and other administrative functions. General and administrative expenses also include corporate facility costs not otherwise included in research and development expenses, legal fees related to intellectual property and corporate matters, insurance costs and fees for accounting and consulting services.

We expect our general and administrative expenses to increase for the foreseeable future to support continued research and development activities, including our ongoing and planned research and development of our product candidate for multiple indications.

Other Income

Other income consists of interest income on our cash, cash equivalents and short-term investments.

Results of Operations

Comparison of Year Ended December 31, 2022 and 2021

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

	Year Ended December 31,		
	2022	2021	Change
Operating expenses:			
Research and development	$ 37,705	$ 28,169	$ 9,536
General and administrative	16,143	11,649	4,494
Total operating expenses	53,848	39,818	14,030
Loss from operations	(53,848)	(39,818)	(14,030)
Other income	1,893	48	1,845
Net loss	$ (51,955)	$ (39,770)	$ (12,185)

Operating Expenses

Research and Development Expenses

Research and development expenses increased by $9.5 million during 2022 compared to 2021. This increase was primarily due to an increase of $6.4 million related to clinical and manufacturing costs primarily related to our STRIDE and STRIDE AHEAD studies and an increase of $2.8 million in personnel related costs due to the additional headcount required to support our clinical and manufacturing operations.

General and Administrative Expenses

General and administrative expenses increased by $4.5 million during 2022 compared to 2021. This increase was primarily due to an increase of $2.9 million in outside professional services and an increase of $1.2 million in facility and personnel related costs due to additional headcount.

Other Income

Other income increased by $1.8 million during 2022 compared to 2021. This increase primarily relates to higher interest income attributable to increasing interest rates during 2022.

Liquidity and Capital Resources

Since inception, we have incurred operating losses and negative cash flows from operations and have funded our operations primarily through the sale of preferred and common stock. We do not have any product candidates approved for sale and have not generated any revenue from product sales, and we do not expect to generate revenues from the commercial sale of our product candidate for at least the foreseeable future, if ever. We are subject to all the risks related to the development and commercialization of novel therapeutics, and we may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect our business. We continue to incur additional costs associated with operating as a public company. We anticipate that we will need substantial additional funding in connection with our continuing operations.

In May 2022, we entered into the ATM facility with SVB Securities LLC under which we may offer and sell, from time to time, at our sole discretion, up to $20.0 million in shares of our common stock. As of March 21, 2023, we have sold and issued approximately 500,000 shares of our common stock pursuant to the ATM facility at a weighted-average price of $2.48 per share, resulting in aggregate gross proceeds to us of $1.2 million. Sales

commissions to SVB Securities LLC and other issuance expenses were immaterial. The remaining capacity under the ATM facility was approximately $18.8 million in shares of common stock as of March 21, 2023.

The accompanying consolidated financial statements have been prepared assuming we will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business, and does not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or amounts and classification of liabilities that may result from the outcome of this uncertainty. We have prepared cash flow forecasts which indicate that based on our expected operating losses and negative cash flows, there is substantial doubt about our ability to continue as a going concern for twelve months after the date the consolidated financial statements for the year ended December 31, 2022 are issued. We plan to raise additional capital through public or private equity offerings or debt financings, credit or loan facilities, collaborations, strategic alliances, licensing arrangements or a combination of one or more of these funding sources. While we believe this plan to raise additional funds will alleviate the conditions that raise substantial doubt, these plans are not entirely within its control and cannot be assessed as being probable of occurring. We may not be able to secure additional financing in a timely manner or on favorable terms, if at all.

Cash Flows

The following table summarizes our cash flows for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,	
	2022	**2021**
Net cash used in operating activities	$ (47,362)	$ (37,983)
Net cash used in investing activities	(57,842)	(23,376)
Net cash provided by financing activities	471	132,406
Net (decrease) increase in cash and cash equivalents	$ (104,733)	$ 71,047

Operating Activities

Net cash used in operating activities for the year ended December 31, 2022 was $47.4 million, consisting primarily of our net loss of $52.0 million adjusted for non-cash items of $3.6 million primarily due to stock-based compensation expense and $1.0 million related to net change in operating assets and liabilities. The change in net operating assets and liabilities was primarily due to a decrease in prepaid and other assets of $0.9 million as a result of a decrease in prepayments made for clinical trial activities and an increase in accrued expenses of $0.5 million due to timing of receipt of invoices and payments, offset by a decrease in operating lease liabilities of $0.4 million as a result of lease payments.

Net cash used in operating activities for the year ended December 31, 2021 was $38.0 million, consisting primarily of our net loss of $39.8 million adjusted for non-cash items of $4.6 million primarily due to stock-based compensation expense and $2.8 million net change in operating assets and liabilities. The change in net operating assets and liabilities was primarily due to an increase in prepaid and other assets of $4.7 million as a result of prepayments made for clinical trial activities, offset by the increase in accounts payable, accrued expense and other of $1.8 million due to timing of receipt of invoices and payments.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2022 was $57.8 million consisting primarily of purchases of $101.6 million of available for sale short term investments, offset by $44.1 million of proceeds received from maturities of available for sale short term investments.

Net cash used in investing activities for the year ended December 31, 2021 was $23.4 million consisting primarily of purchases of $31.4 million of available for sale short term investments, offset by $8.2 million of proceeds received from maturities of available for sale short term investments.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2022 was $0.5 million, consisting primarily of $0.3 million of proceeds from the exercise of stock options and employee stock purchase plan (ESPP) purchases and net proceeds of $0.2 million from the sale of common stock under our ATM facility.

Net cash provided by financing activities for the year ended December 31, 2021 was $132.4 million, consisting primarily of $93.8 million of gross proceeds raised from our IPO, net of $6.6 million in underwriters' discount and commissions and issuance costs of $2.6 million, as well as $47.2 million of net proceeds from the issuance of shares of Series B convertible preferred stock, and $0.6 million of proceeds from the exercise of stock options and ESPP purchases.

Funding Requirements

We will need to raise additional capital through public or private equity offerings or debt financings, credit or loan facilities, collaborations, strategic alliances, licensing arrangements or a combination of one or more of these funding sources. Additional funds may not be available to us on acceptable terms or at all. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and disruptions to, and volatility in, the credit and financial markets in the United States and worldwide, including those resulting from the ongoing COVID-19 pandemic, bank failures, actual or perceived changes in interest rates and economic inflation. If we fail to obtain necessary capital when needed on acceptable terms, or at all, it could force us to delay, limit, reduce or terminate our product development programs, commercialization efforts or other operations.

Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of clinical trials and preclinical studies for mavodelpar;
- the scope, prioritization and number of our research and clinical indications we pursue;
- the costs and timing of manufacturing for our product candidates;
- the costs, timing, and outcome of regulatory review of mavodelpar;
- the timing and amount of the milestone or other payments we must make to vTv Therapeutics and any future licensors;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of securing manufacturing arrangements for commercial production;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market any product candidates.

As of December 31, 2022, we had $101.2 million in cash, cash equivalents and short-term investments.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive, and uncertain process that takes many years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidate, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of a product candidate that we do not expect to be commercially available for many years, if at all. Until such time as we can generate significant revenue from sales of our product candidate, if ever, we expect to finance our operations through public or private equity offerings or debt financings, credit or loan facilities, collaborations, strategic alliances, licensing arrangements or a combination of one or more of these funding sources. 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 stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends.

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

Material Cash Requirements

The discussion below summarizes our significant contractual obligations and commitments as of December 31, 2022.

Leases. See Note 6 of Notes to Consolidated Financial Statements included in this Annual Report for information regarding our leases, including the future operating lease minimum payments.

Performance Award. See Note 8 of Notes to Consolidated Financial Statements included in this Annual Report for information regarding a special performance award that our chief executive officer may be entitled to receive, including the maximum payout.

vTv License Agreement. See Note 9 of Notes to Consolidated Financial Statements included in this Annual Report for information regarding the vTv License Agreement, including potential milestone and royalty payments.

In addition to the contractual obligations above, we also expect to have future material cash requirements related to our contract manufacturing, preclinical and clinical programs, and personnel expenses.

Critical Accounting Policies and Estimates

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

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report, we believe the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

All research and development costs are expensed as incurred. Research and development costs consist primarily of costs associated with manufacturing drug substance and drug product, costs associated with preclinical studies, clinical trials managed through CROs and other third parties, license fees, salaries and employee benefits.

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves the following:

- communicating with appropriate internal and external personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost;
- estimating and accruing expenses in our consolidated financial statements as of each balance sheet date based on facts and circumstances known to us at the time; and
- periodically confirming the accuracy of our estimates with service providers and making adjustments, if necessary.

We base our expense accruals related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing costs, we estimate the time period over which services will be performed and the level of effort to be expended in each period.

Nonrefundable advance payments for goods and services, including fees for process development or manufacturing and distribution of clinical supplies that will be used in future research and development activities, are deferred and recognized as expense in the period that the related goods are consumed, or services are performed.

To date, we have not experienced significant changes in our estimates of accrued research and development expenses after a reporting period. However, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials and other research activities.

Stock-Based Compensation

We recognize stock-based compensation expense for grants under our 2014 and 2021 Equity Incentive Plans and ESPP. We account for all stock-based awards granted to employees and directors at their fair value and recognize compensation expense over the award's vesting period. Determining the amount of stock-based compensation to be recorded requires us to develop estimates of fair values of stock options as of the grant date. We calculate the grant date fair values of stock options using the Black-Scholes valuation model, which requires the input of subjective assumptions, including but not limited to expected stock price volatility over the term of the awards and the expected term of stock options. The fair value of restricted stock awards granted to employees is based on the quoted closing market price per share on grant date.

We granted restricted stock awards with performance conditions that are based upon the achievement of pre-specified clinical development or regulatory performance events. As the outcome of each event has inherent risks and uncertainties, and a positive outcome may not be known until the event is achieved, we will begin to recognize the value of the performance-based restricted stock awards when the achievement of each performance condition is deemed probable, a determination that requires significant judgment by management. Compensation cost is recognized under the accelerated method and is adjusted in future periods for subsequent changes in the expected outcome of the performance-related conditions.

We also granted restricted stock awards with market conditions. We measure the fair value of stock-based awards with market-based vesting conditions on the date of grant using a Monte Carlo simulation model. In accordance with accounting guidance for awards with market conditions, the stock-based compensation expense will be recognized over the derived service period regardless of whether the award achieves the market condition and will only be adjusted to the extent the service condition is not met.

Stock-based compensation expenses year-over-year have increased due to more equity grants awarded in 2022 to attract and retain key scientific or management personnel.

Recent Accounting Pronouncements

A description of recent accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 2 to our consolidated financial statements included elsewhere in this Annual Report.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Not required for smaller reporting companies.

Item 8. Financial Statements and Supplementary Data

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Reneo Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Reneo Pharmaceuticals, Inc. (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, changes in convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses and negative cash flows from operations and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Adoption of ASU No. 2016-02

As discussed in Note 1 to the consolidated financial statements, the Company changed its method of accounting for leases in 2022 due to the adoption of ASU No. 2016-02, *Leases (Topic 842)* and related amendments.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.

San Diego, California
March 27, 2023

RENEO PHARMACEUTICALS, INC.

Consolidated Balance Sheets
(In thousands, except par value and share data)

	December 31,	
	2022	**2021**
Assets		
Current assets:		
Cash and cash equivalents	$ 19,927	$ 124,660
Short-term investments	81,246	23,010
Prepaid expenses and other current assets	5,180	6,064
Total current assets	106,353	153,734
Property and equipment, net	453	212
Right-of-use assets	1,292	—
Other non-current assets	84	78
Total assets	$ 108,182	$ 154,024
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,893	$ 2,022
Accrued expenses	4,827	4,180
Operating lease liabilities, current portion	404	—
Total current liabilities	7,124	6,202
Operating lease liabilities, less current portion	1,059	—
Other long-term liabilities	—	167
Performance award	29	444
Total liabilities	8,212	6,813
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.0001 par value; 200,000,000 shares authorized at December 31, 2022 and December 31, 2021; 24,699,553 shares issued and outstanding at December 31, 2022; and 24,457,838 and 24,455,390 shares issued and outstanding at December 31, 2021, respectively	3	3
Additional paid-in capital	236,693	231,902
Accumulated deficit	(136,683)	(84,728)
Accumulated other comprehensive (loss) income	(43)	34
Total stockholders' equity	99,970	147,211
Total liabilities and stockholders' equity	$ 108,182	$ 154,024

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

RENEO PHARMACEUTICALS, INC.

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Year Ended December 31,	
	2022	**2021**
Operating expenses:		
Research and development	$ 37,705	$ 28,169
General and administrative	16,143	11,649
Total operating expenses	53,848	39,818
Loss from operations	(53,848)	(39,818)
Other income	1,893	48
Net loss	(51,955)	(39,770)
Unrealized (loss) gain on short-term investments	(77)	34
Comprehensive loss	$ (52,032)	$ (39,736)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.12)	$ (2.19)
Weighted-average shares used in computing net loss per share, basic and diluted	24,496,425	18,143,487

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

RENEO PHARMACEUTICALS, INC.

Consolidated Statements of Changes in Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share data)

	Convertible Preferred Stock						Additional	Accumulated Other		Total
	Series A		Series B		Common Stock		Paid-In	Comprehensive	Accumulated	Stockholders'
	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Income (Loss)	Deficit	Equity (Deficit)
Balances, December 31, 2020	**24,302,472**	**$ 45,652**	**23,440,514**	**$ 47,068**	**2,053,070**	**$ —**	**$ 2,843**	**$ —**	**$ (44,958)**	**$ (42,115)**
Issuance of series B convertible preferred stock, net of issuance costs of $29	—	—	23,440,514	47,356	—	—	—	—	—	—
Conversion of convertible preferred stock into common stock upon initial public offering	(24,302,472)	(45,652)	(46,881,028)	(94,424)	15,907,629	2	140,076	—	—	140,078
Issuance of common stock in initial public offering, net of offering costs					6,250,000	1	84,532	—	—	84,533
Stock based compensation	—	—	—	—	—	—	3,891	—	—	3,891
Issuance of common stock in connection with equity plans	—	—	—	—	244,691	—	560	—	—	560
Other comprehensive income	—	—	—	—	—	—	—	34	—	34
Net loss	—	—	—	—	—	—	—	—	(39,770)	(39,770)
Balances, December 31, 2021	**—**	**$ —**	**—**	**$ —**	**24,455,390**	**$ 3**	**$ 231,902**	**$ 34**	**$ (84,728)**	**$ 147,211**
Stock based compensation	—	—	—	—	—	—	4,320	—	—	4,320
Issuance of common stock in connection with the at-the-market facility	—	—	—	—	92,085	—	193	—	—	193
Issuance of common stock in connection with equity plans	—	—	—	—	152,078	—	278	—	—	278
Other comprehensive loss	—	—	—	—	—	—	—	(77)	—	(77)
Net loss	—	—	—	—	—	—	—	—	(51,955)	(51,955)
Balances, December 31, 2022	**—**	**$ —**	**—**	**$ —**	**24,699,553**	**$ 3**	**$ 236,693**	**$ (43)**	**$ (136,683)**	**$ 99,970**

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

RENEO PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2022	**2021**
Cash flows from operating activities		
Net loss	$ (51,955)	$ (39,770)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	4,320	3,891
Depreciation and amortization	88	50
Amortization/accretion on short-term investments	(817)	202
Changes in the fair value of performance award	(415)	444
Non-cash lease expense	441	—
Loss on disposal of fixed asset	17	—
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	878	(4,711)
Accounts payable and accrued expenses	518	1,780
Operating lease liabilities	(437)	—
Other current and long-term liabilities	—	131
Net cash used in operating activities	(47,362)	(37,983)
Cash flows from investing activities		
Purchases of property and equipment	(346)	(198)
Purchase of available-for-sale short-term investments	(101,596)	(31,406)
Proceeds from maturities of available-for-sale short-term investments	44,100	8,228
Net cash used in investing activities	(57,842)	(23,376)
Cash flows from financing activities		
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	—	47,238
Proceeds from initial public offering, net of offering costs	—	84,612
Proceeds from at-the-market facility, net of offering costs	193	—
Proceeds from issuance of common stock in connection with equity plans	278	556
Net cash provided by financing activities	471	132,406
Net (decrease) increase in cash and cash equivalents	(104,733)	71,047
Cash and cash equivalents, beginning of year	124,660	53,613
Cash and cash equivalents, end of year	$ 19,927	$ 124,660
Noncash operating activities:		
Right-of-use assets obtained in exchange for lease obligations	$ 1,733	$ —
Noncash investing and financing activities:		
Vesting of unvested exercised options	$ —	$ 4

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

RENEO PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements

1. Organization and Business

Organization

Reneo Pharmaceuticals, Inc. (Reneo or the Company) commenced operations on September 22, 2014 as a clinical-stage pharmaceutical company focused on the development of therapies for patients with rare genetic mitochondrial diseases. In December 2017, the Company in-licensed mavodelpar (REN001), a novel oral peroxisome proliferator-activated receptor delta (PPARδ) agonist.

Public Offerings

On April 13, 2021, the Company completed an initial public offering (IPO) of its common stock. In connection with its IPO, the Company sold and issued 6,250,000 shares of its common stock at a price to the public of $15.00 per share. The gross proceeds from the IPO were approximately $93.8 million before deducting underwriting discounts and commissions of $6.6 million and offering expenses of approximately $2.6 million payable by the Company.

At the closing of the IPO, 71,183,500 shares of outstanding convertible preferred stock were automatically converted into 15,907,629 shares of common stock. Following the IPO, there were no shares of preferred stock outstanding.

In May 2022, the Company entered into an at-the-market equity offering sales agreement with SVB Securities LLC (ATM facility) under which it may offer and sell, from time to time at its sole discretion, up to $20.0 million in shares of its common stock. For the year ended December 31, 2022, the Company has sold and issued approximately 100,000 shares of its common stock under the ATM facility.

Liquidity

The Company follows Accounting Standards Codification (ASC) Topic 205-40, *Presentation of Financial Statements—Going Concern*, which requires that management perform a two-step analysis over its ability to continue as a going concern. Management must first evaluate whether there are conditions and events that raise substantial doubt about the Company's ability to continue as a going concern and to meet its obligations as they become due within one year after the date that the consolidated financial statements are issued (step 1). If management concludes that substantial doubt is raised, management is also required to consider whether its plans alleviate that doubt (step 2).

From its inception in 2014, the Company has incurred significant losses and negative cash flows from operations. As of December 31, 2022, the Company had cash, cash equivalents and short-term investments of $101.2 million and an accumulated deficit of $136.7 million. The Company had a net loss of $52.0 million and used cash of $47.4 million for operating activities for the year ended December 31, 2022. Since inception through December 31, 2022, the Company has funded its operations primarily with the net proceeds from the issuance of convertible preferred stock and common stock. Management has prepared cash flow forecasts which indicate that based on the Company's expected operating losses and negative cash flows, there is substantial doubt about the Company's ability to continue as a going concern for twelve months after the date the consolidated financial statements for the year ended December 31, 2022 are issued. The accompanying consolidated financial statements have been prepared assuming the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business, and do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or amounts and classification of liabilities that may result from the outcome of this uncertainty.

Due to the Company's continuing research and development activities, the Company expects to continue to incur net losses into the foreseeable future and may never become profitable. The Company plans to fund its losses from operations and capital funding needs through public or private equity offerings or debt financings, credit or loan facilities, collaborations, strategic alliances, licensing arrangements or a combination of one or more of these funding sources.

There can be no assurance that the Company will be successful in obtaining additional funding, that the Company's projections of its future working capital needs will prove accurate, or that any additional funding would be sufficient to continue operations in future years. If the Company is not able to secure adequate additional funding, the Company may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, and/or suspend or curtail planned programs. Any of these actions could negatively impact the Company's business, results of operations, and future prospects. The Company's ability to raise additional capital may be adversely impacted by potential worsening global economic conditions, disruptions to, and volatility in, financial markets in the United States and worldwide, including those resulting from the ongoing COVID-19 pandemic, bank failures, actual or perceived changes in interest rates and economic inflation. The Company may not be able to secure additional financing in a timely manner or on favorable terms, if at all. In addition, successful transition to attaining profitable operations is dependent upon achieving a level of revenues adequate to support the Company's cost structure.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The Company's consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States (GAAP) and reflect the operation of the Company and its wholly owned subsidiary. All intercompany balances and transactions among the consolidated entities have been eliminated in consolidation.

Use of Estimates

The preparation of the Company's consolidated financial statements requires management to make estimates and assumptions that impact the reported amounts of assets, liabilities and expenses and the disclosure in the Company's consolidated financial statements and accompanying notes. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances. By their nature, estimates are subject to an inherent degree of uncertainty and, as such, actual results may differ from management's estimates.

Risks and Uncertainties

Any product candidates developed by the Company will require approvals from the U.S. Food and Drug Administration or foreign regulatory agencies prior to commercial sales. There can be no assurance that the Company's current product candidates will meet desired efficacy and safety requirements to obtain the necessary approvals. If approval is denied or delayed, it may have a material adverse impact on the Company's business and its financial statements.

The Company is subject to a number of risks similar to other clinical-stage pharmaceutical companies including, but not limited to, dependency on the clinical and commercial success of the Company's product candidate, mavodelpar, ability to obtain regulatory approval of mavodelpar, the need for substantial additional financing to achieve its goals, uncertainty of broad adoption of its approved products, if any, by physicians, consumers and third-party payors, significant competition and untested manufacturing capabilities, and dependence on key individuals and sole source suppliers.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less, when purchased, to be cash equivalents. As of December 31, 2022 and 2021, the Company had cash balances deposited at major financial institutions. Cash balances are subject to minimal credit risk as the balances are with high credit quality financial institutions. Cash and cash equivalents include cash in readily available checking, money market accounts and repurchase agreements.

Short-term Investments

The Company accounts for short-term investments in accordance with ASC Topic 320, *Investments – Debt and Equity Securities*. Management determines the appropriate classification of its investments at the time of purchase and reevaluates such determinations at each reporting period.

At December 31, 2022, the Company's investments comprised of U.S. treasury securities and commercial paper classified as available-for-sale securities. Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported in accumulated other comprehensive income (loss) in stockholders' equity (deficit). Realized gains and losses on sales of investments are included in interest income and are derived using the specific identification method for determining the cost of securities.

The Company recognizes an impairment charge when a decline in the fair value of its investments in debt securities below the amortized cost basis of such securities is judged to be other-than temporary impaired. Factors considered in making such a determination include the duration and severity of the impairment, the reason for the decline in value, the potential recovery period and if the entity has the intent to sell the security, or if it is more likely than not that it will be required to sell the security before recovery of its amortized cost basis. The Company did not recognize any other-than-temporary impairment charges on its short-term investments during the years ended December 31, 2022 and 2021.

Money market account balances are included as cash and cash equivalents on the consolidated balance sheets, which are also disclosed in Note 3, Fair Value Measurements.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to significant concentration of credit risk, consist primarily of cash, cash equivalents and short-term investments. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held.

Property and Equipment, Net

Property and equipment are stated at cost, less accumulated depreciation and amortization. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets. Maintenance and repairs are expensed as incurred.

The following estimated useful lives were used to depreciate or amortize the Company's assets:

	Estimated Useful Life
Furniture and fixtures	5 years
Computers and software	3 years
Leasehold improvements	Shorter of useful life or remaining lease term

Impairment of Long-Lived Assets

Long-lived assets consist primarily of property and equipment. Long-lived assets are evaluated for impairment when events and circumstances indicate the assets might be impaired by first comparing the estimated future undiscounted cash flows of the asset or asset group to the carrying value. If the carrying value exceeds the estimated future undiscounted cash flows, an impairment loss is recognized based on the amount that the carrying value exceeds the fair value of the asset or asset group. The Company did not recognize impairment losses during the years ended December 31, 2022 and 2021.

Leases

The Company determines if an arrangement includes a lease at inception. Leases with an initial term of 12 months or less are not recorded on the balance sheet. The Company's lease terms may include options to extend or terminate a lease when it is reasonably certain that it will exercise that option. The Company combines lease and non-lease components when determining lease payments.

Right-of-use (ROU) assets and lease liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term, unless there is a transfer of title or purchase option the Company is reasonably certain to exercise. For leases where an implicit rate is not readily determinable, the Company uses its incremental borrowing rate based on information available at the lease commencement date to determine the present value of future lease payments. Lease expense for operating leases is recognized on a straight-line basis over the expected lease term.

Research and Development Costs and Accruals

All research and development costs are expensed as incurred. Research and development costs consist primarily of costs associated with manufacturing drug substance and drug product, costs associated with preclinical studies, clinical trials managed through contract research organizations (CROs) and other third parties, license fees, salaries and employee benefits.

The Company bases its expense accruals related to clinical trials on its estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on its behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under certain contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing costs, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. Nonrefundable advance payments for goods and services, including fees for process development or manufacturing and distribution of clinical supplies that will be used in future research and development activities, are deferred and recognized as expense in the period that the related goods are consumed, or services are performed.

To date, the Company has not experienced significant changes in its estimates of accrued research and development expenses after a reporting period.

License Fees

The Company expenses amounts paid to acquire licenses associated with products under development when the ultimate recoverability of the amounts paid is uncertain and the technology has no alternative future use when acquired. Acquisitions of technology licenses are charged to expense or capitalized based upon management’s assessment regarding the ultimate recoverability of the amounts paid and the potential for alternative future use. The Company has determined that technological feasibility for its product candidate would be reached when the requisite regulatory approvals are obtained to make the product available for sale. Contingent milestone payments are recognized when the related contingency is resolved, and the amounts are paid or become payable. These amounts are expensed to research and development if there is no alternative future use associated with the license or capitalized as an intangible asset if alternative future use of the license exists.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

The Company recognizes net deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their net recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company records uncertain tax positions on the basis of a two-step process whereby (1) management determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (2) for those tax positions that meet the more-likely-than-not recognition threshold, management recognizes the largest amount of tax benefit that is more than 50% likely to be realized upon ultimate settlement with the related tax authority. The Company's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, there have been no interest or penalties charged in relation to unrecognized tax benefits.

The Company is subject to taxation in the United States and the United Kingdom (UK). As of December 31, 2022, the Company's tax years since inception are subject to examination by taxing authorities in the United States, and the UK tax returns from 2018 forward are subject to examination.

Stock-Based Compensation

The Company recognizes stock-based compensation expense for grants under its 2014 and 2021 Equity Incentive Plans and employee stock purchase plan (ESPP). The Company accounts for all stock-based awards granted to employees and directors at their fair value and recognizes compensation expense over the award's vesting period. Determining the amount of stock-based compensation to be recorded requires the Company to develop estimates of fair values of stock options as of the grant date. The Company calculates the grant date fair values of stock options using the Black-Scholes valuation model, which requires the input of subjective assumptions, including but not limited to expected stock price volatility over the term of the awards and the expected term of stock options. The fair value of restricted stock awards granted to employees is based on the quoted closing market price per share on grant date.

The Company granted restricted stock awards with performance conditions that are based upon the achievement of pre-specified clinical development or regulatory performance events. As the outcome of each event has inherent risks and uncertainties, and a positive outcome may not be known until the event is achieved, the Company will begin to recognize the value of the performance-based restricted stock awards when the achievement of each performance condition is deemed probable, a determination that requires significant judgment by management. Compensation cost is recognized under the accelerated method and is adjusted in future periods for subsequent changes in the expected outcome of the performance-related conditions.

The Company granted restricted stock awards with market conditions. The Company measures the fair value of stock-based awards with market-based vesting conditions on the date of grant using a Monte Carlo simulation model. In accordance with accounting guidance for awards with market conditions, the stock-based compensation

expense will be recognized over the derived service period regardless of whether the award achieves the market condition and will only be adjusted to the extent the service condition is not met.

Foreign Currency Transactions

The functional currency of Reneo Pharma Ltd, the Company's wholly owned subsidiary in the UK, is the U.S. dollar. All foreign exchange transactional and remeasurement gains and losses are recognized in the consolidated statements of operations and comprehensive loss. For the years ended December 31, 2022 and 2021, total foreign currency gains and losses were immaterial.

Comprehensive Income or Loss

Comprehensive income or loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources.

Net Loss Per Share

The Company computes basic loss per share by dividing the net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share assumes the conversion, exercise or issuance of all potential common stock equivalents, unless the effect of inclusion would be anti-dilutive. For periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company has reported net losses for the years ended December 31, 2022 and 2021. As a result, the Company has, excluded all outstanding common stock equivalents including the Company's stock options, performance-based and market-based RSUs, and employee stock purchase plan, from the diluted net loss per share calculation for the years ended December 31, 2022 and 2021 because such shares are anti-dilutive.

The following potentially issuable common shares were not included in the computation of diluted net loss per share because they would have an anti-dilutive effect:

	As of December 31,	
	2022	**2021**
Common stock options outstanding	5,877,745	4,215,643
Unvested restricted stock units	329,500	299,500
Total	6,207,245	4,515,143

New Accounting Pronouncements

Recently Adopted Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2016-02, *Leases* (ASC 842) in order to increase transparency and comparability among organizations by recognizing lease assets and lease liabilities on the balance sheets for those leases classified as operating leases under previous GAAP. ASU 2016-02 requires a lessee to recognize a liability for lease payments (lease liability) and a ROU asset (representing its right to use the underlying asset for the lease term) on the balance sheet. In July 2018, the FASB issued ASU 2018-11, *Leases (ASC 842): Targeted Improvements*, which provides entities an optional transition method to apply the new guidance as of the adoption date, rather than as of the earliest period presented. In transition, entities may also elect a package of practical expedients that must be applied in its entirety to all leases commencing before the effective date, unless the lease was modified, to not reassess (a) whether a contract is or contains a lease, (b) lease classification or (c) determination of initial direct costs, which effectively allows entities to carryforward accounting conclusions under previous GAAP. The Company adopted

this standard on January 1, 2022, using the optional transitional method and elected the package of practical expedients in transition for leases that commenced prior to January 1, 2022.

As a result of implementing ASC 842, the Company recognized operating lease ROU assets of $1.5 million and lease liabilities of $1.7 million on January 1, 2022, with no impact on its beginning retained earnings, consolidated statements of operations and comprehensive loss, or cash flows. See Note 6, *Leases*, for further details.

In December 2019, the FASB issued ASU 2019-12, *Simplifying the Accounting for Income Taxes*. The standard simplifies the accounting for income taxes, eliminates certain exceptions within ASC 740, *Income Taxes*, and clarifies certain aspects of the current guidance to promote consistency among reporting entities. The new guidance was effective for the Company as of January 1, 2022. Most amendments within the standard are required to be applied on a prospective basis, while certain amendments must be applied on a retrospective or modified retrospective basis. The Company adopted this standard on January 1, 2022. Adoption of this standard had no material impact on the Company's consolidated financial position, results of operations or cash flows.

Recent Accounting Pronouncements Not Yet Adopted

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments - Credit Losses (Topic 326), Measurement of Credit Losses on Financial Instruments*. The standard amends the impairment model by requiring entities to use a forward-looking approach based on expected losses to estimate credit losses for most financial assets and certain other instruments that are not measured at fair value through net income. For available-for-sale debt securities, entities will be required to recognize an allowance for credit losses rather than a reduction in the carrying value of the asset. Entities will no longer be permitted to consider the length of time that fair value has been less than amortized cost when evaluating when credit losses should be recognized. This new guidance is effective for the Company as of January 1, 2023. The Company is currently evaluating the impact of this ASU and does not expect that adoption of this standard will have a material impact on its consolidated financial statements and related disclosures.

Other accounting standard updates effective for interim and annual periods beginning after December 31, 2022 are not expected to have a material impact on the Company's financial position, results of operations or cash flows.

3. Fair Value Measurements

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

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

- Level 1 – Observable inputs such as quoted prices in active markets for identical assets or liabilities.
- Level 2 – Inputs, other than quoted prices in active markets, which are observable for the asset or liability, either directly or indirectly.
- Level 3 – Unobservable inputs in which there is little or no market data, which requires the Company to develop its own assumptions.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. The Company's financial assets are subject to fair value measurements on a recurring basis.

The Company categorizes its money market funds as Level 1, using the quoted prices in active markets. Commercial paper and U.S. treasury securities are categorized as Level 2, using significant other observable inputs. The fair value of the Company's investments in certain money market funds is their face value and such instruments are classified as Level 1 and are included in cash and cash equivalents on the consolidated balance sheets.

Investments are reviewed periodically to identify possible other-than-temporary impairments. As the Company has the ability and intends to hold these investments with unrealized losses for a reasonable period of time sufficient for the recovery of fair value, which may be maturity, the Company does not consider these investments to be other-than-temporarily impaired for any of the periods presented.

In connection with the Company's chief executive officer's (CEO) employment agreement, he is entitled to receive a special performance bonus in the amount of $7.5 million (Performance Award), payable in cash, common stock or a combination of cash and common stock, at the election of the Company, based on achievement of certain conditions as described in more detail in Note 8. The Company estimated the fair value of the Performance Award using a Monte Carlo simulation, which incorporates the stock price at the date of the valuation and utilizes Level 3 inputs such as volatility, probabilities of success, and other inputs that are not observable in active markets. The Performance Award is required to be measured at fair value on a recurring basis each reporting period, with changes in the fair value recognized in general and administrative expense in the consolidated statements of operations and comprehensive loss over the derived service period of the award.

No assets or liabilities were transferred into or out of their classifications during the years ended December 31, 2022 and 2021.

The recurring fair value measurement of the Company's assets and liabilities measured at fair value at December 31, 2022 consisted of the following (in thousands):

	Quoted Prices in Active Markets For Identical Items (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets				
Cash and cash equivalents:				
Money market investments	$ 9,365	$ —	$ —	$ 9,365
Commercial paper	—	4,978	—	4,978
Short-term Investments:				
U.S. treasury securities	—	76,253	—	76,253
Commercial paper	—	4,993	—	4,993
Total	$ 9,365	$ 86,224	$ —	$ 95,589
Liabilities				
Performance award	$ —	$ —	$ 29	$ 29
Total	$ —	$ —	$ 29	$ 29

The recurring fair value measurement of the Company's assets and liabilities measured at fair value at December 31, 2021 consisted of the following (in thousands):

	Quoted Prices in Active Markets For Identical Items (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets				
Cash and cash equivalents:				
Money market investments	$ 118,535	$ —	$ —	$ 118,535
Short-term Investments:				
Commercial paper	—	23,010	—	23,010
Total	$ 118,535	$ 23,010	$ —	$ 141,545
Liabilities				
Performance award	$ —	$ —	$ 444	$ 444
Total	$ —	$ —	$ 444	$ 444

The following table sets forth a summary of changes in the fair value of the Company's performance award liability (in thousands):

	Performance Award
Balance as of January 1, 2022	$ 444
Change in fair value	(415)
Balance as of December 31, 2022	$ 29

The following tables summarize the gross unrealized gains and losses of the Company's available-for-sale securities as of December 31, 2022 and 2021 (in thousands):

	As of December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Market Value
Available-for-sale securities:				
U.S. treasury securities	$ 76,297	$ 2	$ (46)	$ 76,253
Commercial paper	4,993	—	—	4,993
Total	$ 81,290	$ 2	$ (46)	$ 81,246

	As of December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Market Value
Available-for-sale securities:				
Commercial paper	$ 23,013	$ —	$ (3)	$ 23,010
Total	$ 23,013	$ —	$ (3)	$ 23,010

4. Property and Equipment, Net

Property and equipment, net, consisted of the following (in thousands):

	As of December 31,	
	2022	2021
Computer, software and office equipment	$ 300	$ 315
Leasehold improvements	255	30
Total property and equipment, gross	555	345
Less: accumulated depreciation and amortization	(102)	(133)
Total property and equipment, net	$ 453	$ 212

5. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	As of December 31,	
	2022	2021
Accrued clinical and regulatory	$ 1,872	$ 1,236
Accrued contract manufacturing cost	1,583	1,482
Accrued compensation	807	1,027
Accrued research and development-other	565	435
Total accrued expenses	$ 4,827	$ 4,180

6. Leases

The Company's headquarters are located in Irvine, California, where it leases office space. The Company leases additional office space located in San Diego, California, and in Sandwich, United Kingdom. The lease terms for the Irvine, San Diego, and Sandwich offices extend through November 30, 2026, July 31, 2023, and October 23, 2027, respectively.

On October 20, 2022, the Company entered into a lease agreement for of office space located in Sandwich, United Kingdom, with a term of 5 years and a termination option after three years, which commenced in December 2022. In connection with the lease, the Company recorded $0.2 million in ROU and lease liabilities at commencement date.

At December 31, 2022, the weighted average incremental borrowing rate was 5% and the weighted average remaining lease term was 3.9 years for the operating leases held by the Company. For the year ended December 31, 2022, cash paid for amounts included for the measurement of lease liabilities was $0.5 million. For the year ended December 31, 2022, the Company recorded operating lease expense of $0.5 million.

Maturities of lease liabilities by fiscal year for the Company's operating leases are as follows:

	As of December 31, 2022
2023	$ 473
2024	381
2025	381
2026	343
2027	34
Total lease payments	1,612
Less: Imputed interest	(149)
Present value of lease liabilities	$ 1,463

7. Convertible Preferred Stock

Preferred Stock

The Company has authorized up to 10,000,000 shares of preferred stock, $0.0001 par value per share, for issuance. The Company's preferred stock will have such rights, preferences, privileges, and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, which will be determined by its board of directors upon its issuance. As of December 31, 2022, there were no shares of preferred stock outstanding.

In connection with the IPO in April 2021, all outstanding shares of Series A convertible preferred and Series B convertible preferred stock were converted into 5,430,957 and 10,476,672 shares of common stock, respectively.

8. Stock-Based Compensation

In March 2021, the Company's board of directors adopted the Company's 2021 Equity Incentive Plan (2021 Plan), which is the successor to the Company's 2014 Equity Incentive Plan (2014 Plan). As of the effective date of the 2021 Plan, awards granted under the 2014 Plan that are forfeited or otherwise become available under the 2014 Plan will be included and available for issuance under the 2021 Plan. Under the 2021 Plan, the Company may grant stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other awards to individuals who are employees, officers, directors or consultants of the Company, and employees and consultants of the Company's affiliates.

Under the 2014 Plan, certain employees were granted the ability to early exercise their options. The shares of common stock issued pursuant to the early exercise of unvested stock options are restricted and continue to vest over the requisite service period after issuance. The Company has the option to repurchase any unvested shares at the original purchase price upon any voluntary or involuntary termination. The shares purchased by the employees pursuant to the early exercise of stock options are not deemed, for accounting purposes, to be outstanding until those shares vest. As of December 31, 2022, there were no shares subject to stock options that have been early exercised.

Shares Reserved for Future Issuance

As of December 31, 2022, the Company had reserved shares of its common stock for future issuance as follows:

	Shares Reserved
Common stock options outstanding	5,877,745
Unvested restricted stock units	329,500
Available for future grants under the 2021 Equity Incentive Plan	546,521
Available for future grants under the 2021 Employee Stock Purchase Plan	383,917
Total shares of common stock reserved	7,137,683

Stock Options

A summary of the Company's stock option activity and related information for the year ended December 31, 2022 is as follows:

	Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	4,215,643	$ 5.49	8.5	$ 13,530
Granted	2,067,976	2.51		
Exercised	(54,535)	2.01		
Forfeited/Expired	(351,339)	5.60		
Outstanding at December 31, 2022	5,877,745	$ 4.47	8.2	$ 907
Vested at December 31, 2022	2,159,499	$ 5.20	6.7	$ 101
Exercisable at December 31, 2022	2,947,283	$ 5.12	7.0	$ 101

Options exercisable at December 31, 2022 include vested options and options eligible for early exercise. All outstanding options as of December 31, 2022 are expected to vest.

Unrecognized stock-based compensation expense at December 31, 2022 was $10.0 million, which is expected to be recognized over a weighted-average vesting term of 2.9 years.

The weighted-average assumptions used in the Black-Scholes option pricing model to determine the fair value of the employee stock option grants were as follows:

	Year Ended December 31,	
	2022	2021
Risk-free interest rate	3.4%	0.9%
Expected volatility	84.8%	78.3%
Expected term (in years)	6.0	6.0
Expected dividend yield	—%	—%

Risk-free interest rate. The Company bases the risk-free interest rate assumption on the U.S. Treasury's rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the award being valued.

Expected volatility. Since the Company does not have sufficient trading history for its common stock the expected volatility assumption is based on volatilities of a peer group of similar companies whose share prices are publicly available. The peer group was developed based on companies in the biotechnology industry.

Expected term. The expected term represents the period of time that options are expected to be outstanding. Because the Company does not have historical exercise behavior, it determines the expected life assumption using the simplified method, which is an average of the contractual term of the option and its vesting period.

Expected dividend yield. The Company bases the expected dividend yield assumption on the fact that it has never paid cash dividends and has no present intention to pay cash dividends.

Fair value of common stock. For periods prior to the Company's IPO in April 2021, since there had been no public market for the Company's common stock, the Company's board of directors, with input from management, determined the fair value of the Company's common stock on each grant date by considering a number of

objective and subjective factors, including the most recent independent third-party valuations of the Company's common stock, sales of the Company's convertible preferred stock to unrelated third-parties, operating and financial performance of the Company, the lack of liquidity of capital stock and general and industry-specific economic outlook, and the Company's board of directors' assessment of additional objective and subjective factors that it believed were relevant.

Restricted Stock Units (RSUs)

RSUs consist of performance-based units (PSUs) and market-based units (MSUs). The following table summarizes RSU activities as of December 31, 2022:

	Number of RSUs	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2021	299,500	$ 6.32
Granted	60,000	2.95
Cancelled	(30,000)	6.69
Unvested at December 31, 2022	329,500	$ 5.67

Performance-Based Units

The PSUs vest based on the Company achieving certain regulatory milestones and are subject to the employee's continued employment with the Company through the achievement date. The fair value of the awards was based on the value of the Company's common stock at the grant date of the award and expense recognition is based on the probability of achieving the performance conditions. Stock-based compensation expense is adjusted in future periods for subsequent changes in the expected outcome of the performance conditions. The Company has 209,500 unvested shares underlying PSUs as of December 31, 2022. The Company concluded that achievement of the performance conditions was not probable as of December 31, 2022 and 2021, and therefore no stock-based compensation expense was recognized for the years ended December 31, 2022 and 2021 in connection with the PSUs. As of December 31, 2022, unrecognized stock-based compensation expense related to the PSUs that were deemed not probable was $1.4 million.

Market-Based Units

The MSUs vest based on the Company's closing stock price trading above $20 per share for 30 consecutive trading days subject to the employee's continued employment with the Company through the date of achievement. The share price of the Company's common stock on the date of issuance of the MSUs was $2.78 per share. The fair value was based on Monte Carlo simulation model on the grant date. Stock-based compensation expense is recognized over the derived service period of approximately 3 years. The Company has 120,000 unvested shares underlying MSUs as of December 31, 2022. Stock-based compensation expense related to the MSUs during the years ended December 31, 2022 and 2021 was immaterial. As of December 31, 2022, there was $0.3 million of unrecognized stock-based compensation expense related to this MSU.

Performance Award

In connection with the CEO's employment agreement, he is entitled to receive a Performance Award in the amount of $7.5 million, payable in cash, common stock or a combination of cash and common stock, at the election of the Company, in the event that (i) the Company's market value exceeds $750 million utilizing the volume-weighted average of the closing sale price of its common stock on the Nasdaq Stock Market or other principal exchange for each of the 30 trading days immediately prior to the measurement date, or (ii) the fair market value of the net proceeds available for distribution to the Company's stockholders in connection with a

change in control as defined in the Company's severance benefit plan, as determined in good faith by its board of directors, exceeds $750 million. The Company has determined that the Performance Award is subject to ASC 718, *Compensation – Stock Compensation* and includes both market and performance conditions. Since the IPO, neither of the events have yet been satisfied. The Company estimated the fair value of the Performance Award at each reporting period using the Monte Carlo simulation (Note 3), which is recognized as stock-based compensation expense over the derived service period.

For the year ended December 31, 2022, the Company reversed approximately $0.4 million in stock-based compensation expenses as a direct result of decreased value of the Performance Award caused by a decline in the Company's common stock price.

2021 Employee Stock Purchase Plan

In March 2021, the Company's board of directors adopted the ESPP, which became effective immediately prior to the execution of the underwriting agreement in connection with the Company's IPO. As of December 31, 2022, 103,719 shares have been issued under the ESPP.

In September 2021, the Company's board of directors adopted the Company's 2021 UK Sharesave Sub-plan (SAYE). An allocation of 25,875 shares of common stock from the ESPP reserve pool was approved and reserved for issuance under the SAYE. No shares have been issued under the SAYE through December 31, 2022.

The stock-based compensation expense related to the ESPP and the SAYE for the year ended December 31, 2022, was $0.2 million and was immaterial for the year ended December 31, 2021.

Stock-Based Compensation Expense

The following table summarizes stock-based compensation expense, including expense associated with award modifications for unvested options, reflected in the consolidated statements of operations and comprehensive loss (in thousands):

	Year Ended December 31,	
	2022	2021
Research and development	$ 1,593	$ 1,036
General and administrative	2,727	2,855
Total	$ 4,320	$ 3,891

In December 2022, the Company's Compensation Committee approved an extension of the post-termination exercise period applicable to each outstanding stock option, approximately 613,000 shares, held by the Company's non-employee directors, such that upon the termination of service, each option will remain exercisable through the lessor of i) three years or ii) end of the term of such option from the date of grant. The Company recognized $0.2 million in stock-based compensation expense related to this modification in December 2022.

9. License Agreement

In December 2017, the Company entered into a license agreement with vTv Therapeutics LLC (vTv Therapeutics) (the vTv License Agreement), under which the Company obtained an exclusive, worldwide, sublicensable license under certain vTv Therapeutics intellectual property to develop, manufacture and commercialize peroxisome proliferator-activated receptor delta (PPARδ) agonists and products containing such PPARδ agonists, including mavodelpar, for any therapeutic, prophylactic or diagnostic application in humans. To date, the Company has paid a $3.0 million upfront payment and $2.0 million in milestone payments and issued an aggregate of 576,443 shares of its common stock to vTv Therapeutics.

Upon the achievement of certain pre-specified development and regulatory milestones, the Company is also required to pay vTv Therapeutics milestone payments totaling up to $64.5 million. The Company is also required to pay vTv Therapeutics up to $30.0 million in total sales-based milestones upon achievement of certain sales thresholds of the licensed product. In addition, the Company is obligated to make royalty payments to vTv Therapeutics at mid-single digit to low teen percentage royalty rates, based on tiers of annual net sales of licensed products, subject to certain customary reductions. A milestone payment of $2.0 million was achieved and recorded for the year ended December 31, 2021. There were no milestone payments achieved or recorded for the year ended December 31, 2022.

10. Income Taxes

The Company's net loss was generated in the following jurisdictions (in thousands):

	Year Ended December 31,	
	2022	2021
Domestic	$ (51,994)	$ (39,718)
Foreign	39	(52)
Net loss	$ (51,955)	$ (39,770)

The components of net deferred taxes consisted of the following (in thousands):

	As of December 31,	
	2022	2021
Deferred tax assets:		
NOL carryforwards	$ 16,381	$ 13,446
Capitalized research and development expenses	7,465	—
Credit carryforwards	4,061	2,155
Intangible assets	3,202	3,469
Compensation accruals	989	653
Operating lease liabilities	316	—
Depreciation	78	104
Other accruals and reserves	—	35
Other	2	2
Gross deferred tax assets	32,494	19,864
Less valuation allowance	(32,214)	(19,864)
Total deferred tax assets	280	—
Deferred tax liabilities:		
ROU assets	(280)	—
Net deferred tax assets (liabilities)	$ —	$ —

For the years ended December 31, 2022 and 2021, the Company recorded no provision for income taxes. A reconciliation of the effective tax rate to the amount computed by applying the statutory federal income tax rate to the loss from operations is summarized for the years ended December 31, 2022 and 2021, as follows:

	As of December 31,	
	2022	2021
U.S. federal statutory income tax rate	21.0%	21.0%
Tax credits, net	3.4%	3.5%
Return-to-provision adjustment	0.5%	(0.1)%
Other	(0.8)%	(1.0)%
GILTI inclusion	(0.3)%	(0.5)%
Valuation allowance	(23.8)%	(22.9)%
U.S. federal effective tax rate	0.0%	0.0%

The Company had federal net operating loss (NOL) carryforwards available of approximately $74.7 million as of December 31, 2022, before consideration of limitations under Section 382 of the Internal Revenue Code of 1986, as amended (Section 382), as further described below. The federal NOLs generated after 2017 of $73.1 million will carry forward indefinitely. NOLs generated prior to 2018 of $1.6 million will begin to expire in 2034. Additionally, the Company had state NOL carryforwards available of $1.6 million as of December 31, 2022. The state NOLs may be used to offset future taxable income and will begin to expire in 2034. The Company has generated UK NOLs of $2.2 million which carryforward indefinitely.

At December 31, 2022, the Company had federal and state tax credit carry forwards of approximately $10.6 million and $0.5 million, respectively. The Company has not performed a formal research and development credit study with respect to these credits. The federal credits will begin to expire in 2034, if unused, and the state credits carry forward indefinitely.

The future utilization of the Company's NOL and tax credit carryforwards to offset future taxable income may be subject to a substantial annual limitation as a result of changes in ownership by stockholders that hold 5% or more of the Company's common stock. An assessment of such ownership changes under Section 382 was not completed through December 31, 2022. To the extent that an assessment is completed in the future, the Company's ability to utilize tax attributes could be restricted on a year-by-year basis and certain attributes could expire before they are utilized. The Company will examine the impact of any potential ownership changes in the future.

The Company has elected to record the inclusion related to the Global Intangible Low-Taxed Income (GILTI) in the period incurred. The estimated GILTI inclusion generated by the Company's wholly-owned controlled foreign corporation in the United Kingdom for the year ended December 31, 2022 was $0.8 million. This amount is included in the income tax provision, however, has zero impact to the provision due to the full valuation allowance.

The Company has established a full valuation allowance for its deferred tax assets due to uncertainties that preclude it from determining that it is more likely than not that the Company will be able to generate sufficient taxable income to realize such assets. Management assesses the available positive and negative evidence to estimate if sufficient future taxable income will be generated to utilize the existing deferred tax assets. A significant piece of objective negative evidence evaluated was the cumulative loss incurred over the three-year period ended December 31, 2022. Such objective evidence limits the ability to consider other subjective evidence such as the Company's projections for future growth. Based on this evaluation, as of December 31, 2022, a full valuation allowance of $32.2 million has been recorded against the Company net deferred tax assets, as the Company has determined that none of the Company's balance of deferred tax assets is more likely than not to be realized. The amount of the deferred tax assets considered realizable, however, could be adjusted in the future if objective negative evidence in the form of cumulative losses is no longer present and additional weight is given to subjective evidence, such as estimates of future taxable income during carryforward periods and the Company's projections for growth.

The following table summarizes the changes to unrecognized tax benefits (in thousands):

	Year Ended December 31,	
	2022	2021
Beginning balance of unrecognized tax benefits	$ 2,999	$ 258
Additions based on tax positions related to the current year	4,095	2,741
Ending balance of unrecognized tax benefits	$ 7,094	$ 2,999

The amount of the unrecognized tax benefits that would impact the effective tax rate, absent the valuation allowance, would be $7.1 million. Due to the full valuation allowance, the impact, however, is zero. At December 31, 2022 and 2021, the Company has not accrued any interest or penalties related to uncertain tax positions. The Company does not anticipate that there will be a significant change in the amount of unrecognized

tax benefits over the next 12 months. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

The Company is subject to taxation in the United States and the UK. The Company's federal and state returns since inception are subject to examination due to the carryover of net operating losses. The Company has not been, nor is it currently, under examination by any tax authorities. The UK tax returns from 2018 forward are subject to examination by the UK tax authorities.

11. Commitments and Contingencies

Legal Proceedings

The Company is currently not a party to any legal proceedings, nor is the Company aware of any threatened or pending litigation. However, from time-to-time in the future, the Company could be involved in disputes, including litigation, relating to claims arising out of operations in the normal course of business, which may have a material adverse effect on the Company's consolidated results of operations or financial position.

401(k) Plan

The Company maintains a defined contribution 401(k) plan available to eligible employees. Employee contributions are voluntary and are determined on an individual basis, limited to the maximum amount allowable under federal tax regulations. Matching contributions to the 401(k) plan are made for certain eligible employees to meet non-discrimination provisions of the plan. During the years ended December 31, 2022 and 2021, the expense recorded by the Company was immaterial.

12. Subsequent Events

Subsequent to December 31, 2022 through the date of this report, the Company has sold and issued approximately 400,000 shares of common stock under the ATM facility.

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

Our management, with the participation and supervision of our principal executive officer and our principal financial officer, have evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act), as of the end of the period covered by this Annual Report. Based on that evaluation, our principal executive officer and our principal financial officer have concluded that as of December 31, 2022, our disclosure controls and procedures were effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and our principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's 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 Rule 13a-15(f) and 15(d)-15(f) under the Exchange Act. Our management conducted an evaluation of the effectiveness of our internal control over financial reporting based on the 2013 framework in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the

Treadway Commission (COSO framework). Management believes that the COSO framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of our internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of our internal control over financial reporting are not omitted, and is relevant to an evaluation of internal control over financial reporting.

Based on its evaluation under the COSO framework, our management concluded that the Company maintained effective internal control over financial reporting at a reasonable assurance level as of December 31, 2022, based on those criteria.

Attestation Report of the Independent Registered Public Accounting Firm

This Annual Report does not include an attestation report of our independent registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2022 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item and not set forth below is incorporated by reference to our definitive proxy statement to be filed with the Securities and Exchange Commission in connection with our 2023 Annual Meeting of Stockholders (the Proxy Statement), which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2022, under the sections headed "Election of Directors," "Information Regarding the Board of Directors and Corporate Governance," and "Executive Officers."

Code of Business Conduct and Ethics

We maintain a Code of Conduct that applies to all our employees, officers and directors. This includes our principal executive officer, principal financial officer and principal accounting officer or controller, or persons performing similar functions. The full text of our Code of Conduct is posted on our website at www.reneopharma.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report. If we make any substantive amendments to the Code of Conduct or grant any waiver from a provision of the Code of Conduct to any executive officer or director that are required to be disclosed pursuant to SEC rules, we will promptly disclose the nature of the amendment or waiver on our website or in a current report on Form 8-K.

Item 11. Executive Compensation

The information required by this item is incorporated by reference to our Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2022, under the section headed "Executive Compensation."

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item is incorporated by reference to our Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2022, under the sections headed "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information."

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item is incorporated by reference to our Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2022, under the sections headed "Transactions with Related Persons and Indemnification" and "Information Regarding the Board of Directors and Corporate Governance."

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference to our Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2022, under the section headed "Ratification of Selection of Independent Registered Public Accounting Firm."

PART IV

Item 15. Exhibit and Financial Statement Schedules

(a) The following documents are filed as part of this Annual Report:

(1) Financial statements

The financial statements filed as part of this Annual Report are included in Part II, Item 8 of this Annual Report.

(2) Financial statement schedules

Financial statement schedules have been omitted in this Annual Report because they are not applicable, not required under the instructions, or the information requested is set forth in the financial statements or related notes thereto.

(3) Exhibits

The exhibits listed in the accompanying Exhibit Index are filed as part of, or incorporated by reference into, this Annual Report.

Item 16. Form 10-K Summary

None.

EXHIBIT INDEX

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on April 13, 2021).
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K, filed with the SEC on April 13, 2021).
4.1	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
4.2	Amended and Restated Investors' Rights Agreement, by and among the Registrant and certain of its stockholders, dated December 9, 2020 (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on March 19, 2021).
4.3	Description of Common Stock of the Registrant (incorporated by reference to Exhibit 4.3 to the Registrant's Annual Report on Form 10-K (File No. 001-40315), filed with the SEC on March 23, 2022).
Agreements with Executive Officers and Directors	
10.1+	Employment Agreement by and between the Registrant and Alejandro Dorenbaum, M.D., dated January 1, 2018 (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.2+	Letter Agreement by and between the Registrant and Michael Grey, dated February 12, 2018, as amended on December 7, 2020 (incorporated by reference to Exhibit 10.16 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.3+	Employment Agreement by and between the Registrant and Gregory J. Flesher, dated November 2, 2020 (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.4+	Employment Agreement by and between the Registrant and Michael Cruse, dated November 20, 2020 (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.5+	Letter Agreement by and between the Registrant and Eric M. Dube, Ph.D., dated March 10, 2021 (incorporated by reference to Exhibit 10.19 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.6+	Employment Agreement by and between the Registrant and Vineet R. Jindal, dated March 19, 2021 (incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).

Exhibit Number	Description
10.7+	Employment Agreement by and between the Registrant and Ashley F. Hall, J.D., dated October 11, 2021 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed with the SEC on November 12, 2021 (File No. 001-40315).
10.8+	Form of Indemnity Agreement by and between the Registrant and its directors and executive officers (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.9+*	Reneo Pharmaceuticals, Inc. Non-Employee Director Compensation Policy, as amended.
10.10+	Letter Agreement by and between Registrant and Paul W. Hoelscher, dated January 20, 2022 (incorporated by reference to Exhibit 10.13 to the Registrant's Annual Report on Form 10-K (File No. 001-40315), filed with the SEC on March 23, 2022).
10.11+	Transition, Separation and Consulting Agreement by and between the Registrant and Vineet R. Jindal, dated February 2, 2022 (incorporated by reference to Exhibit 10.14 to the Registrant's Annual Report on Form 10-K (File No. 001-40315), filed with the SEC on March 23, 2022).
10.12+	Letter Agreement by and between the Registrant and Roshawn Blunt, dated August 2, 2022 (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-40315), filed with the SEC on August 9, 2022).
Patent and License Agreements	
10.13#	License Agreement by and between the Registrant and vTv Therapeutics LLC, dated December 21, 2017 (incorporated by reference to Exhibit 10.17 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
Sales Agreements	
10.14	Sales Agreement, dated May 2, 2022, by and between the Registrant and SVB Securities LLC (incorporated by reference to Exhibit 1.2 to the Registrant's Registration Statement on Form S-3 (File No. 333-264616), filed with the SEC on May 2, 2022).
Equity Compensation Plans and Policies	
10.15+	Reneo Pharmaceuticals, Inc. 2014 Equity Incentive Plan, as amended, and UK Sub-Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.16+	Forms of Grant Notice, Stock Option Agreement and Notice of Exercise under the Reneo Pharmaceuticals, Inc. 2014 Equity Incentive Plan, as amended, and UK Sub-Plan (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.17+	Reneo Pharmaceuticals, Inc. 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).

Exhibit Number	Description
10.18+*	Forms of (i) Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise, (ii) Stock Option Grant Notice - International, Stock Option Agreement - International and Notice of Exercise - International and (iii) Non-Employee Director Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise – Non-Employee Director under the Reneo Pharmaceuticals, Inc. 2021 Equity Incentive Plan.
10.19+	Forms of (i) Restricted Stock Unit Award Grant Notice and Award Agreement and (ii) Restricted Stock Unit Award Grant Notice - International and Award Agreement - International under the Reneo Pharmaceuticals, Inc. 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.20+	Forms of Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise for Inducement Grant Outside of the Reneo Pharmaceuticals, Inc. 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q, filed with the SEC on November 12, 2021).
10.21+	Forms of RSU Award Grant Notice and Award Agreement (RSU Award) for Inducement Grant Outside of the Reneo Pharmaceuticals, Inc. 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Quarterly Report on Form 10-Q, filed with the SEC on November 12, 2021).
10.22+	Reneo Pharmaceuticals, Inc. 2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.23+	Reneo Pharmaceuticals, Inc. Severance Benefit Plan, as amended as of September 27, 2022, and form of Participation Agreement thereunder (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q, filed with the SEC on November 8, 2022).
10.24+	Reneo Pharmaceuticals, Inc. UK Sharesave Sub-Plan to the Reneo Pharmaceuticals, Inc. 2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q, filed with the SEC on November 12, 2021).
Other	
21.1*	Subsidiaries of the Registrant.
23.1*	Consent of independent registered public accounting firm.
24.1*	Power of Attorney (see signature page).
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as 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.

Exhibit Number	Description
32.1*†	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101. INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

* Filed with this Annual Report on Form 10-K.
† This certification shall not be deemed filed for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that Section, nor shall it be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.
+ Indicates Management contract or compensatory plan.
# Pursuant to Item 601(b)(10) of Regulation S-K, certain portions of this exhibit have been omitted by means of marking such portions with asterisks because the Registrant has determined that the information is not material and is the type that the Registrant treats as private or confidential.

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.

RENEO PHARMACEUTICALS, INC.

March 27, 2023

By: /s/ Gregory J. Flesher
Gregory J. Flesher
President & Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Gregory J. Flesher and Jennifer P. Lam and each of them, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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 and in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Gregory J. Flesher Gregory J. Flesher	President and Chief Executive Officer (Principal Executive Officer)	March 27, 2023
/s/ Jennifer P. Lam Jennifer P. Lam	Senior Vice President of Finance (Principal Financial and Accounting Officer)	March 27, 2023
/s/ Michael Grey Michael Grey	Executive Chairman	March 27, 2023
/s/ Roshawn A. Blunt Roshawn A. Blunt	Director	March 27, 2023
/s/ Eric Dube Eric Dube, Ph. D.	Director	March 27, 2023
/s/ Paul W. Hoelscher Paul W. Hoelscher	Director	March 27, 2023
/s/ Edward T. Mathers Edward T. Mathers	Director	March 27, 2023
/s/ Bali Muralidhar Bali Muralidhar, M.D., Ph. D.	Director	March 27, 2023
/s/ Niall O'Donnell Niall O'Donnell, Ph. D.	Director	March 27, 2023
/s/ Stacey D. Seltzer Stacey D. Seltzer	Director	March 27, 2023

Executive Management

Gregory J. Flesher
President & Chief Executive Officer

Michael P. Cruse
Chief Operating Officer

Alejandro Dorenbaum, M.D.
Chief Medical Officer

Ashley F. Hall, J.D.
Chief Development Officer

Jennifer Lam
Principal Financial & Accounting Officer

Board of Directors

Michael Grey
Executive Chairman
Reneo Pharmaceuticals, Inc.

Gregory J. Flesher
President & Chief Executive Officer
Reneo Pharmaceuticals, Inc.

Roshawn A. Blunt
President
Corsaire Corporation

Eric M. Dube, Ph.D.
President & Chief Executive Officer
Travere Therapeutics, Inc.

Paul W. Hoelscher
Retired

Edward T. Mathers
General Partner
New Enterprise Associates, Inc.

Bali Muralidhar, M.D., Ph.D.
Managing Partner &
Chief Investment Officer
Abingworth LLP

Niall O'Donnell, Ph.D.
Managing Director
RiverVest Venture Partners

Stacey D. Seltzer
Partner
Gurnet Point, LLC

Corporate Headquarters

18575 Jamboree Rd. Suite 275-S
Irvine, CA 92612
858-283-0280
www.reneopharma.com

Transfer Agent

American Stock Transfer & Trust Company, LLC
6201 15th Avenue
Brooklyn, NY 11219
(800) 937-5449

Annual Stockholders Meeting

The annual meeting of stockholders will be held on June 6, 2023, at 11:30 a.m. Pacific Time in a virtual-meeting format only via live webcast as detailed in the proxy statement for the annual meeting.

Investor Inquiries

858-283-0280
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This annual report to stockholder contains forward-looking statements relating to Reneo's clinical and preclinical development programs, the potential therapeutic and commercial potential of those drug candidates, and the strength of Reneo's balance sheet and the adequacy of cash on hand. These statements involve risks, uncertainties and other important factors that may cause Reneo's actual results to be materially different from any future results expressed or implied by such forward-looking statements. Information identifying such risks, uncertainties and other important factors is contained in the section entitled "Risk Factors" and elsewhere in our annual report on Form 10-K for the year ended December 31, 2022, as filed with the Securities and Exchange Commission and included as part of this annual report to Stockholder.

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