Table of Contents

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, 2021

OR

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

For The Transition Period From To

Commission file number: 001-40315

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: (619) 733-3852

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 Par Value per Share	**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. ☐

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 $9.33 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, 2021 (the last business day of the registrant's most recently completed second fiscal quarter) was approximately $93,281,340. 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 17, 2022 was 24,458,550 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 2022 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, 2021. Except with respect to information specifically incorporated by reference in 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

TABLE OF CONTENTS

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 REN001 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 REN001, if approved;
- our ability to develop and maintain sales and marketing capabilities, whether alone or with potential future collaborators;
- our plans to research, develop and commercialize REN001, including the timing of our ongoing clinical trials of REN001;
- our expectations regarding the size of target patient populations for REN001, if approved for commercial use, and any additional product candidates we may develop;
- the size and growth potential of the markets for REN001, and our ability to serve those markets;
- the rate and degree of market acceptance of REN001, as well as third-party payor coverage and reimbursement for REN001;
- 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 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 will need substantial additional financing to develop REN001 and any future product candidates and implement our operating plan. If we fail to obtain additional financing, we may be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- We currently depend entirely on the success of REN001, which is our only product candidate. If we are unable to advance REN001 in clinical development, obtain regulatory approval, and ultimately commercialize REN001, 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 REN001, 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.
- 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.
- 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, clinical research organizations (CROs), or other third parties with whom we conduct business.
- If the market opportunities for REN001 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 REN001 in the future. We may expend our limited resources to pursue a particular indication or formulation for REN001 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 REN001 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 REN001.
- 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 REN001 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

- 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.

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, REN001, is a potent and selective agonist of the peroxisome proliferator-activated receptor delta (PPARδ). REN001 has been shown to increase transcription of genes involved in mitochondrial function and increase fatty acid oxidation, and may increase production of new mitochondria.

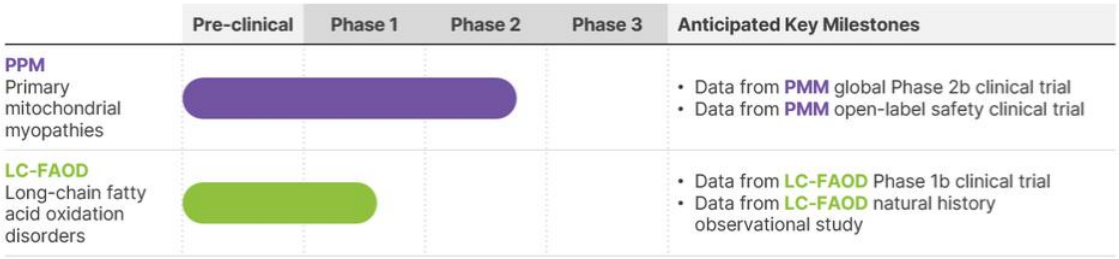
The PPAR family of nuclear hormone receptors, PPARa, PPARg, and PPARδ, control the transcription of genes critical for regulating energy metabolism and homeostasis. PPARδ is highly expressed in muscle, kidney, brain, and liver tissue. Activation of PPARδ results in changes in the expression of genes 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. REN001 was studied in healthy volunteers with one leg immobilized to produce muscle atrophy. Compared to placebo, administration of REN001 resulted in statistically significant increases in expression of genes involved in mitochondrial oxidative phosphorylation, and statistically significant improvements in muscle strength. REN001 was also studied in an open-label trial in patients with primary mitochondrial myopathies (PMM). In this trial, administration of REN001 improved function, reduced symptoms, and increased expression of genes involved in mitochondrial activity.

As a PPARδ agonist, REN001 may benefit patients with genetic mitochondrial myopathies who experience weakness, fatigue, or deterioration in muscle due to impaired mitochondrial energy production. We are currently developing REN001 in rare genetic diseases that typically present with myopathy and have high unmet medical needs, including PMM and long-chain fatty acid oxidation disorders (LC-FAOD). 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.

Our Product Pipeline

The following table summarizes our pipeline for REN001.



We are currently developing REN001 in the following rare genetic diseases that are associated with a deficit of energy production in mitochondria and typically present with myopathy:

- PMM: This rare genetic mitochondrial disease has an estimated prevalence of 20:100,000, 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 oxidative phosphorylation (OxPhos) is compromised. We are initially targeting adult patients with PMM.

- 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.

Muscle cells mainly rely on three sources to generate energy: phosphocreatine, carbohydrates (glycogen), and fatty acids. Muscle cells initially use readily available phosphocreatine 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.

REN001 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 REN001 will act to help patients with mitochondrial diseases.

We completed an open-label Phase 1b study in patients with PMM to assess the safety and tolerability of REN001, and measure changes in functional tests such as walk distance, exercise capacity and patient-reported symptoms that could serve as potential endpoints in future clinical studies. REN001 was well-tolerated and had an adequate safety profile in this trial. Compared to baseline, patients receiving REN001 once-daily for 12 weeks experienced an average increase in distance of 104.4 meters in the 12-minute walk test (12MWT), an average increase in weight-adjusted peak oxygen consumption (VO2) of 1.7 mL/kg/min, a reduction in fatigue and pain, and increased expression of genes involved with transport and metabolism of nutrients in the mitochondria including Pyruvate dehydrogenase lipoamide kinase isozyme 4 (PDK4), Angiopoietin-like 4 (ANGPTL4), and Solute carrier family 25 member 34 (SLC25A34).

Based on these results, we initiated a global, randomized, double-blind, placebo-controlled Phase 2b study of REN001 in patients with PMM (STRIDE study). The first patient was dosed in July 2021 and we expect to complete enrollment by year-end 2022 and announce results in 2023. We are also conducting an open-label, long-term safety trial outside the United States in a subset of patients from the STRIDE study (STRIDE AHEAD study). The first patient was dosed in January 2022 and we anticipate preliminary data from this study in 2023. Following our interactions with United States and several European regulatory agencies, we believe that positive results from these trials could support registration of REN001 for PMM in both the United States and in Europe.

We completed enrollment of an open-label Phase 1b study in patients with four different LC-FAOD enzyme defects to assess the safety and tolerability of REN001, and measure changes in functional tests such as walk distance, exercise capacity and patient-reported symptoms that could serve as potential endpoints in future clinical studies. We also completed enrollment of a natural history study in patients with LC-FAOD (FORWARD study). The FORWARD study

is an observational, non-interventional study to better understand the changes in patient function and symptoms over time. We anticipate results from both studies in the second calendar quarter of 2022.

We completed an open-label Phase 1b study in patients with glycogen storage disease type V (McArdle Disease) to assess the safety and tolerability of REN001, and measure changes in functional tests such as walk distance, exercise capacity and patient-reported symptoms that could serve as potential endpoints in future clinical studies. Patients with McArdle disease are unable to break down glycogen in the muscle, and during the first several minutes of muscle activity experience acute fatigue and pain, and a significant increase in heart rate. REN001 was well-tolerated and had an adequate safety profile in this study. Compared to baseline, patients receiving REN001 once-daily for 12 weeks experienced an average increase in distance of 25.0 meters in the 12MSWT and an increase in fat oxidation of 38.5% as measured by indirect calorimetry. No corresponding changes in heart rate, fatigue, pain, or other symptoms were observed. Based on these results, we will not pursue a subsequent Phase 2 study in McArdle Disease at this time.

As of March 4, 2022, REN001 has been dosed in 225 individuals across multiple clinical trials. In these trials, REN001 was well tolerated, with no drug-related serious adverse events (SAE) reported.

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 REN001 initially for patients with PMM and LC-FAOD and will continue to explore other patient populations where REN001 may provide benefit. We intend to establish REN001 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 REN001 in PMM.** REN001 is an oral small molecule PPARδ agonist that is designed to modulate multiple genes critical for cellular metabolism and the generation of energy in the cell. Our lead clinical program targets PMM, a rare genetic mitochondrial disease with an estimated prevalence of 20:100,000, and a high unmet medical need due to the lack of any approved pharmaceutical treatment option. We established proof-of-concept in a Phase 1b study in patients with PMM in which REN001 was shown to be well-tolerated and improvements in exercise performance and patient-reported symptoms were observed. We also observed increases in the expression of genes responsible for the transport and metabolism of nutrients within the mitochondria. The first patient in the STRIDE study was dosed in July 2021, and we expect to complete enrollment by year-end 2022 and announce results in 2023. We are also conducting the STRIDE AHEAD study, an open-label, long-term, safety trial outside the United States in a subset of patients from the STRIDE study, with the first patient dosed in January 2022 and preliminary data anticipated to be available in 2023. Based on interactions with U.S. and several European regulatory agencies, we believe that positive results from these trials could support registration of REN001 for PMM in both the United States and in Europe.

- **Maximize the commercial potential of REN001 in additional rare genetic mitochondri**al **disease indications.** We are also studying REN001 in a Phase 1b study in patients with LC-FAOD, a rare genetic disease with high unmet medical need, plus the FORWARD study. Preliminary data from the Phase 1b study have demonstrated an improvement in a subset of patients in both exercise tests and symptoms, with tolerability of REN001 that is consistent with that observed in other REN001 studies. We anticipate that data for the full cohort of patients from our Phase 1b study and the FORWARD study will be available in the second calendar quarter of 2022. We will assess the potential for continued development of REN001 in LC-FAOD following receipt of full data from both studies, and discussion with key opinion leaders. We also plan to explore further development of REN001 in other diseases that are defined by the inability of mitochondria to produce cellular energy.

- **Commercialize REN001 in the United States and key European markets, and establish REN001 as standard of care.** 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 REN001 to patients. Our goal is to establish REN001 as the standard of care for rare genetic mitochondrial diseases around the world.

- **Expand our rare genetic mitochondrial 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.

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 phosphocreatine (P-Cr) as a source of fuel to create ATP (Figure 1, step 1). When phosphocreatine is consumed, muscles turn to carbohydrate metabolism (glucose utilization) as the next source of fuel to create ATP (Figure 1, step 2). Finally, after several minutes of exercise when phosphocreatine and carbohydrates are depleted, mitochondria turn to fatty acids as the source of fuel to create ATP (Figure 1, step 3). Fatty acid oxidation (FAO) becomes the primary pathway to generate energy for muscle and other cells during long periods of exercise.

Oxidative phosphorylation

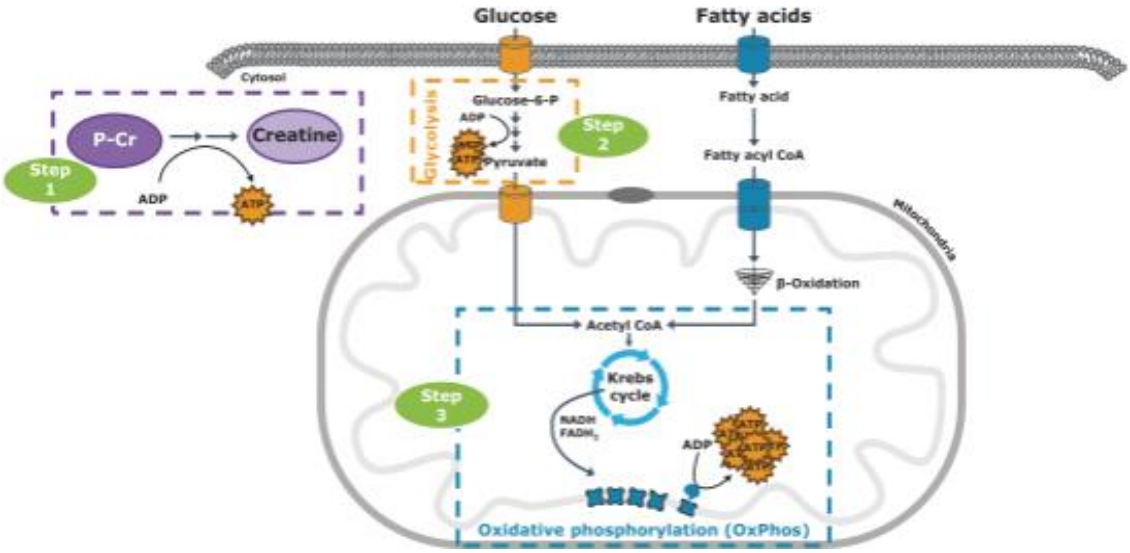
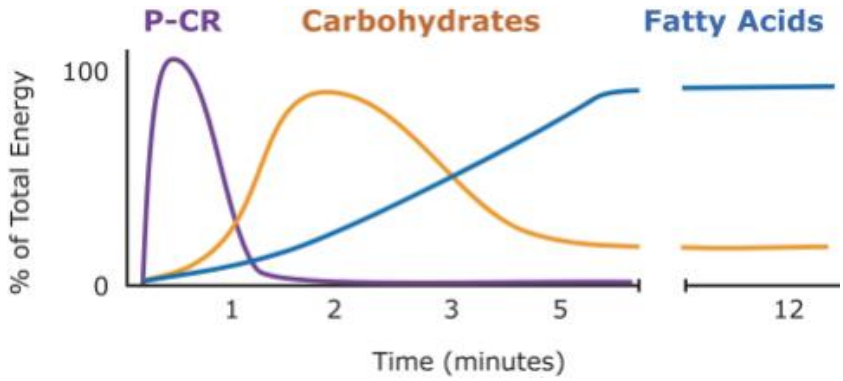


Figure 1. The energy source used by muscles shifts from phosphocreatine (P-Cr) and carbohydrates to fatty acids as short-term supplies of phosphocreatine and carbohydrates are depleted



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.

Disease overview

PMM background

PMM are a group of disorders caused by genetic mutations within the mitochondrial DNA (mtDNA) or nuclear DNA (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 PMM patients 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, long-chain 3-hydroxy acyl-CoA dehydrogenase deficiency (LCHAD), mitochondrial trifunctional protein deficiency, and carnitine palmitoyltransferase (CPT) deficiency. 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 LC-FAOD patients. However, DOJOLVI has not demonstrated clear functional benefits on endurance in randomized, controlled clinical trials.

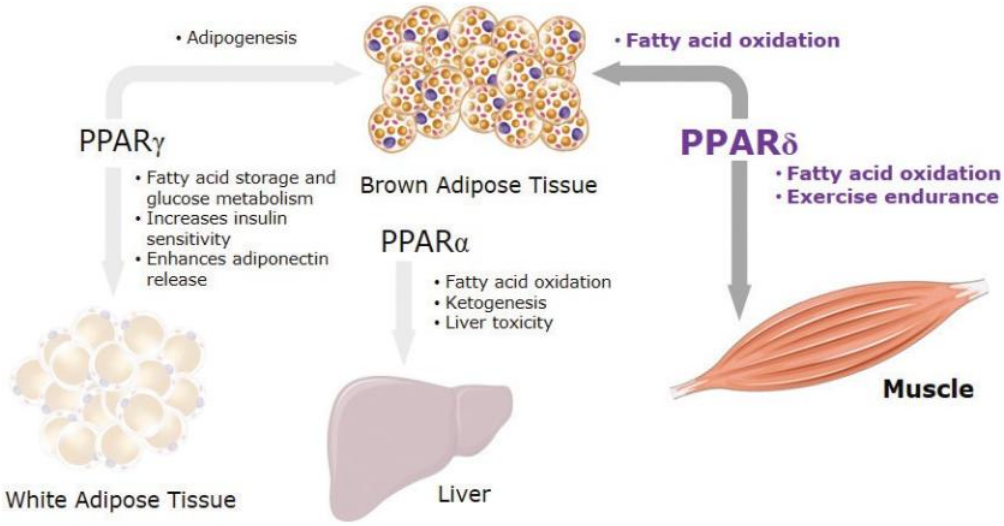
PPARδ, a regulator of FAO

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 REN001, 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



Our Solution, REN001

REN001 is an oral, small molecule selective PPARδ agonist designed to modulate genes critical to metabolism and generation of energy. By selectively targeting PPARδ, REN001 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.

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 PMM patients 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 REN001 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 REN001 in healthy volunteers who were randomized to receive 4 weeks of treatment with 100 mg REN001 orally twice-daily (n=12) or placebo (n=12) showed increased expression of PPARδ regulated genes. Compared to placebo, analysis of muscle biopsies from REN001 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 REN001 in the United States for PMM and LC-FAOD. Additionally, we have received orphan drug designations for REN001 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 licensed exclusive, worldwide rights to develop and commercialize REN001 and other related compounds from vTv Therapeutics in 2017.

REN001 for the Treatment of PMM

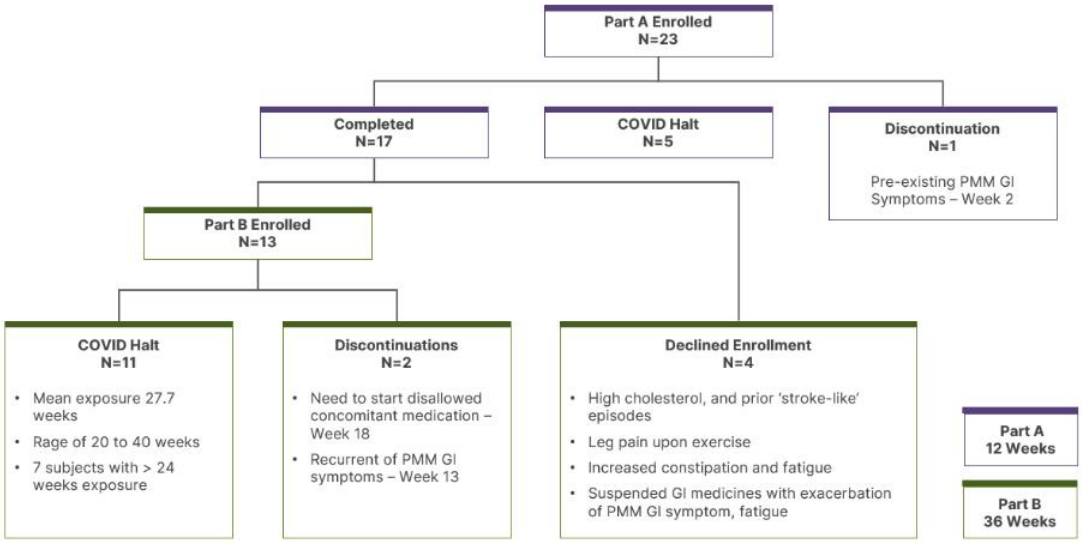
Phase 1b clinical results in PMM

We completed an open-label Phase1b clinical trial of REN001 in patients with PMM and myopathy due to mtDNA mutations, which was conducted under a Clinical Trial Authorisation submitted to the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK) and accepted in November 2018. The primary objective of the trial was to evaluate the safety and tolerability of REN001, and REN001 was generally well-tolerated. We selected PMM patients with mtDNA mutations and excluded PMM patients with nDNA mutations to reduce heterogeneity in the study. Also, in contrast to PMM patients with nDNA mutations who have all their mitochondria affected, patients with mtDNA mutations harbor both normal and mutated mitochondria within their cells (heteroplasmy). In PMM patients with mtDNA mutations, REN001 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 PMM patients.

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 REN001 once daily. A total of 24 patients were enrolled and 23 patients received REN001 in Part A. The planned maximum treatment duration for each patient in both Part A and Part

B was 48 weeks. The Phase 1b study 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. REN001 PMM Phase 1b study enrollment



To evaluate changes in patient function, we used a 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 phosphocreatine and carbohydrate metabolism into FAO in the mitochondria.

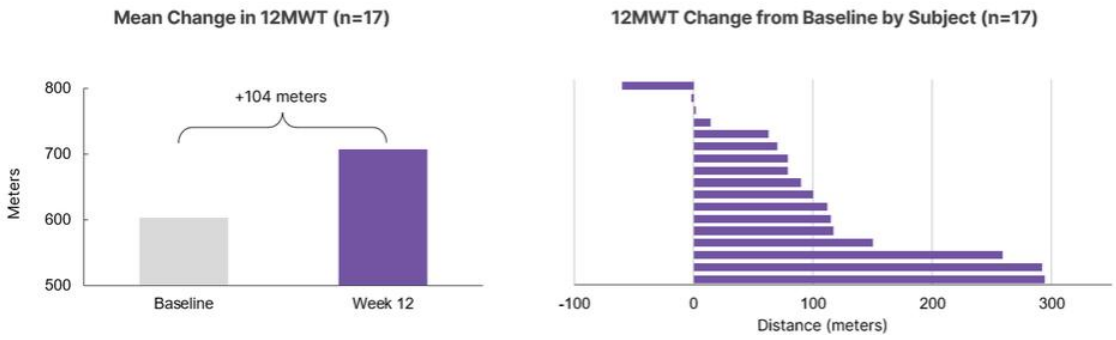
REN001 was generally well tolerated with no drug related SAEs observed. There were 114 treatment emergent adverse events (TEAE) experienced by 21 out of 23 subjects, with 66 of the 114 TEAEs (57.9%) experienced by 15 subjects which are considered related to study drug. The majority of these TEAEs were 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 study was 603.2 meters. Following 12 weeks of 100 mg once-daily dosing with REN001, patients achieved an average increase of 104.4 meters (95% CI: 53.1, 155.6) in distance walked during the

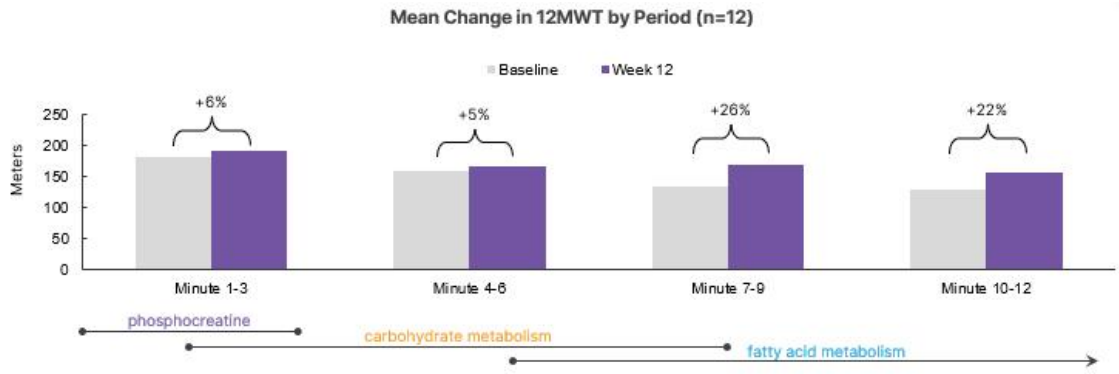
12MWT compared to baseline. An increase in distance walked was observed in 15 of 17 patients (88%), with 13 of 17 (76%) increasing by 60 meters or greater as illustrated in Figure 5a.

Figure 5a. REN001-treated PMM patients had improved 12MWT distances after 12 weeks of treatment



The largest improvement in distance walked in the 12MWT at week 12 occurred in the second half of the 12-minute period (Figure 5b), which we believe is consistent with REN001's mechanism of action. We expect REN001 to improve muscle cell energy by increasing mitochondrial oxidative phosphorylation, and this process occurs several minutes into exercise (See Figure 1 above).

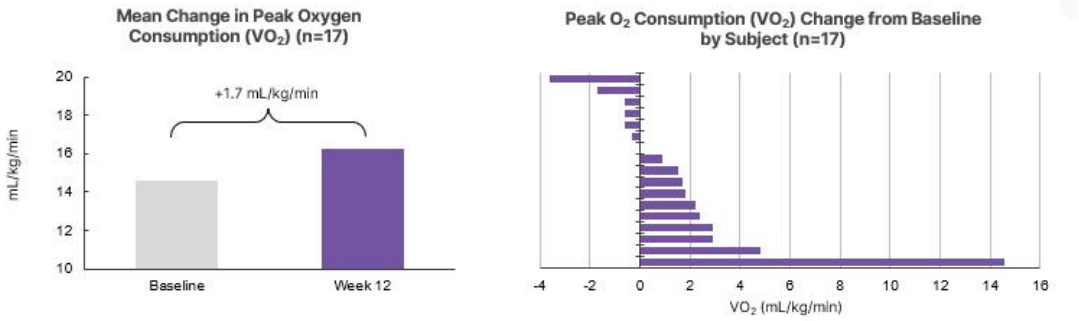
Figure 5b. REN001-treated PMM patients had greatest improvement in walking distances in the latter half of the 12MWT, consistent with the proposed mechanism of REN001 to stimulate fatty acid metabolism



An additional outcome measure in our Phase 1b study was measurement of peak oxygen consumption 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 oxygen consumption of 35 to 40 ml/kg/min for males and 27 to 30 ml/kg/min for females. A weight-adjusted peak oxygen consumption of 14 mL/kg/min or lower has been determined to predict increased mortality in other patient populations (congestive heart failure).

Baseline weight-adjusted peak oxygen consumption in the Phase 1b study was 14.6 mL/kg/min. Following 12 weeks of 100 mg once-daily dosing with REN001, patients achieved an average increase in weighted average peak oxygen consumption of 1.7 mL/kg/min (95% CI: -0.329, 3.665) compared to baseline (Figure 5c).

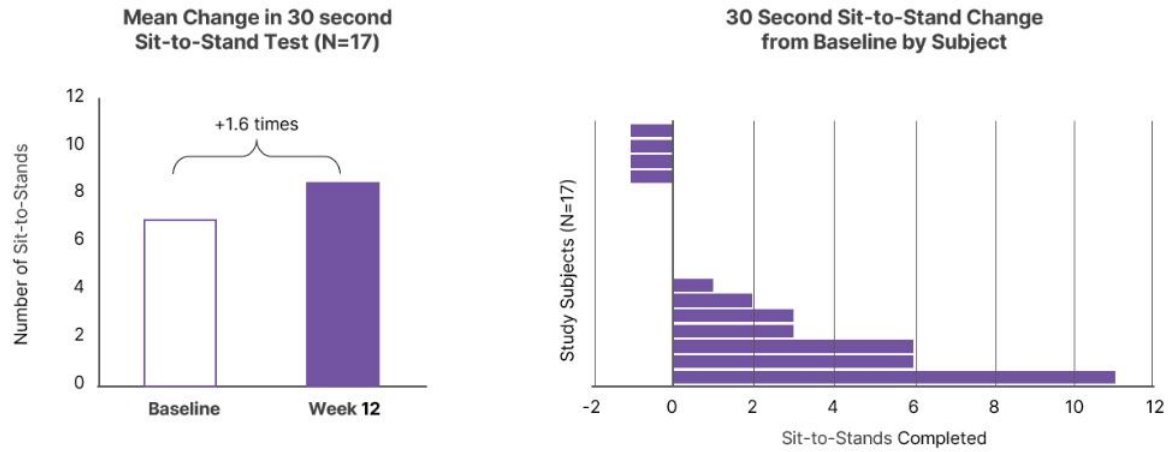
Figure 5c. Peak exercise oxygen consumption increased in PMM patients after 12 weeks of REN001 treatment



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 REN001 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 test was also performed. The 30-second sit-to-stand 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 PMM patients in our Phase 1b study 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 REN001, 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 PMM patients showed improvements in lower extremity muscle strength and stamina after 12 weeks of REN001 treatment as evaluated with the 30-second sit-to-stand test.

Figure 5d. PMM patients showed improvements in lower extremity muscle strength and stamina after 12 weeks of REN001 treatment as evaluated with the 30-second sit to stand test



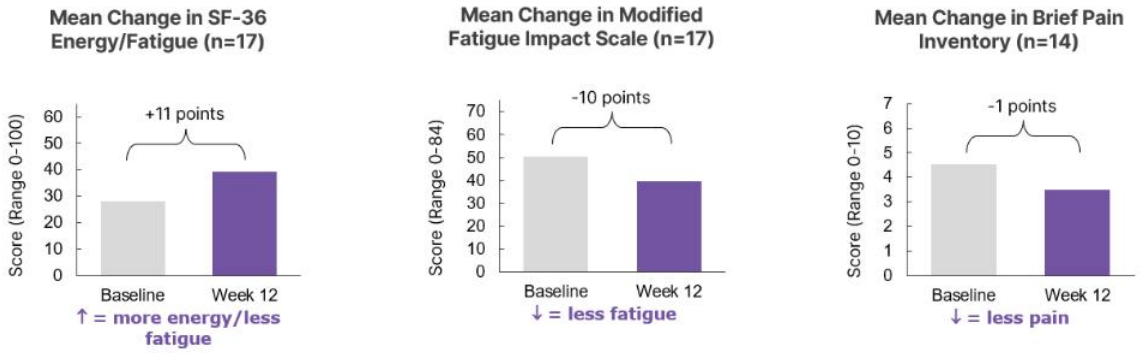
Patient reported outcomes (evaluation of symptoms)

The 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 in the right chart in Figure 5e, after 12 weeks of 100 mg once-daily dosing with REN001, 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 in the middle chart in Figure 5e, after 12 weeks of 100 mg once-daily dosing with REN001, 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 REN001, 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.

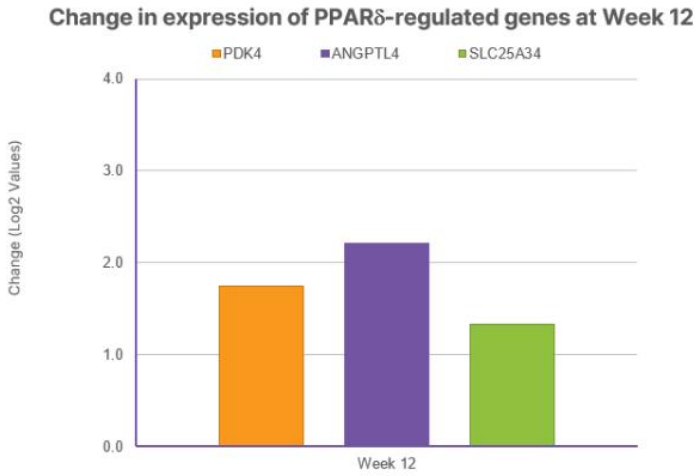
Figure 5e. Mean change from baseline to week 12 in patient reported outcome questionnaires in patients with PMM participating in the Phase 1b study



Muscle biopsies (evaluation of gene expression)

Muscle biopsies were performed at baseline and after 12 weeks of treatment with REN001 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 PDK4, ANGPTL4, and SLC25A34.

Figure 5f. Change in PPARδ-regulated gene expression from human muscle following REN001 treatment from a Phase 1b clinical trial in PMM patients



Clinical development plans in PMM

We have initiated the STRIDE study, a global Phase 2b study of REN001 in patients with PMM and dosed the first patient in July 2021. STRIDE is a randomized, double-blind, placebo-controlled, multi-center clinical trial designed to investigate the efficacy and safety of 100 mg REN001 administered once-daily over a 24-week period to PMM patients with mtDNA mutations. We anticipate enrolling approximately 200 adult patients with a history of myopathy. The primary endpoint of the trial is the change from baseline in the distance walked during the 12MWT at 24 weeks. Secondary endpoints include changes from baseline in the MFIS and the patient global impression of change scale.

Other exploratory endpoints include the 30-second sit-to-stand test, step counts, patient global impression of severity scale, BPI, and additional patient-reported outcome measures. Results from the STRIDE study is expected to be available in 2023. We have also initiated the STRIDE AHEAD study, an open-label extension trial, which will enroll a subset of the patients from the STRIDE study. Based on interactions with the U.S. Food and Drug Administration (FDA) and several European regulatory agencies, we believe that positive results from the STRIDE study and the STRIDE AHEAD study could support registration of REN001 for PMM in both the United States and in Europe.

REN001 for the Treatment of LC-FAOD

Phase1b Study in LC-FAOD

In December 2021, we completed enrollment in an open-label Phase 1b study in adult patients with LC-FAOD. The primary objective of the trial is to evaluate the safety and tolerability of REN001 in the LC-FAOD patient population, and we will also explore multiple clinical outcomes. 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. We completed enrollment of this study in late 2021, and we expect results to be available in the second calendar quarter of 2022. We obtained data from the first six patients who completed 12 weeks of dosing, and both doses have been well tolerated. As shown in Figure 6, after 12 weeks of treatment with REN001, 5 of the 6 patients showed an improvement in the 12MWT, with 4 of the 6 showing an

improvement over 50 meters. Improvements in symptoms, including a decrease in MFIS and BPI and an increase in SF-36, were also observed in several patients.

Figure 6. Results from the first six LC-FAOD patients dosed with REN001 in a Phase 1b Study

Mean Change from Baseline to Week 12					
Patient	12MWT (meters)	MFIS	BPI	SF-36 Physical Functioning	SF-36 Energy/ Fatigue
1	-82	-5	0	10	5
2	3	16	0.75	-15	-15
3	58	2	0	5	-5
4	61	-9	-0.5	10	20
5	74	-10	-1.5	5	40
6	120	-8	-0.75	10	25

LC-FAOD natural history study

We completed enrollment in the FORWARD study, an observational, non-interventional study of REN001 in patients with LC-FAOD, to better understand these patients' natural history and disease characteristics through exercise tests and symptom questionnaires. The FORWARD study will also include work for validation of a new Reneo-developed patient questionnaire focused on muscle symptoms in LC-FAOD, which we plan to use in future trials.

We expect to announce results of both the LC-FAOD Phase 1b study and the FORWARD study in the second calendar quarter of 2022.

Additional Clinical Trials for REN001

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*

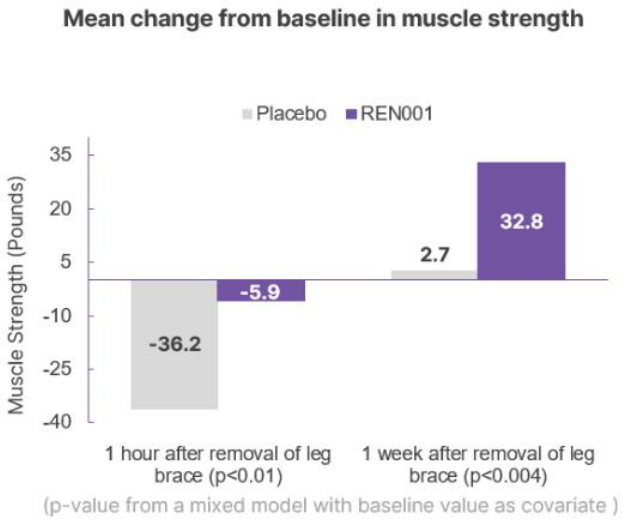
† randomized double-blind placebo-controlled clinical trial

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 REN001 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. REN001 treated volunteers had substantially more leg strength than

placebo treated volunteers immediately and one week after the removal of the leg brace. No SAEs related to REN001 were reported, and TEAEs were similar among subjects who received REN001 or placebo.

Figure 7. Results from the muscle strength test from a Phase 1 clinical trial in healthy volunteers

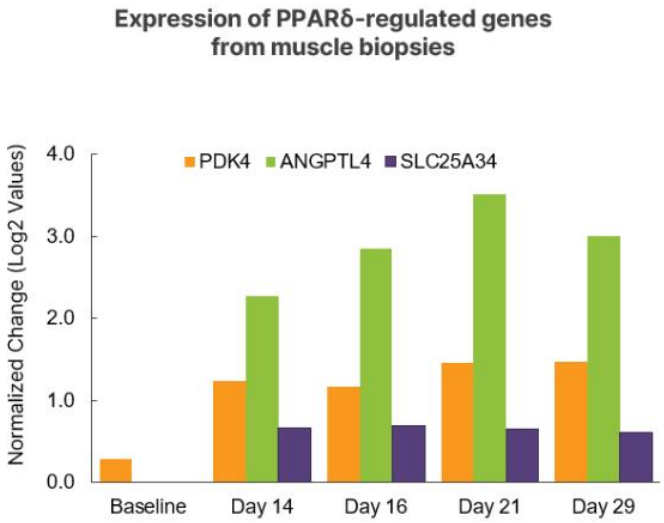


In the description of the Phase 1 clinical results in Figure 7 above, a p-value represents the probability that random chance caused the result. For example, a p-value of 0.001 means that there is a 0.1% probability that the difference between the control group and the treatment group is purely due to 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 8). Muscle biopsies obtained from REN001 treated individuals showed substantial increases in the mRNA of the following PPAR-regulated genes compared to placebo-treated controls:

- **Pyruvate dehydrogenase lipoamide kinase isozyme 4 (PDK4)**, encodes a mitochondrial protein. This kinase plays a key role in regulation of glucose and fatty acid metabolism.
- **Angiopoietin-like 4 (ANGPTL4)** is a target of PPARs. The encoded protein is a serum hormone directly involved in regulating lipid metabolism.
- **Solute carrier family 25 member 34 (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 8. Change in PPARδ-regulated Gene Expression from Human Muscle Following REN001 Treatment from a Phase 1 clinical trial in healthy volunteers.



Safety

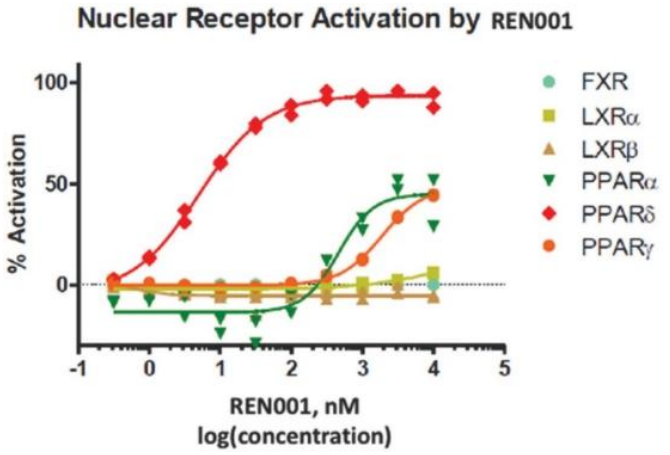
Overall, REN001 has been well tolerated in all clinical trials conducted and there have been no drug related deaths or SAEs reported to date. Most observed TEAEs were mild or moderate in severity. In clinical trials where patients were randomized to REN001 or placebo, the incidence and severity of adverse events were similar among individuals who received REN001 or placebo.

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 REN001. In these studies, it has been observed that REN001 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. REN001 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

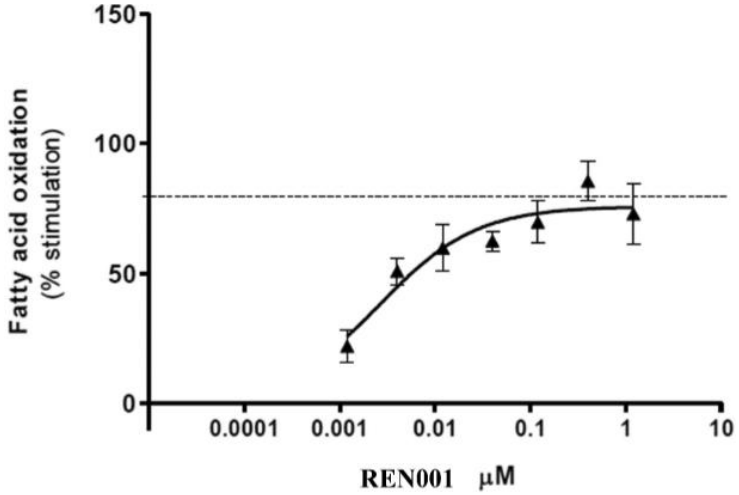
metabolism. REN001 has also been evaluated for these receptors in transcriptional assays with similar findings (Figure 9).

Figure 9. REN001 is a selective agonist of PPARδ



To access effects of REN001 on fatty acid oxidation, incubation of REN001 on XM5 human muscle cell line with REN001 demonstrated a concentration-dependent increase in FAO as shown in Figure 10 below.

Figure 10. REN001 led to a concentration-dependent increase in FAO in XM5 human muscle cell line



In an *in vivo* experiment, administration of REN001 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 11).

Figure 11. The transcription of fatty acid metabolism genes was increased after seven days of dosing with REN001 in mice

Gene	Name	Description	Fold-change over vehicle (SEM)
PGCα	PPARϒ 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 REN001 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 2023.

We are unaware of any data suggesting that there is a clinical cancer risk with selective PPARδ agonists. CymaBay Therapeutics' clinical development programs includes dosing the selective PPARδ agonist seladelpar for up to 52 weeks and is currently conducting a 60-month open-label, long-term safety and tolerability study. Astellas Pharma has announced it intends to conduct a Phase 2/3 clinical trial of up to 52-weeks with ASP0367, a selective PPARδ agonist. Collectively, this suggests that both seladelpar and ASP0367 have 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 REN001.

We have completed a 6-month toxicology study in rats and a 12-month toxicology study in primates. No adverse effects associated PPARα or PPARγ agonists were observed with administration of REN001 at any dose level.

COVID-19

The COVID-19 pandemic continues to evolve, and we will continue to monitor the COVID-19 situation closely. The extent of the impact of COVID-19 on our business, operations and clinical development timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the pandemic, including new variants of the virus, and its impact on our clinical trial enrollment, trial sites, contract research organizations, third-party manufacturers, and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. For example, our Phase 1b study of REN001 in PMM patients was closed early as a result of COVID-19, and we may face future clinical trial disruptions. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. As a result of COVID-19, we have taken precautionary measures in order to minimize the risk of the virus to our employees and the communities in which we operate. While we have experienced impacts to our clinical development activities as a result of COVID-19 as set forth in this Annual Report, there has been a minimal disruption to date in our ability to ensure the effective operation of our business. We will continue to actively monitor the rapidly evolving situation related to COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with whom we do business. At this point, the extent to which the COVID-19 pandemic may affect our business, operations and clinical development timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain.

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 REN001 in the United States and key European markets. For other territories, we will seek strategic partnerships to bring REN001 to market with the goal of establishing REN001 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 REN001, 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 REN001, 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 REN001 for treatment of 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, REN001, 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 international (*i.e.*, PCT) 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 REN001. We have licensed from vTv Therapeutics seven issued patents in the United States and 19 issued patents in foreign countries, including Australia, Canada, Great Britain, Germany, France, Austria, Belgium, Switzerland, Spain, Ireland, Italy, the Eurasian Patent Organization, Israel, Japan, South Korea, Mexico, New Zealand, South Africa, and Taiwan covering composition of matter of REN001, 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, including Canada, Germany, Spain, France, Great Britain, and Italy, one pending application in the United States, and one pending application in Europe, from vTv Therapeutics covering methods of using REN001, 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 REN001, we have filed our own patent applications. We co-own one international application, and own three pending applications in the United States, one pending international patent application, an issued patent in Lebanon, and over 25 pending applications in foreign countries, directed to various methods of use of REN001. These 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, two pending international patent applications, and two pending applications in foreign countries directed to methods of manufacturing, and crystalline forms (polymorphs) of REN001. The issued patent, and patent applications if issued, are expected to expire in 2041, absent any patent term adjustments or extensions. Patents related to REN001 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 REN001 for the treatment of LC-FAOD and PMM in the United States and LCHAD deficiency and mitochondrial encephalomyopathy, lactic acidosis, and neurological stroke-like episodes 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 REN001 has not previously been approved in the United States for any indication, REN001 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 REN001 has not previously been approved in the EU for any indication, REN001 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 REN001 is approved for a new indication that provides a significant clinical benefit.

In addition to patent protection around REN001, we have also licensed from vTv Therapeutics three issued patents in the United States and 20 issued patents in foreign countries, including Germany, France, Great Britain, Switzerland, Spain, Ireland, Italy, Canada, India, Japan, South Korea, Mexico, and Taiwan directed to composition of matter around other PPARδ agonists, which are expected to expire in 2026, 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 REN001, 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 REN001 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 REN001. As REN001 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. Astellas Pharma is also developing a PPARδ agonist for PMM and has announced that it has initiated a Phase 2/3 trial in April 2021. Other companies are developing therapies for mitochondrial diseases, including, Stealth BioTherapeutics Corp., Abliva AB, Cyclerion Therapeutics, Inc. and Khondrion B.V.

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 LC-FAOD patients. 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 that operates in the United States, 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 IND, 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 (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.

Among the Affordable Care Act's provisions of importance to the pharmaceutical industry, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and a cap on the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, including individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act. For example, the Tax Cuts and Jobs Act of 2017 (the Tax Act) was enacted, which includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." 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. Thus, the Affordable Care Act will remain in effect in its current form. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. 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, including the Infrastructure Investment and Jobs Act, will remain in effect through 2031, except for a temporary suspension from May 1, 2020 through March 31, 2022, unless additional congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% 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. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to drug pricing in an effort to implement several of the administration's proposals. As a result, the FDA concurrently released a final rule and guidance in September 2020 providing pathways for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the U.S. Department of Health and Human Services (HHS) finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden Administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which

have also been delayed until January 1, 2023. On November 20, 2020, the Centers for Medicare & Medicaid Services (CMS) issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. As a result of litigation challenging the Most Favored Nation model, on December 27, 2021, CMS published a final rule that rescinded the Most Favored Nation model interim final rule. 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. No legislation or administrative actions have been finalized to implement these principles. In addition, Congress is considering drug pricing as part of other health reform initiatives. It is unclear whether these or similar policy initiatives will be implemented in the future. 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. Further, it is also possible that additional governmental action is taken in response to the COVID-19 pandemic.

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, guidance, and industry standards related to data privacy, security, and protection. Such obligations may include, without limitation, the Federal Trade Commission Act, the California Consumer Privacy Act of 2018 (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 by virtue of section 3 of the European Union (EU) (Withdrawal) Act 2018 (UK GDPR). In addition, several states within the United States have enacted or proposed data privacy laws. For example, Virginia passed the Consumer Data Protection Act, and Colorado passed the Colorado Privacy Act.

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 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 delete the individual's personal data, and to opt out of certain personal data disclosures). Also, the CCPA provides for civil penalties and a private right of action for certain data breaches. In addition, the California Privacy Rights Act of 2020 (CPRA), effective January 1, 2023, will expand the CCPA. The CPRA will, among other things, give California residents the ability to limit use of certain sensitive personal data, establish restrictions on personal data retention, expand the types of data breaches that are subject to the CCPA's private right of action, and establish a new California Privacy Protection Agency to implement and enforce the new law. U.S. federal and state consumer protection laws require us to publish statements that accurately and fairly describe how we handle personal data and choices individuals may have about the way we handle their personal data.

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. As one 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.

See the section titled “Risk Factors” for additional information about the laws and regulations to which we are 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 must be conducted in accordance with EU and national regulations and the International Conference on Harmonization (ICH) guidelines on Good Clinical Practices (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, or 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.

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 two years from January 1, 2021, the 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) will not be applicable in GB. The United Kingdom may diverge from the EU to maintain regulatory flexibility and changes impacting the ability to conduct trials spanning several EU countries will need to be closely monitored going forward. Already, as a result of Brexit various benefits of membership no longer apply to the United Kingdom, 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 United Kingdom 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 December 31, 2021, we employed 32 employees, 20 of whom are full-time. Further, 15 of our employees are located in the United States and 17 are located in the United Kingdom. None of our employees is subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

We expect to continue to add employees in 2022, 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, CA 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 $1.07 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 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, REN001. 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 REN001 is not successfully developed and approved in the United States or Europe, we may never generate any revenue. For the years ended December 31, 2021 and 2020, we reported a net loss of $39.8 million and $19.5 million, respectively. As of December 31, 2021, we had an accumulated deficit of $84.7 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, REN001 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.

We will need substantial additional financing to develop REN001 and any future product candidates and implement our operating plan. If we fail to obtain additional financing, 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 to continue the clinical development of, and seek regulatory approval for, REN001 and any future

product candidates. We will require significant additional amounts in order to prepare for commercialization, and, if approved, to launch and commercialize REN001.

As of December 31, 2021, we had cash, cash equivalents and short-term investments of $147.7 million. We believe, based on our current operating plan, that our cash, cash equivalents and short-term investments as of December 31, 2021 will be sufficient to fund our planned operations into 2024. 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 REN001;
- the scope, prioritization and number of our research and indications we pursue;
- the costs and timing of manufacturing for our product candidate;
- the costs, timing, and outcome of regulatory review of REN001;
- 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 REN001 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. 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 resulting from the ongoing COVID-19 pandemic, as well as 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 REN001 or other research and development initiatives. We also could be required to seek collaborators for REN001 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 REN001 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 REN001, which is our only product candidate. If we are unable to advance REN001 in clinical development, obtain regulatory approval, and ultimately commercialize REN001, or experience significant delays in doing so, our business will be materially harmed.

We currently only have one product candidate, REN001, and our business and future success depends entirely on our ability to develop, obtain regulatory approval for, and then successfully commercialize, REN001, which is currently in clinical development for 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 REN001 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 European Medicines Agency (EMA) of data from our global Phase 2b or future clinical trials in patients with PMM;
- demonstrating safety and efficacy to the satisfaction of applicable regulatory authorities;
- 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 new drug applications (NDAs) from the FDA and marketing authorizations from 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 REN001, 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 REN001;
- maintaining an acceptable safety profile of REN001 following approval; and
- maintaining and growing an organization of people who can develop REN001.

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 REN001.

Even if regulatory approvals are obtained, we may never be able to successfully commercialize REN001. 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 REN001 to continue our business.

Our clinical trials may fail to adequately demonstrate the safety and efficacy of REN001, 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 REN001 of PMM, such as the Modified Fatigue Impact Scale, the Brief Pain Inventory assessment, and a 36-item short form survey (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 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 Phase 2b study of REN001 in patients with PMM and our Phase 1b study in patients with LC-FAOD utilize a 12MWT as an assessment of functionality in patients with genetic mitochondrial diseases who commonly lack endurance rather than the more commonly used six minute walk test (6MWT). Although we believe the 12MWT is the appropriate assessment tool, we cannot guarantee you that the FDA or other regulators will not require clinical results from a 6MWT for approval. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of REN001 in other indications.

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 REN001 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 the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. Also, because there are generally no approved drugs for our clinical indications, there are few regulatory precedents by which we can be guided with respect to clinical endpoints.

As such, we cannot be certain that our ongoing and planned clinical trials will be successful. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to 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 clinical trials have involved a limited number of patients and clinical trial sites. 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 REN001. Any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of REN001 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 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 REN001 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 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 REN001 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 REN001. 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 certain of the 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 REN001 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 chemistry, manufacturing and controls, and our proposed clinical trial protocol, as part of an investigational new drug application (IND) 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 REN001 or any future product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of REN001 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 REN001 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 REN001 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 REN001 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 serious adverse events (SAEs) in clinical trials of the same class of agents conducted by other companies;
- a facility manufacturing REN001 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 REN001 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 REN001;
- impact of possible trade disputes with countries where REN001 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, good clinical practice (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 REN001 in PMM patients 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 REN001 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 REN001.

If we experience delays in the completion of, or termination of, any clinical trial of REN001 or any future product candidates, the commercial prospect of REN001 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 REN001 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 REN001 and our competitors may be able to bring products to market before we do, and the commercial viability of REN001 could be significantly reduced. Any of these occurrences may harm our business, financial condition, results of operations and prospects significantly.

Use of REN001 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 REN001 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 REN001 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 REN001 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 REN001 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 form 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 REN001 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 REN001 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 REN001 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 REN001 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 REN001 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 REN001 and any future product candidates either prior to or post-approval, or may object to elements of our clinical development program.

REN001 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 REN001 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 REN001, 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 REN001 or any future product candidates and could substantially increase the costs of commercializing REN001 or any future product candidates. The demand for REN001 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 REN001 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 REN001 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 risk evaluation and mitigation strategy (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, including:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site; investigators and clinical site staff;
- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruption in global shipping that may affect the transport of clinical trial materials;
- changes in local regulations as part of a response to the COVID-19 outbreak which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;
- interruptions or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- risk that participants enrolled in our clinical trials will acquire COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- refusal of the FDA or comparable foreign regulatory authorities to accept data from clinical trials in affected geographies; and
- increased costs relating to mitigating the impact of COVID-19 on any of the foregoing factors.

These and other disruptions in our operations and the global economy could negatively impact our business, operating results and financial condition.

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 REN001 in PMM patients 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, the UK and Spain 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, ongoing or planned clinical trials may also be impacted by interruptions or delays in the operations of the FDA and comparable foreign regulatory agencies. For example, in certain locations, Ethics Committees' clinical protocol reviews have been delayed due to a backlog of applications requiring review. Such approvals are required to conduct studies at clinical trial sites.

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.

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 or third-party manufacturing facilities upon which we rely, or the availability or cost of materials, which could disrupt the supply chain for REN001. To the extent our suppliers and service providers are unable to comply with their obligations under our agreements with them or they are otherwise unable to deliver or are delayed in delivering goods and services to us due to the COVID-19 pandemic, our ability to continue meeting clinical supply demand for REN001 or otherwise advancing development of REN001 may become impaired.

The spread of COVID-19 and actions taken to reduce its spread may also materially affect us economically. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, there could be a significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity and financial position. In addition, the trading prices for other companies have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms.

COVID-19 and actions taken to reduce its spread continue to evolve. The extent to which COVID-19 may impede the development of REN001, reduce the productivity of our employees, disrupt our supply chains, delay our clinical trials, reduce our access to capital or limit our business development activities, will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this “Risk Factors” section.

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 Phase 1b studies of REN001 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, REN001 and any future product candidates may be harmed, which could harm our business, operating results, prospects, or financial condition.

If the market opportunities for REN001 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 REN001 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 REN001 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 REN001, 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, 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 REN001, if approved. Further, even if we obtain significant market share for REN001 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 REN001 in the future. We may expend our limited resources to pursue a particular indication or formulation for REN001 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 REN001. As a result, we may fail to generate additional clinical development opportunities for REN001 for a number of reasons, including, REN001 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 REN001 for PMM to regulatory approval, we plan to conduct several clinical trials for REN001 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 forgo 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 REN001. Furthermore, research programs to identify additional indications for REN001 require substantial technical, financial, and human resources. We may also pursue additional formulations for REN001 such as a tablet form. 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 REN001 is also subject to approval.

We expect to submit a Marketing Authorization Application (MAA) to the EMA for approval of REN001 in the European Union (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 EMA's Committee for Medicinal Products for Human Use, 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 REN001 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 REN001 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 REN001 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 REN001 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 REN001, 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 REN001 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 REN001. To the extent we rely on third parties to commercialize REN001, 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 REN001 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 REN001 or any future product candidates.

If we receive regulatory approval for REN001 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 requires 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 REN001 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 REN001 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 REN001 and any future product candidates, REN001 and any future product candidates may not gain market acceptance among physicians, patients, healthcare payors and others in the medical community.

REN001 and any future product candidates may not be commercially successful. The commercial success of REN001 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 REN001 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 REN001 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 REN001 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 REN001 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 REN001 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 REN001, 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 REN001 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 REN001 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 REN001 and any future product candidates, which could make it difficult for us to sell REN001 and any future product candidates profitably.

Successful sales of REN001 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 REN001 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 REN001 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 REN001 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 REN001 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 REN001 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 REN001 in the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for REN001, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly 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 REN001 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, legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act of 2017 (the Tax Act), included a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." 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. Thus, the Affordable Care Act will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. 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 through 2031. However, COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2022. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% 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. In addition, Congress is considering additional health reform measures.

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, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to drug pricing in an effort to implement several of the administration's proposals. As a result, the FDA concurrently released a final rule and guidance in September 2020 providing pathways for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden Administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1,

2021. As a result of litigation challenging the Most Favored Nation model, on December 27, 2021, CMS published a final rule that rescinded the Most Favored Nation Model interim final rule. 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. No legislation or administrative actions have been finalized to implement these principles. It is unclear whether these 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. This could reduce the ultimate demand for REN001, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition, and prospects.

We cannot predict the likelihood, nature, or extent of health reform initiatives that may arise from future legislation or administrative action, particularly as a result of the new presidential administration. 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. In addition, it is possible that additional governmental action will be taken in response to the COVID-19 pandemic. 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 REN001, if approved.

A variety of risks associated with marketing REN001 and any future product candidates internationally could materially adversely affect our business.

We plan to seek regulatory approval for REN001 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, 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 REN001. We believe the key competitive factors that will affect the development and commercial success of REN001 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. Astellas is also developing a PPARδ agonist for PMM and has announced that it has initiated a Phase 2/3 trial in April 2021. Other companies are developing therapies for mitochondrial diseases, including Abliva AB, Cyclerion Therapeutics, Inc., Khondrion B.V. and Stealth Bio Therapeutics Corp.

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 LC-FAOD patients. 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 REN001 are likely to be efficacy, safety, and convenience.

Even though we have obtained orphan drug designation for REN001 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 REN001. 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 REN001 for the treatment of PMM and LC-FAOD in the United States and LCHAD and MELAS in the EU, if we receive approval for REN001 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 REN001, 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 REN001.

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 REN001 for the treatment of PMM, 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 clinical 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 REN001 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 REN001 could delay the development and commercialization of REN001 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 and San Diego, California, and Sandwich, United Kingdom. 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 December 31, 2021, we had 34 employees, 24 of whom are 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 REN001 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 REN001 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 REN001 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 REN001 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 REN001 and begin commercializing those products in the United States, the EU and other countries, our potential exposure under the laws of such countries 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; 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 REN001 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 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; loss of customers or sales; 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 (commonly known as processing) sensitive data, including personal data, 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 subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contracts, and other obligations that govern the processing of Sensitive Data by us and on our behalf.

In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations that govern the processing of health-related and other personal data could apply to our operations or the operations of our partners. We may obtain health data from third parties that is subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to penalties if we violate HIPAA. In addition to HIPAA, the Federal Trade Commission (FTC) enforces data privacy under Section 5 of the Federal Trade Commission Act against companies for failing to take appropriate steps to keep consumers' personal data secure. Individually identifiable health data is considered sensitive data that merits stronger safeguards, so the FTC could bring action against us if it felt the security measures we use are not reasonable or appropriate under the circumstances.

At the state level, California recently enacted the CCPA, which became effective on January 1, 2020 and creates new individual privacy rights for California consumers (as defined in the law). The CCPA also places increased privacy and security obligations on entities handling certain personal data of consumers or households. Further, the CPRA was recently passed in California. The CPRA, which goes into effect on January 1, 2023, will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Additional compliance investment and potential business process changes may be required for the CPRA and other recently passed laws, including in Virginia, the Consumer Data Protection Act (CDPA), which goes into effect on January 1, 2023 and the Colorado Privacy Act (CPA), which goes into effect on July 1, 2023. The CCPA, CPRA, CDPA, CPA, and other similar laws pending in several states may impact our business activities and exemplify the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

Outside the United States, an increasing number of laws, regulations, and industry standards apply to data privacy and security. For example, the EU GDPR and the UK GDPR impose strict requirements for processing personal data. For example, under the EU GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines of up to 20 million euros or 4% of annual global revenue, whichever is greater. Further, individuals may initiate litigation related to processing.

Certain jurisdictions have enacted data localization laws and cross-border personal data transfer laws, which could make it more difficult to transfer information across jurisdictions (such as transferring or receiving personal data that originates in the EU or in other foreign jurisdictions). Existing mechanisms that facilitate cross-border personal data transfers may change or be invalidated. For example, absent appropriate safeguards or other circumstances, the EU GDPR generally restricts the transfer of personal data to countries outside of the EEA that the European Commission does not consider to provide an adequate level of data privacy and security, such as the United States. The European Commission released a set of "Standard Contractual Clauses" (SCCs) that are designed to be a valid mechanism to facilitate personal data transfers out of the EEA to these jurisdictions. Currently, these SCCs are a valid mechanism to transfer personal data outside of the EEA, but there exists some uncertainty regarding whether the SCCs will remain a valid mechanism. Additionally, the SCCs impose additional compliance burdens, such as conducting transfer impact assessments to determine whether additional security measures are necessary to protect the at-issue personal data. In addition, Switzerland and the UK similarly restrict personal data transfers outside of those jurisdictions to countries such as the United States that do not provide an adequate level of personal data protection, and certain countries outside Europe (e.g., China) have also passed or are considering laws requiring local data residency or otherwise impeding the transfer of personal data across borders, any of which could increase the cost and complexity of doing business. If we cannot implement a valid compliance mechanism for cross-border data transfers, we may face increased exposure to regulatory actions, substantial fines, and injunctions against processing or transferring personal data from Europe or other foreign jurisdictions. The inability to import personal data to the United States could significantly and negatively impact our business operations, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere; limiting our ability to collaborate with parties that are subject to such cross-border data transfer or localization laws; or requiring us to increase our personal data processing capabilities and infrastructure in foreign jurisdictions at significant expense.

Our obligations related to data privacy and security are quickly changing in an increasingly stringent fashion, creating some uncertainty as to the effective future legal framework. 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 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. In addition, these obligations may require us to change our business model.

Although we endeavor to comply with all applicable data privacy and security obligations, we may at times fail (or be perceived to have failed) to do so. 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 and compliance posture. For example, any failure by a third-party processor to comply with applicable law, regulations, or contractual obligations could result in adverse effects, including inability to or interruption in our ability to operate our business and proceedings against us by governmental entities or others. If we fail, or are perceived to have failed, to address or comply with 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-related 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, as relevant, 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 EMA and a separate MA will be required to market our product candidates in GB, including REN001 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 REN001 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 may be additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period. Further, should the UK 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 REN001 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. 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, 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 REN001 and any future product candidates.

We face an inherent risk of product liability as a result of the clinical testing of REN001 and any future product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if REN001 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 REN001. 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 REN001 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 REN001 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 9, *Income Taxes* of Notes to Consolidated Financial Statements 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. For example, California imposed limits on the usability of California state NOLs and certain tax credits to offset California taxable income and California tax, respectively, in tax years beginning after 2019 and before 2023, but has recently changed its law to eliminate those limitations for the 2022 tax year.

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, proposals have recently been made in Congress to make various changes to the federal corporate income tax rules, although they have not yet been enacted. 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, 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.

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 REN001, 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 REN001.

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 REN001.

We currently rely on, and intend to continue relying on, third-party CROs in connection with our clinical trials for REN001. 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 REN001 and any future product candidates. As a result, our financial results and the commercial prospects for REN001 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 REN001 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 REN001 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 REN001 used in our current product format and we rely on single-source suppliers for clinical supply of API and drug product of REN001. 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 REN001 or commercialize it, if approved. Further, any delay in identifying and qualifying a manufacturer for commercial production could delay the potential commercialization of REN001 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 REN001 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 REN001 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 REN001 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 REN001and 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 REN001 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 REN001 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 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 REN001, 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 REN001, any future product candidates, and other proprietary technologies we develop. If we are unable to obtain or maintain patent protection with respect to REN001, 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 REN001 and have licensed rights to a number of U.S. and non-U.S. patents and patent applications for REN001. Some of our owned and licensed patents and patent applications cover or relate to REN001, including composition of matter, uses to treat particular conditions and methods of manufacturing.

We have licensed patents and patent applications from vTv Therapeutics directed to REN001, some of which are expected to expire as early as 2026, absent any patent term adjustments or extensions. In addition, we own pending patent applications directed to REN001. 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 United States Patent and Trademark Office (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 REN001, which are set to expire in 2026, absent any patent term adjustments or extensions.

If we do not obtain patent term extension for REN001, our business may be materially harmed.

Depending upon the timing, duration, and specifics of any FDA marketing approval of REN001, 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 REN001 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 REN001. 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 REN001, 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 REN001, 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 REN001, 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 REN001, 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 REN001 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 REN001 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 REN001 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 REN001 and any future product candidates. Furthermore, even if they are unchallenged, our patents may not adequately protect our intellectual property, provide exclusivity for REN001 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 REN001 or any future product candidates is threatened, it could dissuade companies from collaborating with us to develop, or threaten our ability to commercialize, REN001 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 REN001, those patents will likely expire, absent patent term adjustment or extension, before the expiration of any regulatory exclusivity period that we may receive for REN001. We also own pending patent applications directed to polymorphs of REN001. We cannot be certain that the claims in our pending patent applications directed to the polymorph of REN001 will be considered patentable by the USPTO or by patent offices in foreign countries, or that the claims in any of our issued patents will be considered valid 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 REN001, 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 REN001, 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. 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.

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 REN001 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 REN001. 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, REN001 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 REN001. 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. Where 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 REN001. 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, REN001. 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 REN001.

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 REN001, 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 REN001 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 REN001.

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, and there may be additional delays in such proceeding due to the ongoing COVID-19 pandemic. 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 REN001 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 REN001.

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 of 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 REN001. 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 REN001, 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 REN001 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 REN001 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 REN001 to market and be precluded from developing, manufacturing or selling REN001.

We do not always conduct independent reviews of pending patent applications of 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, REN001, and any future product candidates or the use of REN001 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 REN001 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 REN001. 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 REN001. 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 REN001, 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 REN001 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 unable to be obtained, challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential 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 REN001 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, it 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 REN001 or any future clinical trials we may conduct for any future product candidates, or changes in the development status of REN001 or any future product candidates;
- acceptance by the FDA and EMA of data from our global Phase 2b study or any future clinical trials we conduct;
- any delay in our regulatory filings for REN001 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 REN001 and any future product candidates;
- changes in laws or regulations applicable to REN001 and any future product candidates, including but not limited to clinical trial requirements for approvals;

- our failure to commercialize REN001 and any future product candidates;
- the failure to obtain coverage and adequate reimbursement of REN001 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 REN001 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 the COVID-19 pandemic.

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 control 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 $1.07 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. Commencing with our fiscal year ending December 31, 2022, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. We may experience difficulty in meeting these reporting requirements in a timely manner.

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.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the Securities and Exchange Commission (the SEC) or other regulatory authorities.

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, 2021, there were 24,457,838 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 13,460,408 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.

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 REN001. Our ability to obtain clinical supplies of REN001 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 Sensitive 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 collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (commonly known as processing) sensitive data, including personal data, 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). We may rely upon third parties service providers and technologies to operate critical business systems to process Sensitive Data in a variety of contexts, including, without limitation, third-party providers of cloud-based infrastructure, encryption and authentication technology, employee email, and other functions. Our ability to monitor these third parties' cybersecurity practices is limited, and these third parties may not have adequate information security measures in place. We may share or receive Sensitive Data with or from third parties.

Cyberattacks, malicious internet-based activity, and online and offline fraud are prevalent and continue to increase. These threats are becoming increasingly difficult to detect. These threats come from a variety of sources. In addition to traditional computer "hackers," threat actors, sophisticated nation-states, and nation-state-supported actors now engage in attacks. Despite the implementation of security and back-up measures, our internal computer, server, and other information technology systems as well as those of third-parties upon which we rely, may be vulnerable to damage from physical or electronic break-ins, malicious code (such as computer viruses or bugs), actions or inactions 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), and other cyberattacks or disruptive incidents that could result in unauthorized access to, use or disclosure of, corruption of, or loss of Sensitive Date, and could subject us to significant liabilities and regulatory and enforcement actions, and contractual violations, or reputational damage. For example, 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.

Ransomware attacks, including those perpetrated by organized criminal threat actors, nation-states, and nation-state-supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, loss of data and income, 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. Similarly, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain or our third-party partners' supply chains have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems (including our products) or the third-party information technology systems that support us and our services. Further, the COVID-19 pandemic and our remote workforce poses increased risks to our information technology systems and Sensitive Data, as more of our employees work from home, utilizing network connections outside our premises.

Any of the previously identified or similar threats could cause a security incident or other interruption. A security incident or other interruption could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to Sensitive Data. A security incident or other interruption could disrupt our ability (and that of third parties upon whom we rely) to provide our products. While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We may be unable in the future to detect vulnerabilities in our information technology systems because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after a security

incident has occurred. Despite our efforts to identify and remediate vulnerabilities, if any, in our information technology systems, our efforts may not be successful. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities.

If we or third-parties upon which we rely were to suffer a security incident, we may have to notify relevant stakeholders. Such disclosures are costly, and the disclosures or the failure to comply with such requirements could lead to adverse consequences. These consequences may include government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing 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 REN001 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 events relating to their computer systems 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.

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 1,400 square feet of space for an office in the UK under an agreement that expires in November 2022. 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 17, 2022, there were 24,458,550 shares of our common stock outstanding held by approximately 30 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.

Issuer Purchases of Equity Securities

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, 2021, 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 REN0001 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, REN001, is a potent and selective agonist of the PPARδ. REN001 has been shown to increase transcription of genes involved in mitochondrial function and increase fatty acid oxidation, and may increase production of new mitochondria.

The PPAR family of nuclear hormone receptors 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. REN001 was studied in healthy volunteers with one leg immobilized to produce muscle atrophy. Compared to placebo, administration of REN001 resulted in statistically significant increases in expression of genes involved in mitochondrial oxidative phosphorylation, and statistically significant improvements in

muscle strength. REN001 was also studied in an open-label trial in patients with PMM. In this trial, administration of REN001 improved function, reduced symptoms, and increased expression of genes involved in mitochondrial activity.

As a PPARδ agonist, REN001 may benefit patients with genetic mitochondrial myopathies who experience weakness, fatigue, or deterioration in muscle due to impaired mitochondrial energy production. We are currently developing REN001 in rare genetic diseases that typically present with myopathy and have high unmet medical needs, including PMM and LC-FAOD. 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.

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 REN001. 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 $39.8 million and $19.5 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $84.7 million, and cash, cash equivalents and short-term investments of $147.7 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, protect our intellectual property and incur additional expenses as a result of operating as a public company.

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 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 resulting from the ongoing COVID-19 pandemic, 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, 2021 will enable us to fund our operating expenses and capital expenditure requirements through our planned near-term clinical milestones.

We do not own or operate manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of REN001 for preclinical studies and clinical trials, as well as for commercial manufacturing if REN001 obtains marketing approval. We also rely, and expect to continue to rely, on third parties to manufacture, package, label, store, and distribute REN001, if marketing approval is obtained. We believe that this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment, and personnel while also enabling us to focus our expertise and resources on the development of REN001.

COVID-19

The COVID-19 pandemic continues to evolve, and we will continue to monitor the COVID-19 situation closely. The extent of the impact of COVID-19 on our business, operations and clinical development timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the pandemic, including new

variants of the virus, and its impact on our clinical trial enrollment, trial sites, contract research organizations, third-party manufacturers, and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. For example, our Phase 1b study of REN001 in PMM patients was closed early as a result of COVID-19, and we may face future clinical trial disruptions. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. As a result of COVID-19, we have taken precautionary measures in order to minimize the risk of the virus to our employees and the communities in which we operate. While we have experienced impacts to our clinical development activities as a result of COVID-19 as set forth in this Annual Report, there has been a minimal disruption to date in our ability to ensure the effective operation of our business. We will continue to actively monitor the rapidly evolving situation related to COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with whom we do business. At this point, the extent to which the COVID-19 pandemic may affect our business, operations and clinical development timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain.

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 REN001, 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 payment of $3.0 million and issued to vTv Therapeutics shares of our common stock subject to antidilution provisions under the agreement. Upon the achievement of certain pre-specified development and regulatory milestones, we are also required to pay vTv Therapeutics up to an aggregate of $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 pay vTv Therapeutics tiered royalty payments 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. In July 2021, a milestone under the vTv License Agreement was achieved, and we made a payment of $2.0 million to vTv Therapeutics.

Components of Our Results of Operations

Operating Expenses

Research and Development Expenses

Research and development expenses primarily relate to preclinical and clinical development of REN001. 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 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, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Clinical and regulatory	$ 14,863	$ 7,894
Contract manufacturing cost	6,450	4,254
Nonclinical	2,339	4,026
Research and development-other expense (income)	4,517	(230)
Total	$ 28,169	$ 15,944

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, compliance and human resource and other

administrative functions. General and administrative expense also includes 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 significantly 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.

Critical Accounting Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with 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 and clinical trials (including amounts paid to clinical research organizations and other professional services), license fees, salaries and employee benefits.

Research and development costs, comprising payments for work performed by third party contractors, laboratories, participating clinical trial sites and others. 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 reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We accrue and expense clinical trial activities performed by third parties based upon estimates of the proportion of work completed over the life of the individual study and patient enrollment rates in accordance with agreements established with clinical research organizations, clinical trial sites and other vendors associated with the clinical trials. We determine the estimates by reviewing contracts, vendor agreements and purchase orders and through discussions with internal clinical personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services. We make estimates of accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments, if necessary. 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.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result

in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Accrued research and development expenses year-over-year have increased by approximately 10% due to increased activities in our research and development as we advance our pipeline, and management anticipates the expense to continue to increase in 2022.

Stock-Based Compensation

We recognize stock-based compensation expense for grants under our 2014 and 2021 Equity Incentive Plans and employee stock purchase plan (ESPP). We account for all stock-based awards granted to employees and board of 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. Since we have recently completed our IPO and do not have sufficient trading history our common stock the expected volatility assumption is based on volatilities of a peer group of similar companies whose share prices are publicly available. 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 performance 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 an accumulative expense catch-up, with remaining expense amortized over the remaining service period.

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 appropriate 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 2021 to attract and retain key scientific or management personnel. We anticipate an increase in our stock-based compensation expense in 2022.

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.

Results of Operations

Comparison of Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020 (in thousands):

	Year ended December 31,		
	2021	2020	Change
Operating expenses:			
Research and development	$ 28,169	$ 15,944	$ 12,225
General and administrative	11,649	3,608	8,041
Total operating expenses	39,818	19,552	20,266
Loss from operations	(39,818)	(19,552)	(20,266)
Other income	48	87	(39)
Net loss	$ (39,770)	$ (19,465)	$ (20,305)

Operating Expenses

Research and Development Expenses

Research and development expenses increased by $12.2 million during 2021 compared to 2020. This increase was primarily due to an increase of $5.7 million related to clinical and manufacturing activities for REN0001, $3.0 million in personnel related costs due to support growth in our development activities, and $2.0 million in milestone costs under the vTv License Agreement, offset by a $1.5 million tax rebate received from the UK government in 2020 for qualifying research expense incurred in the UK.

General and Administrative Expenses

General and administrative expenses increased by $8.0 million during 2021, compared to 2020 primarily as a result of our IPO in April 2021 and increased operating activities necessary to operate as a public company, which consisted of increases in personnel-related expenses of $5.1 million, insurance premiums of $1.1 million, and outside professional services of $1.3 million.

Other Income

Other income for the years ended December 31, 2021 and 2020 was immaterial.

Liquidity and Capital Resources

Since inception, we have incurred operating losses and negative cash flows from operations and have funded our operation 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.

Cash Flows

The following table summarizes our cash flows for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Net cash used in operating activities	$ (37,983)	$ (18,536)
Net cash (used in) provided by investing activities	(23,376)	7,376
Net cash provided by financing activities	132,406	47,272
Net increase in cash and cash equivalents	$ 71,047	$ 36,112

Operating Activities

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 our 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.

Net cash used in operating activities for the year ended December 31, 2020 was $18.5 million, consisting primarily of our net loss of $19.5 million, partially offset by a $0.5 million net change in operating assets and liabilities and $0.5 million in non-cash adjustment primarily consisting of stock-based compensation expense.

Investing Activities

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.

Net cash provided investing activities for the year ended December 31, 2020 was $7.4 million consisting primarily of proceeds received from maturities of available for sale short term investments.

Financing Activities

Net cash provided by financing activities in 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.

Net cash provided by financing activities in the year ended December 31, 2020 was $47.3 million, consisting primarily of $47.2 million of net proceeds from the issuance of Series B convertible preferred stock and $0.1 million of proceeds from the exercise of stock options.

Funding Requirements

To date, we have not generated any revenue. We do not expect to generate revenue from product sales unless and until we obtain regulatory approval and commercialize REN001 or any future product candidates, and we do not know when, or if at all, that will occur. We will continue to require additional capital to develop REN001 and fund operations for the foreseeable future. Our primary uses of cash are to fund our operations, which consist primarily of research and development expenses related to our clinical development programs, and to a lesser extent, general and administrative expenses. We expect our expenses to continue to increase in connection with our ongoing activities as we continue to advance REN001 through clinical development and regulatory approval and additional costs associated with operating as

a public company. 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 activities.

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 resulting from the ongoing COVID-19 pandemic, 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.

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

- the scope, progress, results and costs of clinical trials and preclinical studies for REN001;
- 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 REN001;
- 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.

In December 2020 and March 2021, we raised net proceeds of $94.4 million from the sale of Series B convertible preferred stock. In April 2021, we raised net proceeds of approximately $84.6 million in connection with our IPO. As of December 31, 2021, we had $147.7 million in cash, cash equivalents and short-term investments. We believe, based upon our current operating plan, that our cash, cash equivalents and short-term investments as of December 31, 2021 will be sufficient to fund our planned operations into 2024.

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, 2021.

vTv License Agreement. See Note 8 of Notes to Consolidated Financial Statements included in this Annual Report for information, including the milestone payments, associated with the vTv License Agreement.

Operating Leases. See Note 10 of Notes to Consolidated Financial Statements included in this Annual Report for information, including the future operating lease minimum payments.

Performance bonus. See Note 7 of Notes to Consolidated Financial Statements included in this Annual Report for information, including the maximum payout.

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

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, 2021 and 2020, 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, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

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 23, 2022

RENEO PHARMACEUTICALS, INC.

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

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 124,660	$ 53,613
Short-term investments	23,010	—
Prepaid expenses and other current assets	6,064	1,412
Total current assets	153,734	55,025
Property and equipment, net	212	69
Other non-current assets	78	127
Total assets	$ 154,024	$ 55,221
Liabilities, convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 2,022	$ 908
Accrued expenses	4,180	3,672
Total current liabilities	6,202	4,580
Deferred rent	167	36
Performance award	444	—
Total liabilities	6,813	4,616
Commitments and contingencies		
Series A convertible preferred stock, $0.0001 par value; zero and 24,302,472 shares authorized and outstanding at December 31, 2021 and 2020, respectively; liquidation preference of $0 and $49,127 at December 31, 2021 and 2020, respectively	—	45,652
Series B convertible preferred stock, $0.0001 par value; zero and 46,881,028 shares authorized at December 31, 2021 and 2020, respectively; zero and 23,440,514 shares issued and outstanding at December 31, 2021 and 2020, respectively; liquidation preference of $0 and $47,385 as of December 31, 2021 and 2020, respectively	—	47,068
Stockholders' equity (deficit):		
Common stock, $0.0001 par value; 200,000,000 and 105,000,000 shares authorized at December 31, 2021 and 2020, respectively; 24,457,838 and 24,455,390 shares issued and outstanding at December 31, 2021, respectively; and 2,053,070 shares issued and outstanding at December 31, 2020	3	—
Additional paid-in capital	231,902	2,843
Accumulated deficit	(84,728)	(44,958)
Accumulated other comprehensive income	34	—
Total stockholders' equity (deficit)	147,211	(42,115)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 154,024	$ 55,221

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,	
	2021	2020
Operating expenses:		
Research and development	$ 28,169	$ 15,944
General and administrative	11,649	3,608
Total operating expenses	39,818	19,552
Loss from operations	(39,818)	(19,552)
Other income	48	87
Net loss	(39,770)	(19,465)
Unrealized gain (loss) on short-term investments	34	(3)
Comprehensive loss	$ (39,736)	$ (19,468)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.19)	$ (9.60)
Weighted-average shares used in computing net loss per share, basic and diluted	18,143,487	2,028,198

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									
	Series A		Series B		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount				
Balances, December 31, 2019	**24,302,472**	**$ 45,652**	**—**	**$ —**	**2,008,905**	**$ —**	**$ 2,363**	**$ 3**	**$ (25,493)**	**$ (23,127)**
Issuance of series B convertible preferred stock, net of issuance costs of $317	—	—	23,440,514	47,068	—	—	—	—	—	—
Stock based compensation	—	—	—	—	—	—	393	—	—	393
Stock option exercise	—	—	—	—	44,165	—	87	—	—	87
Other comprehensive loss	—	—	—	—	—	—	—	(3)	—	(3)
Net loss	—	—	—	—	—	—	—	—	(19,465)	(19,465)
Balances, December 31, 2020	**24,302,472**	**$ 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 public offering, net of offering costs of $2,654	—	—	—	—	6,250,000	1	84,532	—	—	84,533
Stock-based compensation	—	—	—	—	—	—	3,891	—	—	3,891
Stock option exercise	—	—	—	—	236,067	—	507	—	—	507
Employee stock purchase plan	—	—	—	—	8,624	—	53	—	—	53
Net loss	—	—	—	—	—	—	—	—	(39,770)	(39,770)
Other comprehensive loss	—	—	—	—	—	—	—	34	—	34
Balances, December 31, 2021	**—**	**$ —**	**—**	**$ —**	**24,455,390**	**$ 3**	**$ 231,902**	**$ 34**	**$ (84,728)**	**$ 147,211**

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,	
	2021	2020
Cash flows from operating activities		
Net loss	$ (39,770)	$ (19,465)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	50	37
Amortization/accretion on short-term investments	202	(17)
Changes in the fair value of performance award	444	—
Loss on disposal of property, plant & equipment	—	2
Stock-based compensation	3,891	393
Changes in operating assets and liabilities:		
Accounts payable, accrued expenses and other	1,780	1,486
Prepaid expenses and other assets	(4,711)	(967)
Deferred rent	131	(5)
Net cash used in operating activities	(37,983)	(18,536)
Cash flows from investing activities		
Purchases of property and equipment	(198)	(24)
Purchase of available-for-sale short-term investments	(31,406)	—
Proceeds from maturities of available-for-sale short-term investments	8,228	7,400
Net cash (used in) provided by investing activities	(23,376)	7,376
Cash flows from financing activities		
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	47,238	47,185
Proceeds from initial public offering, net of offering costs	84,612	—
Proceeds from issuance of common stock pursuant to equity award plans	556	87
Net cash provided by financing activities	132,406	47,272
Effect of exchange rates on cash and cash equivalents		—
Net increase in cash and cash equivalents	71,047	36,112
Cash and cash equivalents, beginning of period	53,613	17,501
Cash and cash equivalents, end of period	$ 124,660	$ 53,613
Supplemental cash flow information:		
Vesting of unvested exercised options	$ 4	$ —
Unpaid Series B convertible preferred stock issuance costs	$ —	$ 117
Costs incurred in connection with initial public offering included in accrued expenses	$ —	$ 33
Property and equipment in accounts payable	$ —	$ 5

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 REN001, a novel oral peroxisome proliferator-activated receptor (PPAR) agonist.

Reverse Stock Split

On April 5, 2021, the Company effected a 1-for-4.4748 reverse stock split of its common stock. The par value and the authorized number of shares of the common stock were not adjusted as a result of the reverse stock split. The reverse stock split resulted in an adjustment to the Series A and Series B convertible preferred stock conversion prices to reflect a proportional decrease in the number of shares of common stock to be issued upon conversion. The accompanying consolidated financial statements and notes to the consolidated financial statements give retroactive effect to the reverse stock split for all periods presented.

Initial Public Offering

On April 13, 2021, the Company completed an initial public offering (IPO) of its common stock. In connection with its IPO, the Company issued and sold 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.

Liquidity

The Company has incurred significant losses and negative cash flows from operations. As of December 31, 2021, the Company had cash, cash equivalents and short-term investments of $147.7 million and an accumulated deficit of $84.7 million. The Company had a net loss of $39.8 million and used cash of $38.0 million for operating activities for the year ended December 31, 2021. In accordance with Accounting Standards Codification (ASC) Topic 205-40, *Presentation of Financial Statements - Going Concern*, management is required to perform a two-step analysis over the Company's 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 for a period of 12 months from the date the consolidated financial statements are issued. If management concludes that substantial doubt is raised, management is also required to consider whether its plans alleviate that doubt.

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. As a result, the Company will need to raise capital through public or private equity or debt financings, government or other third-party funding, collaborations, strategic alliances and licensing arrangements or a combination of these.

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 materially harm 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 and disruptions to, and volatility in, financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic, as well as 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.

As of December 31, 2021, the Company had $147.7 million in cash, cash equivalents and short-term investments, which management believes will be sufficient to fund operations for at least one year from date on which this Annual Report on Form 10-K is issued.

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 Reneo 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 (FDA) 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, REN001, ability to obtain regulatory approval of REN001, 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.

The Company's business has been and could continue to be adversely affected by the evolving COVID-19 pandemic. For example, the COVID-19 pandemic has resulted in and could result in delays to the Company's clinical trials for numerous reasons including additional delays or difficulties in enrolling patients, diversion of healthcare resources away from the conduct of clinical trials, interruption or delays in the operations of the FDA or other regulatory authorities, and delays in clinical sites receiving the supplies and materials to conduct the Company's clinical trials. At this time, the extent to which the COVID-19 pandemic impacts the Company's business will depend on future developments, which are highly uncertain and cannot be predicted.

Segment Reporting

The Company operates and manages its business as one operating segment, which is the business of developing novel therapies for rare genetic mitochondrial diseases. The Company's chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for allocating and evaluating financial performance.

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, 2021 and 2020, 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, and 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, 2021, the Company's investments consisted of U.S. treasury bills and they were 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 in stockholders' 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-temporarily 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, 2021 and 2020.

Money market account balances are included as cash and cash equivalents on the consolidated balance sheets, which are also disclosed in Note 4, 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, 2021 and 2020.

Leases

Leases are accounted for under ASC Topic 840, *Leases*, and classified as operating leases. The Company records rent expense on a straight-line basis over the term of the lease. The difference between rent payments and straight-line rent expense is recorded as deferred rent.

Convertible Preferred Stock

The Company records convertible preferred stock at fair value on the dates of issuance, net of issuance costs. Prior to the IPO, upon the occurrence of certain potential events that would have been outside the Company's control, including a "deemed liquidation event" such as a merger, acquisition and sale of all or substantially all of the Company's assets, holders of the convertible preferred stock could cause redemption for cash. Therefore, convertible preferred stock was classified as temporary equity (mezzanine) on the consolidated balance sheets as events triggering the liquidation preferences are not solely within the Company's control. All convertible preferred stock was converted to common stock in connection with the IPO in April 2021.

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 and clinical trials (including amounts paid to clinical research organizations and other professional services), license fees, salaries and employee benefits.

The Company records accruals for estimated research and development costs, comprising payments for work performed by third party contractors, laboratories, participating clinical trial sites and others. Some of these contractors bill monthly based on actual services performed, while others bill periodically based upon achieving certain contractual milestones. Payments made in advance of or after performance are reflected in the consolidated balance sheets as prepaid expenses or accrued liabilities, respectively. Up-front costs, such as costs associated with setting up clinical trial sites for participation in the trials, are expensed immediately once the set-up has occurred as research and development expenses. The Company accrues the costs incurred under agreements with these third parties based on estimates of actual work completed in accordance with the respective agreements. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company adjusts accrued expenses or prepaid expenses accordingly, which impact research and development expenses.

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.

Patent Costs

Costs related to filing and pursuing patent applications are expensed as incurred, as recoverability of such expenditures is uncertain. These costs are included in general and administrative expenses.

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 on the basis of 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 UK. As of December 31, 2021, 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 board of 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 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, 2021 and 2020, total foreign currency gains and losses were a loss of $0.3 million and gain of $0.1 million, respectively.

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 loss for the years ended December 31, 2020 and 2021, therefore, excluded all outstanding common stock equivalents including the Company's stock options, performance-based and market-based RSUs, employee stock purchase, and convertible preferred stock, from the diluted net loss per share calculation for the years ended December 31, 2021 and 2020 because such shares are anti-dilutive.

Historical outstanding anti-dilutive securities not included in the diluted net loss per share calculation include the following:

	As of December 31,	
	2021	2020
Convertible preferred stock (as converted)	—	10,669,291
Common stock options outstanding	4,215,643	935,478
Unvested restricted stock units	299,500	—
Total	4,515,143	11,604,769

New Accounting Pronouncements

Recent Accounting Pronouncements Not Yet Adopted

In December 2019, the Financial Accounting Standards Board (FASB) issued Accounting Standard Update (ASU) 2019-12, *Simplifying the Accounting for Income Taxes*. The standard simplifies the accounting for income taxes, eliminates certain exceptions within ASC Topic 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 is in the process of evaluating the impact of the application of this ASU on its consolidated financial statements.

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.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 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 (the lease liability) and a right-of-use 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 (Topic 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 U.S. GAAP. This ASU is effective for annual reporting periods beginning after December 15, 2021, and interim periods within fiscal years beginning after December 15, 2022, with early adoption permitted. The Company will adopt the standard using the modified retrospective method and elect a package of practical expedients for leases that commenced prior to January 1, 2022 and will not reassess: (i) whether any expired or existing contracts are or contain leases; (ii) lease classification for any expired or existing leases; and (iii) initial direct costs capitalization for any existing leases. The Company is finalizing its assessment of the impact of this guidance and anticipates establishing liabilities and corresponding right-of-use assets on its consolidated balance sheets with no material impact to its consolidated statements of operation and comprehensive loss.

Other accounting standard updates effective for interim and annual periods beginning after December 31, 2021 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 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 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 and convertible preferred stock purchase right liability are subject to fair value measurements on a recurring basis.

The Company categorized its money market funds as Level 1, using the quoted prices in active markets. Commercial papers are valued using level 2 significant other observable inputs. The Company considers all highly liquid investments purchased with a remaining maturity of three months or less to be cash equivalents. 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.

For the years ended December 31, 2021 and 2020, gains or losses realized on the sale of investments were not material. Investments are reviewed periodically to identify possible other-than-temporary impairments. As the Company has the ability and intent 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 November 2020, the Company hired a new chief executive officer who 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 7. 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, 2021 and 2020.

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 papers	—	23,010	—	23,010
Total	$ 118,535	$ 23,010	$ —	$ 141,545
Liabilities				
Performance award	$ —	$ —	$ 444	$ 444
Total	$ —	$ —	$ 444	$ 444

The recurring fair value measurement of the Company's assets and liabilities measured at fair value at December 31, 2020 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:				
Money market investments	$ 49,632	$ —	$ —	$ 49,632
Total	$ 49,632	$ —	$ —	$ 49,632

The following table sets forth a summary of changes in the fair value of the Company's performance award liability (in thousands):

Balance as of January 1, 2021	$ —
Expense recorded upon consummation of the IPO	590
Change in fair value	(146)
Balance as of December 31, 2021	$ 444

4. Property and Equipment, Net

Property and equipment, net, consisted of the following (in thousands):

	As of December 31,	
	2021	2020
Computer, software and office equipment	$ 315	$ 122
Leasehold improvements	30	30
Total property and equipment, gross	345	152
Less: accumulated depreciation and amortization	(133)	(83)
Total property and equipment, net	$ 212	$ 69

Depreciation and amortization expense related to property and equipment was immaterial for the years ended December 31, 2021 and 2020, respectively.

5. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	As of December 31,	
	2021	2020
Accrued clinical and regulatory	$ 1,236	$ 1,019
Accrued contract manufacturing cost	1,482	1,443
Accrued compensation	1,027	888
Accrued research and development-other	435	322
Total accrued expenses	$ 4,180	$ 3,672

6. Convertible Preferred Stock and Stockholders' Deficit

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, 2021, there were no shares of preferred stock outstanding.

Series A Convertible Preferred Stock

As of December 31, 2020, there were 24,302,472 shares of Series A convertible preferred stock outstanding with a liquidation preference of $49.1 million. In connection with the IPO (Note 1) in April 2021, all outstanding shares of Series A convertible preferred stock were converted into 5,430,957 shares of common stock.

Series B Convertible Preferred Stock

In December 2020, the Company and certain investors entered into a Series B preferred stock purchase agreement, whereby the Company issued 23,440,514 shares of Series B convertible preferred stock at $2.0215 per share for total gross proceeds of approximately $47.4 million, which constituted the closing of the first tranche of the Series B convertible preferred stock. In connection with the closing of the first tranche of Series B convertible preferred stock in December 2020, the Company issued rights to the purchasers for the purchase of an additional 23,440,514 shares of Series B convertible preferred stock (Series B Tranche

Rights). The Company evaluated the Series B Tranche Right and concluded that it was not a free-standing instrument that met the definition of a derivative that required separate accounting.

In March 2021, the Company completed the Series B Tranche Right at $2.0215 per share. A total of 23,440,514 shares of Series B convertible preferred stock were issued for aggregate net proceeds of approximately $47.4 million.

In connection with the IPO in April 2021, all outstanding shares of Series B convertible preferred stock were converted into 10,476,672 shares of common stock.

7. 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 2014 Equity Incentive Plan (2014 Plan). A total of 2,187,524 new shares of common stock were approved to be initially reserved for issuance under the 2021 Plan, which includes 117,639 shares reserved and available for issuance pursuant to the grant of new awards under the 2014 Plan as of the effectiveness of the 2021 Plan and will include any shares subject to stock awards granted under the 2014 Plan that, after the date the 2021 Plan became effective, are forfeited or otherwise become available under the 2014 Plan. Under the 2021 Plan, the Company may grant stock options, stock appreciation rights, restricted stock, restricted stock units, and other awards to individuals who are then employees, officers, directors or consultants of the Company, and employees and consultants of the Company's affiliates. As of December 31, 2021, there were 760,267 shares available for future grant under the 2021 Plan.

Under the 2014 Plan, certain employees may be 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, 2021, 2,447 shares subject to stock options have been early exercised, which vested in January 2022. Cash received in exchange for early exercises of stock options has been recorded as a liability for the early exercise of stock options and were transferred into common stock and additional paid-in capital as the shares vested. As of December 31, 2021, such liability for early exercises of stock options was immaterial.

In October 2021, the Company granted inducement awards, in accordance with Nasdaq Listing Rule 5635(c)(4) (Inducement Awards), in the aggregate amount of 210,000 shares, which included options to purchase 180,000 shares and performance-based restricted stock units (PSUs) of 30,000 shares.

Shares Reserved for Future Issuance

As of December 31, 2021, the Company had reserved shares of its common stock for future issuance as follows:

	Shares Reserved
Common stock options outstanding and unvested restricted stock units	4,515,143
Available for future grants under the 2021 Equity Incentive Plan	970,267
Available for future grants under the 2021 Employee Stock Purchase Plan	234,434
Total shares of common stock reserved	5,719,844

Stock Options

The Company estimates stock awards fair value on the date of grant using the Black-Scholes valuation, with the vesting being subject to service requirements. The Company accounts for forfeitures when they occur.

The following table summarizes stock options as of December 31, 2021, and changes during the year ended December 31, 2021 (in thousands, except share and per share data):

	Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at December 31, 2020	935,478	$ 2.56	7.7	
Granted	3,537,885	$ 6.03		
Exercised	(238,515)	$ 2.13		
Forfeited/Expired	(19,205)	$ 4.54		
Outstanding at December 31, 2021	4,215,643	$ 5.49	8.5	$ 13,530
Vested at December 31, 2021	1,179,617	$ 3.84	7.1	$ 5,553
Exercisable at December 31, 2021	2,695,756	$ 4.50	7.9	$ 8,089

Options exercisable at December 31, 2021 include vested options and options eligible for early exercise. All outstanding options as of December 31, 2021 are expected to vest.

Unrecognized stock-based expense at December 31, 2021 was $11.4 million, which is expected to be recognized over a weighted-average vesting term of 3.0 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,	
	2021	2020
Risk-free interest rate	0.88 %	1.00 %
Expected volatility	78.3 %	71.7 %
Expected term (in years)	6.0	5.8
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 recently completed its IPO and 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.

Performance-Based Restricted Stock Units

In December 2021, the Company granted 169,500 PSUs to employees pursuant to the 2021 Plan and 30,000 PSUs Inducement Awards. 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 date of the award and expense recognition is based on the probability of achieving the performance metric. The Company concluded that achievement of the performance conditions was not probable as of December 31, 2021, and therefore no compensation expense was recognized for the year ended December 31, 2021 in connection with the PSU awards. Compensation cost is adjusted in future periods for subsequent changes in the expected outcome of the performance related conditions.

Market-Based Awards

Restricted Stock Units

In December 2021, the Company granted 100,000 market-based restricted stock units (MRSUs) to an employee pursuant to the 2021 Plan. The MRSUs 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 MRSUs was $6.69 per share. The fair value was $0.4 million based on Monte Carlo simulation model on the grant date. Compensation expense is recognized over the derived service period of 3 years. During the year ended December 31, 2021, the Company recognized $8 thousand of stock-based compensation expense in connection with the MRSUs. As of December 31, 2021, there was $0.4 million of unrecognized compensation expense related to this MRSU.

Performance Award

In November 2020, the Company hired a new chief executive officer who is entitled to receive a Performance Awards 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 Topic 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 compensation cost over the derived service period. During the year ended December 31, 2021, the Company recorded a stock-based compensation expense of $0.4 million.

Employee Stock Purchase Plan

In March 2021, the Company's board of directors adopted the Company's 2021 ESPP, which became effective immediately prior to the execution of the underwriting agreement in connection with the Company's IPO. A total of 243,058 shares of common stock were approved to be initially reserved for issuance under the ESPP. As of December 31, 2021, 8,624 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 was approved and reserved for issuance under the SAYE. No shares have been issued under the SAYE through December 31, 2021.

The stock-based compensation expense related to the ESPP and SAYE for the year ended December 31, 2021 was immaterial.

The following table summarizes stock compensation expense, including expense associated with award modifications that accelerated the recognition of expense for unvested options, reflected in the consolidated statements of operations (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	$ 1,036	$ 165
General and administrative	2,855	228
Total	$ 3,891	$ 393

8. 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 PPARδ agonists and products containing such PPARδ agonists, including REN001, for any therapeutic, prophylactic or diagnostic application in humans. Under the terms of the vTv License Agreement, the Company paid vTv Therapeutics an initial upfront license fee payment of $3.0 million and issued an aggregate of 576,443 shares of its common stock to vTv Therapeutics. The vTv License Agreement was accounted for as an asset acquisition and

the upfront cash payment of $3.0 million and the fair value of common stock of $0.7 million issued to vTv Therapeutics was recorded in research and development expenses, as there was no alternative use for the asset.

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. In July 2021, a milestone under the vTv License Agreement was achieved, and the Company made a payment of $2.0 million to vTv Therapeutics that was recognized as research and development expenses.

9. Income Taxes

The Company's net loss was generated in the following jurisdictions (in thousands):

	Year Ended December 31,	
	2021	2020
Domestic	$ (39,718)	$ (21,291)
Foreign	(52)	1,826
Net Loss	$ (39,770)	$ (19,465)

The components of net deferred taxes consisted of the following (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
NOL carryforwards	$ 13,446	$ 6,488
Credit carryforwards	2,155	663
Compensation accruals	653	179
Other accruals and reserves	35	24
Intangible assets	3,469	3,316
Depreciation	104	—
Other	2	1
Gross deferred tax assets	19,864	10,671
Less valuation allowance	(19,864)	(10,662)
Total deferred tax assets	—	9
Deferred tax liabilities:		
Depreciation	—	(9)
Net deferred tax assets (liabilities)	$ —	$ —

For the years ended December 31, 2021 and 2020, 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, 2021 and 2020, as follows:

	December 31,	
	2021	2020
U. S. Federal statutory income tax rate	21.0 %	21.0 %
UK R&D true-up	(0.1)%	6.5 %
UK permanent items	— %	1.8 %
Other	(1.0)%	(0.1)%
Tax credits, net	3.5 %	2.2 %
GILTI inclusion	(0.5)%	(0.2)%
Valuation allowance	(22.9)%	(31.2)%
Effective tax rate	— %	— %

The Company had federal net operating loss (NOL) carryforwards available of approximately $59.7 million as of December 31, 2021, 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 2018 of $58.1 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, 2021. 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 $3.0 million which carryforward indefinitely.

At December 31, 2021, the Company had federal and state tax credit carry forwards of approximately $4.8 million and $0.3 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, 2021. 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, 2021 was $0.9 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, 2021. 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, 2021, a full valuation allowance of $19.9 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,	
	2021	2020
Beginning balance of unrecognized tax benefits	$ 258	$ 168
Additions based on tax positions related to the current year	2,741	90
Ending balance of unrecognized tax benefits	$ 2,999	$ 258

The amount of the unrecognized tax benefits that would impact the effective tax rate, absent the valuation allowance, would be $3.0 million. Due to the full valuation allowance, the impact, however, is zero. At December 31, 2021 and 2020, 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.

10. Commitments and Contingencies

Operating Leases

In June 2018, the Company leased certain office space for its U.S. headquarters in San Diego, California under a non-cancelable operating lease with terms through July 2023, with an option to extend the terms for the entire premises for a period of five years.

In June 2021, the Company leased 5,137 square feet of office space for its U.S. headquarters in Irvine, California under a non-cancelable operating lease with terms through November 2026. The lease provides for a 3% annual rent increase, five months of abated rent and a tenant improvement allowance of $6.50 per square foot. The total minimum lease payment over the life of the lease is $1.6 million.

The rent expense in the United States for the years ended December 31, 2021 and 2020 totaled $0.4 million and $0.2 million for the years ended December 31, 2021 and 2020, respectively.

In December 2018, the Company leased certain office space for its UK subsidiary under a non-cancelable operating lease with lease terms through November 2021. The Company extended the lease for an additional one year per the terms of the agreement. The rent expense in the UK is immaterial.

Future annual minimum payments under the non-cancelable operating leases are as follows (in thousands):

Year Ending December 31,		
2022	$	501
2023		430
2024		322
2025		332
Thereafter		313
Total minimum lease payments	$	1,898

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, 2021 and 2020, the expense recorded by the Company was immaterial.

11. Subsequent Events

On January 28, 2022, Vineet R. Jindal notified the Company that he will resign as Chief Financial Officer effective March 31, 2022. In connection with Mr. Jindal's resignation, the Company entered into a Transition, Separation and Consulting Agreement with Mr. Jindal (Separation Agreement). Mr. Jindal's resignation and his Separation Agreement is not expected to have material impact on the Company's consolidated financial statements.

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 Chief Executive Officer and our Chief 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 Chief Executive Officer and our Chief Financial Officer have concluded that as of December 31, 2021, 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 Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting

This Annual Report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public 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, 2021 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 will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission in connection with our 2022 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, 2021, and is incorporated herein by reference.

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. 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 will be set forth in our Proxy Statement and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Annual Report:

(1) Financial statements

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.
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 Niall O'Donnell, Ph.D., dated February 1, 2018 (incorporated by reference to Exhibit 10.11 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+	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).
10.4+	Letter Agreement by and between the Registrant and Lon Cardon, Ph.D., dated January 30, 2019 (incorporated by reference to Exhibit 10.18 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+	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).
10.6+	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).
10.7+	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).
10.8+	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).
10.9+	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).

Exhibit Number	Description
10.10+	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).
10.11+*	Reneo Pharmaceuticals, Inc. 2021 Non-Employee Director Compensation Policy, as amended.
10.12+*	Transition, Separation and Consulting Agreement by and between the Registrant and Wendy Johnson, dated December 23, 2021.
10.13+*	Letter Agreement by and between Registrant and Paul W. Hoelscher, dated January 20, 2022.
10.14+*	Transition, Separation and Consulting Agreement by and between the Registrant and Vineet R. Jindal, dated February 2, 2022.
Patent and License Agreements	
10.14#	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).
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).
10.18+	Forms of (i) Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise and (ii) Stock Option Grant Notice - International, Stock Option Agreement - International and Notice of Exercise - International under the Reneo Pharmaceuticals, Inc. 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-254534), filed with the SEC on April 5, 2021).
10.19+	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).

Exhibit Number	Description
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, 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 12, 2021).
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.
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 23, 2022

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 Vineet R. Jindal 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 23, 2022
/s/ Vineet R. Jindal Vineet R. Jindal	Chief Financial Officer (Principal Financial and Accounting Officer)	March 23, 2022
/s/ Michael Grey Michael Grey	Executive Chairman	March 23, 2022
/s/ Lon Cardon Lon Cardon, Ph. D.	Director	March 23, 2022
/s/ Eric Dube Eric Dube, Ph. D.	Director	March 23, 2022
/s/ Paul W. Hoelscher Paul W. Hoelscher	Director	March 23, 2022
/s/ Edward T. Mathers Edward T. Mathers	Director	March 23, 2022
/s/ Bali Muralidhar Bali Muralidhar, M.D., Ph. D.	Director	March 23, 2022
/s/ Niall O'Donnell Niall O'Donnell, Ph. D.	Director	March 23, 2022
/s/ Stacey D. Seltzer Stacey D. Seltzer	Director	March 23, 2022

Exhibit 4.3

DESCRIPTION OF COMMON STOCK

General

The following description summarizes the terms of the common stock of Reneo Pharmaceuticals, Inc., or we, our or us. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description of the matters set forth in this "Description of Common Stock," you should refer to our amended and restated certificate of incorporation and amended and restated bylaws, which are included as exhibits to our Annual Report on Form 10-K, and to the applicable provisions of the Delaware General Corporation Law. Our amended and restated certificate of incorporation authorizes us to issue 200,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share. Our board of directors is authorized, without stockholder approval except as required by the listing standards of The Nasdaq Stock Market LLC, to issue additional shares of our capital stock. In addition, under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock.

Voting Rights

Our common stock is entitled to one vote per share on any matter that is submitted to a vote of our stockholders. Our amended and restated certificate of incorporation does not provide for cumulative voting for the election of directors. Our amended and restated certificate of incorporation establishes a classified board of directors that is divided into three classes with staggered three-year terms. Only the directors in one class will be subject to election by a plurality of the votes cast at each annual meeting of our stockholders, with the directors in the other classes continuing for the remainder of their respective three-year terms.

Economic Rights

Except as otherwise expressly provided in our amended and restated certificate of incorporation or required by applicable law, all shares of common stock have the same rights and privileges and rank equally, share ratably and be identical in all respects for all matters, including those described below.

Dividends. Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of our common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine.

Liquidation Rights. On our liquidation, dissolution or winding-up, the holders of our common stock will be entitled to share equally, identically and ratably in all assets remaining after the payment of any liabilities, liquidation preferences and accrued or declared but unpaid dividends, if any, with respect to any outstanding preferred stock, unless a different treatment is approved by the affirmative vote of the holders of a majority of the outstanding shares of such affected class, voting separately as a class.

No Preemptive or Similar Rights

The holders of shares of our common stock are not entitled to preemptive rights and are not subject to conversion, redemption or sinking fund provisions.

Exchange Listing

Our common stock is listed on the Nasdaq Global Market under the symbol “RPHM.”

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent’s address is 6201 15th Avenue, Brooklyn, New York 11219.

Anti-Takeover Provisions

The provisions of Delaware law, our amended and restated certificate of incorporation and amended and restated bylaws, which are summarized below, may have the effect of delaying, deferring or discouraging another person from acquiring control of our company. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

Certificate of Incorporation and Bylaws

Because our stockholders do not have cumulative voting rights, stockholders holding a majority of the voting power of our shares of common stock will be able to elect all of our directors. Our amended and restated certificate of incorporation and amended and restated bylaws provide that stockholders may only take action at a duly called meeting of stockholders. A special meeting of stockholders may be called by a majority of our board of directors, the chair of our board of directors or our chief executive officer. Our amended and restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors. In accordance with our amended and restated certificate of incorporation, our board of directors is divided into three classes with staggered three-year terms.

The foregoing provisions will make it more difficult for another party to obtain control of us by replacing our board of directors. Since our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change our control.

These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of deterring hostile takeovers or delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, subject to certain exceptions.

Choice of Forum

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware shall be 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 Securities Exchange Act of 1934, as amended. Furthermore, Section 22 of the Securities Act of 1933, as amended, or the Security 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 will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, 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.

Further, our amended and restated certificate of incorporation and amended and restated bylaws provide that unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States will be the exclusive forum for resolution of 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. For the avoidance of doubt, this provision is intended to benefit and may be enforced by us, our officers and directors, the underwriters for any offering giving rise to such complaint, and any other professional entity whose profession gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying the offering.

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 and may discourage these types of lawsuits. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation or bylaws has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. We note that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

RENEO PHARMACEUTICALS, INC.

NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

AMENDED EFFECTIVE: FEBRUARY 25, 2022

Each member of the Board of Directors (the "***Board***") who is not also serving as an employee of or consultant to Reneo Pharmaceuticals, Inc. (the "***Company***") or any of its subsidiaries (each such member, an "***Eligible Director***") will receive the compensation described in this Non-Employee Director Compensation Policy for Board service upon and following the date of the underwriting agreement between the Company and the underwriters managing the initial public offering of the Company's common stock (the "***Common Stock***"), pursuant to which the Common Stock is priced in such initial public offering (the "***Effective Date***"). An Eligible Director may decline all or any portion of their compensation by giving notice to the Company prior to the date cash may be earned or equity awards are to be paid, as the case may be, subject to compliance with applicable tax laws. This policy is effective as of the Effective Date and may be amended at any time in the sole discretion of the Board or the Compensation Committee of the Board.

Annual Cash Compensation

The annual cash compensation amount set forth below is payable to Eligible Directors in equal quarterly installments, payable in arrears on the last day of each fiscal quarter in which the service occurred. If an Eligible Director joins the Board or a committee of the Board at a time other than effective as of the first day of a fiscal quarter, each annual retainer set forth below will be pro-rated based on days served in the applicable fiscal year, with the prorated amount paid for the first fiscal quarter in which the Eligible Director provides the service and regular full quarterly payments thereafter. All annual cash fees are vested upon payment.

1. Annual Board Service Retainer:
   a. All Eligible Directors: $40,000
   b. Non-Executive Chair (in addition to Eligible Director Service Retainer): $30,000

2. Annual Committee Chair Service Retainer:
   a. Chair of the Audit Committee: $15,000
   b. Chair of the Compensation Committee: $10,000
   c. Chair of the Nominating and Corporate Governance Committee: $8,000

3. Annual Committee Member Service Retainer (not applicable to Committee Chairs):
   a. Member of the Audit Committee: $7,500
   b. Member of the Compensation Committee: $5,000
   c. Member of the Nominating and Corporate Governance Committee: $4,000

Equity Compensation

The equity compensation set forth below will be granted under the Company's 2021 Equity Incentive Plan (the "***Plan***"), subject to the approval of the Plan by the Company's stockholders. All stock options granted under this policy will be nonstatutory stock options, with an exercise price per share equal to 100% of the Fair Market Value (as defined in the Plan) of the underlying Common Stock on the date of grant, and a term of ten years from the date of grant (subject to earlier termination in connection with a termination of service as provided in the Plan, provided that upon a termination of service other than by death or for cause, the Board may determine that the post-termination exercise period will be 12 months from the date of termination).

1. Initial Grant: For each Eligible Director who is first elected or appointed to the Board following the Effective Date, on the date of such Eligible Director's initial election or appointment to the Board (or, if such date is not a market trading day, the first market trading day thereafter), the Eligible Director will be automatically, and without further action by the Board or the Compensation Committee of the Board, granted an option to purchase 35,000 shares of Common Stock (the "***Initial Grant***"). The shares subject to each Initial Grant will vest in equal monthly installments over a three-year period such that the option is fully vested on the third anniversary of the date of grant, subject to the Eligible Director's Continuous Service (as defined in the Plan) through each such vesting date and will vest in full upon a Change in Control (as defined in the Plan).

2. Annual Grant: On the date of each annual stockholder meeting of the Company held after the Effective Date, each Eligible Director who continues to serve as a non-employee member of the Board following such stockholder meeting (excluding any Eligible Director who is first appointed or elected to the Board at such meeting) will be automatically, and without further action by the Board or the Compensation Committee of the Board, granted an option to purchase 17,500 shares of Common Stock (the "***Annual Grant***"). The shares subject to the Annual Grant will vest in full on the earlier of (x) the one-year anniversary of the date of grant of the Annual Grant or (y) the day prior to the date of the Company's next annual stockholder meeting, subject to the Eligible Director's Continuous Service through such vesting date and will vest in full upon a Change in Control. With respect to an Eligible Director who, following the Effective Date, was first elected or appointed to the Board on a date other than the date of the Company's annual stockholder meeting, upon the Company's first annual stockholder meeting following such Eligible Director's first joining the Board, such Eligible Director's first Annual Grant will be pro-rated to reflect the time between such Eligible Director's election or appointment date and the date of such first annual stockholder meeting.

Non-Employee Director Compensation Limit

Notwithstanding the foregoing, the aggregate value of all compensation granted or paid, as applicable, to any individual for service as a Non-Employee Director (as defined in the Plan) shall in no event exceed the limits set forth in Section 3(d) of the Plan.

December 21, 2021

Wendy Johnson
3115 3rd Avenue
San Diego CA 92103

Re: Transition, Separation and Consulting Agreement

Dear Wendy:

This letter sets forth the substance of the transition, separation and consulting agreement (the "Agreement") that Reneo Pharmaceuticals, Inc. (the "Company") is offering to you to aid in your employment transition.

1. Separation. Your last day of work with the Company and your employment termination date will be December 31, 2021 (the "**Separation Date**"), unless your employment terminates sooner pursuant to Section 3(c) below. If termination occurs earlier or later than December 31, 2021, the actual date of termination shall become the Separation Date for purposes of this Agreement. As of the Separation Date, you hereby resign as Chief Business Officer and from any other officer or director roles you may hold with the Company and its subsidiaries.

2. Accrued Salary and Paid Time Off. On the Separation Date, the Company will payyou all accrued salary and all accrued and unused paid time off earned through the Separation Date, subject to standard payroll deductions and withholdings. You are entitled to this payment by law.

3. Transition Period.

a. Duties. Between now and the Separation Date (the "**Transition Period**"), you will remain in your current role and will continue to perform your regular duties. During the Transition Period, you agree to transition these duties and responsibilities and perform other tasksas requested by the Company. During the Transition Period, you will be allowed a reasonable amount of time to pursue outside professional opportunities and to conduct job search efforts, subject to your satisfying all reasonable Company work deadlines and performing all transition and other tasks as requested of you by the Company. You agree to perform your Transition Periodservices in good faith and to the best of your abilities. During the Transition Period, you must continue to comply with all of the Company's policies and procedures and with all of your statutory and contractual obligations to the Company, including, without limitation, your obligations underyour Employee Confidential Information and Inventions Assignment Agreement (a copy of which is attached hereto as **Exhibit A**), which you acknowledge and agree are contractual commitments

that remain binding upon you, both during and after the Transition Period in accordance with their terms.

b. Compensation/Benefits. During the Transition Period, your base salary will remain the same, and you will continue to be eligible for the Company's standard benefits, subject to the terms and conditions applicable to such plans and programs. During the Transition Period, your Company stock options will continue to vest under the existing terms and conditionsset forth in the governing plan documents and option agreement.

c. Termination. Nothing in this Agreement alters your employment at will status. Accordingly, during the Transition Period you are entitled to resign your employment withor without cause or advance notice, and the Company may terminate your employment with or without Cause (as defined below) or advance notice. If prior to December 31, 2021, you resign your employment for any reason or the Company terminates your employment with Cause, then you will no longer be eligible for participation in any Company benefit plans, and you will not be entitled to the Severance Payment specified in Section 4 or the Consulting Agreement specified in Section 5 below.

d. Definition of Cause. For purposes of this Agreement, "***Cause***" for termination will mean any one or more of the following: (i) commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) the attempted commission of, or participation in, a fraud or act of dishonesty against the Company; (iii) the intentional or material violation of any contract or agreement between you and the Company or of any statutory duty owed to the Company (including violation of any provision or obligation under this Agreement); (iv) the unauthorized use or disclosure of the Company's confidential information or trade secrets; or (v) your gross misconduct.

4. Severance Payment. If you timely sign this Agreement, allow it to become effective, comply with your obligations under this Agreement (including without limitation satisfactorily transitioning your duties during the Transition Period, and, on or after the Separation Date, timelysign and return the Separation Date Release attached hereto as **Exhibit B** (collectively, the "**Severance Preconditions**"), and allow it to become effective, then the Company will pay you, as severance, the total amount of $100,000.00, subject to standard payroll deductions and withholdings (the "**Severance Payment**"). This amount will be paid in a lump sum within ten (10) days after the Effective Date of the Separation Date Release.

5. Bonus Payment. You will remain eligible to receive an Annual Bonus (as defined in the Employment Agreement between the Company and you, dated February 1, 2018) for achievement of 2021 corporate goals as if your employment continued through the date upon which the Annual Bonus is paid by the Company (the "**Agreed Bonus**").

6. Consulting Agreement. As part of this Agreement, and subject to your fulfillment ofthe Severance Preconditions, the Company agrees to engage you as a consultant, pursuant to the following terms and conditions (the "**Consulting Relationship**"):

a. Consulting Period. The Consulting Relationship will be deemed to have commenced on the Separation Date and will continue for eighteen (18) months thereafter (i.e. from December 31, 2021 to June 30, 2023), unless terminated earlier pursuant to the terms below (the "**Consulting Period**"). The Consulting Period can only be extended by a writing signed by you and an authorized representative of the Company.

b. Consulting Services. You agree to provide consulting services at mutually agreeable times to the Company in any area of your expertise, including but not limited to, transitioning your research and development related duties to Ashley Hall, Chief Development Officer, or such other person designated by the Company, perform business development research and engagement with potential partners and licensees/licensors, intellectual property portfolio management services, and completing other assignments as requested (the "**Consulting Services**"). You agree to make yourself available to the Company for Consulting Services for up to thirty-two (32) hours per month ("**Base Availability**") for the duration of the Consulting Period. Should the Company request time in excess of the Base Availability, you will exercise reasonable efforts to accommodate such requests. You agree to exercise the highest degree of professionalism and utilize your expertise and talents in performing these services. You agree to make yourself available to perform such Consulting Services throughout the Consulting Period, on an as-needed basis at reasonable times. When providing such services, you shall abide by the Company's policies and procedures that have been provided to you in writing.

c. Independent Contractor Relationship. Your relationship with the Company during the Consulting Period will be that of an independent contractor, and nothing in this Agreement is intended to, or should be construed to, create a partnership, agency, joint venture or employment relationship after the Separation Date. You will not be entitled to any of the benefits that the Company may make available to its employees, including but not limited to, group health or life insurance, profit-sharing or retirement benefits, and you acknowledge and agree that your relationship with the Company during the Consulting Period will not be subject to the Fair Labor Standards Act or other laws or regulations governing employment relationships. For the avoidance of doubt, nothing in the foregoing affects your right to receive the Agreed Bonus and the Consulting Consideration.

d. Consideration for Consulting Services. During the Consulting Period, you will be eligible for the following consideration (collectively, the "**Consulting Consideration**"):

(i) Equity Vesting; Acceleration. As additional consideration for the Consulting Services, the Company shall consider your change of status from an employee to a consultant (effective as of the Separation Date), and your Consulting Services during the Consulting Period, to constitute "Continuous Service" for purposes of the Company's 2014 Equity Incentive Plan, as amended (the "**Equity Plan**"), and therefore the Equity Awards (as defined in the Company's 2014 Equity Incentive Plan) will continue to vest in accordance with their terms during the Consulting Period; *provided that* any stock options that are "incentive stock options" under Section 422 of the Internal Revenue Code shall cease to be

"incentive stock options" upon the three (3) month anniversary of the Separation Date and thereafter will be non-qualified stock options. In addition, if the Company prevents the Consulting Relationship to commence on the Separation Date or if, prior to June 30, 2023, the Company terminates the Consulting Relationship, in each case, for a reason other than due to your breach of this Agreement or a breachof your continuing obligations owed to the Company (including, but not limited to,the Employee Confidential Information and Inventions Assignment Agreement) pursuant to the first sentence of Section 5(g) below, then the Company shall accelerate the vesting of your outstanding Equity Awards in full. Your rights to exercise or otherwise acquire any vested shares shall be governed and controlled by the Equity Documents. All terms, conditions and limitations applicable to the Equity Awards will continue to be subject to the applicable Equity Documents, subject to the provisions hereof. For the avoidance of doubt, (A) if you unilaterally decide not to enter into the Consulting Relationship, your "Continuous Service" for purposes of the Equity Awards will terminate, and the vesting of the Equity Awards will cease on the Separation Date, or (B) if the Company unilaterally decides not to enter into the Consulting Relationship, the Equity Awards will immediately vest on the Separation Date.

(ii) Consulting Fees. During the Consulting Period, you will receive cash compensation at the rate of $10,000.00 per calendar month for your Consulting Services for Base Availability (the "**Consulting Fees**"). If the numberof Consulting Service hours completed in a month is greater than the number of hours included in Base Availability, you agree to invoice the Company for the actual hours spent above the Base Availability providing Consulting Services at the rate of $300.00 per hour. Such invoices will be provided on a monthly basis, and the Company will provide payment of any owed Consulting Fees within thirty (30)days after receipt of such invoices. The Company will not withhold from the Consulting Fees any amount for taxes, social security or other payroll deductions. The Company will report your Consulting Fees on an IRS Form 1099. You acknowledge that you will be entirely responsible for payment of any taxes that may be due with regard to the Consulting Fees, and you hereby indemnify, defendand save harmless the Company, and its officers and directors in their individual capacities, from any liability for any taxes, penalties or interest that may be assessed by any taxing authority with respect to the Consulting Fees (with the exception of the employer's share of social security, if any). The Company encourages you to obtain professional advice from an advisor of your choice with respect to the tax treatment of, and any and all tax issues with respect to, the Consulting Fees.

e. Limitations on Authority. You will have no responsibilities or authority as a consultant to the Company other than as provided above. You will have no authority to bindthe Company to any contractual obligations, whether written, oral or implied, except with the authorization of the Company's Chief Executive Officer. Further, except as part of your Consulting Services, you agree not to represent or purport to represent the Company in any manner whatsoever

to any third party (including but not limited to customers, potential customers, investors, business partners or vendors), unless authorized by the Company's Chief Executive Officer to do so.

f. Confidential Information and Inventions. You agree that, during the Consulting Period and thereafter, you will not use or disclose, other than in furtherance of the Consulting Services, any confidential or proprietary information or materials of the Company, including any confidential or proprietary information that you obtain or develop in the course of performing the Consulting Services. Any and all work product you create in the course of performing the Consulting Services will be the sole and exclusive property of the Company. You hereby assign to the Company all right, title, and interest in all inventions, techniques, processes, materials, and other intellectual property developed in the course of performing the Consulting Services. Notwithstanding the foregoing nondisclosure obligations, pursuant to 18 U.S.C. Section 1833(b), you will not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that is made: (i) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney, and solely for the purpose of reporting or investigating a suspected violation of law; or (ii) in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.

g. Early Termination of Consulting Period. Without waiving any other rights or remedies, the Company has the immediate right to terminate the Consulting Relationship if the Company determines that you have breached this Agreement (including any breach of any of the representations, warranties or Consulting Service commitments made by you in this Agreement) or your continuing obligations owed to the Company (including, but not limited to, the Employee Confidential Information and Inventions Assignment Agreement during the Transition Period and thereafter in accordance with its terms). Additionally, each of you and the Company have the right to terminate the Consulting Relationship at any time and for any reason, upon thirty (30) days' advance written notice to the other party.

h. Other Work Activities / Representations. Throughout the Consulting Period, you retain the right to engage in employment, consulting, or other work relationships in addition to your Consulting Services for the Company, so long as such activities do not present a conflict of interest with the Company's business, or materially interfere with your continuing obligations owed to the Company. In the event that it is unclear to you whether a particular activity would breach this commitment, you agree to contact the Company's Chief Executive Officer to seek clarification. You represent and warrant that you are self-employed in an independently established trade, occupation, or business, maintains and operate a business that is separate and independent from the Company's business, hold yourself out to the public as independently competent and available to provide applicable services similar to the Consulting Services, have obtained and/or expect to obtain clients or customers other than the Company for whom you will perform services, and will perform work for the Company that you understand is outside the usual course of the Company's business.

i. Indemnification. For the avoidance of doubt, in connection with your services rendered during the Consulting Period, you will be entitled to the indemnification rights

and privileges described in that certain Indemnification Agreement by and between you and the Company, dated December 22, 2017, attached hereto as **Exhibit C**.

7. No Other Compensation or Benefits. You acknowledge that, except as expressly provided in this Agreement, you have not earned and will not receive from the Company any additional compensation (including base salary, bonus, incentive compensation, or equity), severance, or benefits before or after the Separation Date, with the exception of any vested right you may have under the express terms of a written ERISA-qualified benefit plan (e.g., 401(k) account) or any vested options, in each case, other than the Agreed Bonus and the Consulting Consideration.

8. Expense Reimbursements. You agree that, within thirty (30) days after the Separation Date, you will submit your final documented expense reimbursement statement reflecting all business expenses you incurred through the Separation Date, if any, for which you seek reimbursement. The Company will reimburse you for these expenses pursuant to its regular business practice. During the Consulting Period, you will submit expenses in monthly invoices and you will be reimbursed by the Company pursuant to its regular business practice.

9. Return of Company Property. By the Separation Date, or earlier if requested by theCompany, you agree to return to the Company all Company documents (and all copies thereof) and other Company property which you have in your possession or control, including, but not limited to, Company files, notes, drawings, records, plans, forecasts, reports, studies, analyses, proposals, agreements, financial information, research and development information, sales and marketing information, customer lists, prospect information, pipeline reports, sales reports, operational and personnel information, specifications, code, software, databases, computer-recorded information, tangible property and equipment (including, but not limited to, computers, facsimile machines, mobile telephones, servers), credit cards, entry cards, identification badges and keys; and any materials of any kind which contain or embody any proprietary or confidential information of the Company (and all reproductions thereof in whole or in part) (collectively "**Company Materials**"), in each case except those Company Materials that the Company permits you to keep in order to perform the Consulting Services. You agree that you will make a diligent search to locate any Company materials in your possession by the close of business on the Separation Date. If you have used any personally owned computer, server, or e-mail system to receive, store, review, prepare or transmit any Company confidential or proprietary data, materials or information, within five (5) days after the Separation Date, you shall provide the Company with a computer-useable copy of such information and then permanently delete and expunge such Company confidential or proprietary information from those systems except for any such information that the Company permits you to keep; and you agree to provide the Company reasonable access to your system as requested to verify that the necessary copying and/or deletion is done. **Your timely compliance with this paragraph is a condition to your receipt of the consideration provided under this Agreement.** Following your return of Company Materials pursuant to this Section, the Company may permit you to receive and/or use certain Company Materials reasonably necessary or useful to perform the Consulting Services, all of which you shall return to the Company by the last day of the Consulting Period, or earlier upon the Company's request, without retaining any copies or embodiments (in whole or in part). The Company

acknowledges that if it requests that you return Company Materials prior to the end of the Consulting Period it may impact your ability to provide the Consulting Services and your failure to continue to provide Consulting Services thereafter, after your reasonable efforts to do so, will not be considered a breach of this Agreement or an attempt by you to stop the Consulting Relationship.

10. Confidentiality. The provisions of this Agreement will be held in strictest confidence by you and will not be publicized or disclosed by you in any manner whatsoever; *provided, however,* that: (a) you may disclose this Agreement in confidence to your immediate family and to your attorneys, accountants, tax preparers and financial advisors; and (b) you may disclose this Agreement insofar as such disclosure may be necessary to enforce its terms or as otherwise required by law. In particular, and without limitation, you agree not to disclose the terms of this Agreement to any current or former Company employee or independent contractor.

11. Nondisparagement. You agree not to disparage the Company, its officers, directors, employees, shareholders, parents, subsidiaries, affiliates, and agents, in any manner likely to be harmful to its or their business, business reputation, or personal reputation; provided that you may respond accurately and fully to any question, inquiry, or request for information if required by legal process or in connection with a government investigation. In addition, nothing in this provision or this Agreement is intended to prohibit or restrain you in any manner from making disclosures that are protected under the whistleblower provisions of federal or state law or regulation or under other applicable law or regulation, nor prevent you from disclosing information about unlawful acts in the workplace, including, but not limited to, sexual harassment.

12. References. In response to any reference request from a prospective employer, the Company will only confirm your dates of employment and last job title.

13. No Voluntary Adverse Action. You agree that you will not voluntarily (except in response to legal compulsion or as permitted under the Protected Rights section below) assist any person in bringing or pursuing any proposed or pending litigation, arbitration, administrative claimor other formal proceeding against the Company, its parent or subsidiary entities, affiliates, officers, directors, employees or agents.

14. Cooperation. You agree to cooperate fully with the Company in connection with its actual or contemplated defense, prosecution, or investigation of any claims or demands by or against third parties, or other matters arising from events, acts, or failures to act that occurred during the period of your employment by the Company. Such cooperation includes, without limitation, making yourself available to the Company upon reasonable notice, without subpoena, to provide complete, truthful and accurate information in witness interviews, depositions, and trial testimony. The Company will reimburse you for reasonable out-of-pocket expenses you incur in connection with any such cooperation (excluding foregone wages) and will make reasonable efforts to accommodate your scheduling needs.

15. No Admissions. You understand and agree that the promises and payments in consideration of this Agreement shall not be construed to be an admission of any liability or

obligation by the Company to you or to any other person, and that the Company makes no such admission.

16. Release of Claims. In exchange for the consideration provided to you under this Agreement to which you would not otherwise be entitled, you hereby generally and completely release the Company, and its affiliated, related, parent and subsidiary entities, and its and their current and former directors, officers, employees, shareholders, partners, agents, attorneys, predecessors, successors, insurers, affiliates, and assigns from any and all claims, liabilities, demands, causes of action, and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring at any time prior to and includingthe date you sign this Agreement. This general release includes, but is not limited to: (a) all claims arising out of or in any way related to your employment with the Company or the termination of that employment; (b) all claims related to your compensation or benefits from the Company, including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, or any other ownership, equity, or profits interests in the Company, in each case except as related to the Agreed Bonus, the Consulting Consideration and reimbursement of all expenses incurred during your employment; (c) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (d) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (e) all federal, state, and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys' fees, or other claims arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990, the California Labor Code (as amended), the California Family Rights Act, the Age Discrimination in Employment Act ("**ADEA**") and the California Fair Employment and Housing Act (as amended). Notwithstanding the foregoing, you are not releasing the Company hereby from any obligation toindemnify you pursuant to the Articles and Bylaws of the Company, any valid fully executed indemnification agreement with the Company, applicable law, or applicable directors and officers liability insurance. Also, excluded from this Agreement are any claims that cannot be waived by law, including without limitation claims under the California Fair Employment and Housing Act, to the extent such claims are not waivable as a matter of law with this release.

17. ADEA Release. You acknowledge that you are knowingly and voluntarily waiving andreleasing any rights you have under the ADEA, and that the consideration given for the waiver andreleases you have given in this Agreement is in addition to anything of value to which you were already entitled. You further acknowledge that you have been advised, as required by the ADEA,that: (a) your waiver and release does not apply to any rights or claims that arise after the date you sign this Agreement; (b) you should consult with an attorney prior to signing this Agreement (although you may choose voluntarily not to do so); (c) you have twenty-one (21) days to consider this Agreement (although you may choose voluntarily to sign it sooner); (d) you have seven (7) days following the date you sign this Agreement to revoke this Agreement (in a written revocationsent to the Company); and (e) this Agreement will not be effective until the date upon which the revocation period has expired, which will be the eighth day after you sign this Agreement providedthat you do not revoke it (the "**Effective Date**").

18. Section 1542 Waiver. In giving the release herein, which includes claims which may be unknown to you at present, you acknowledge that you have read and understand Section 1542 of the California Civil Code, which reads as follows:

> **"A general release does not extend to claims that the creditor or releasing party does not know or suspect to exist in his or her favor at the time of executing the release and that, if known by him or her, would have materially affected his or her settlement with the debtor or released party."**

You hereby expressly waive and relinquish all rights and benefits under that section and any law of any other jurisdiction of similar effect with respect to your release of claims herein, including but not limited to your release of unknown claims.

19. Protected Rights. You understand that nothing in this Agreement limits your ability to file a charge or complaint with the Equal Employment Opportunity Commission, the Department of Labor, the National Labor Relations Board, the Occupational Safety and Health Administration, the California Department of Fair Employment and Housing, the Securities and Exchange Commission or any other federal, state or local governmental agency or commission ("**Government Agencies**"). You further understand this Agreement does not limit your ability to communicate with any Government Agencies or otherwise participate in any investigation or proceeding that may be conducted by any Government Agency, including providing documents or other information, without notice to the Company. While this Agreement does not limit your right to receive an award for information provided to the Securities and Exchange Commission, you understand and agree that, to maximum extent permitted by law, you are otherwise waiving any and all rights you may have to individual relief based on any claims that you have released and any rights you have waived by signing this Agreement.

20. Representations. You hereby represent that you have been paid all compensation owed and for all hours worked through the date you sign this Agreement, except the Agreed Bonus, have received all the leave and leave benefits and protections for which you are eligible pursuant to the Family and Medical Leave Act, the California Family Rights Act, or otherwise, and have not suffered any on-the-job injury for which you have not already filed a workers' compensation claim.

21. Miscellaneous. This Agreement, including its Exhibits, constitutes the complete, finaland exclusive embodiment of the entire agreement between you and the Company with regard to its subject matter. It is entered into without reliance on any promise or representation, written or oral, other than those expressly contained herein, and it supersedes any other promises, warranties, representations or agreements relating to the subject matter hereof, including that certain Amended Participation Agreement under the Severance Benefit Plan by and between you and the Company, dated March 31, 2021. This Agreement may not be modified or amended except in a writing signed by both you and a duly authorized officer of the Company. This Agreement will bind the heirs, personal representatives, successors and assigns of both you and the Company, and inure to the benefit of both you and the Company, their heirs, successors and assigns. If any provision of this Agreement is determined to be invalid or unenforceable, in whole or in part, this determination will not affect any other provision of this Agreement and the provision in question

will be modifiedby the court so as to be rendered enforceable to the fullest extent permitted by law, consistent withthe intent of the parties. This Agreement will be deemed to have been entered into and will be construed and enforced in accordance with the laws of the State of California without regard to conflict of laws principles. Any ambiguity in this Agreement shall not be construed against eitherparty as the drafter. Any waiver of a breach of this Agreement shall be in writing and shall not bedeemed to be a waiver of any successive breach. This Agreement may be executed in counterpartsand facsimile signatures will suffice as original signatures.

[Signature page to follow]

If this Agreement is acceptable to you, please sign below and return the original to me. You have twenty-one (21) calendar days to decide whether you would like to accept this Agreement, and the Company's offer contained herein will automatically expire if you do not sign and return it within this timeframe.

We wish you the best in your future endeavors.

Sincerely,

By: /s/ Gregory J. Flesher

Gregory J. Flesher

Chief Executive Officer

I HAVE READ, UNDERSTAND AND AGREE FULLY TO THE FOREGOING AGREEMENT:

/s/ Wendy Johnson
Wendy Johnson

23 December, 2021
Date

EXHIBIT A

EMPLOYEE CONFIDENTIAL INFORMATION AND INVENTIONS ASSIGNMENT AGREEMENT

For California Employee

RENEO PHARMACEUTICALS, INC.

EMPLOYEE CONFIDENTIAL INFORMATION AND INVENTION ASSIGNMENT AGREEMENT

In consideration of my employment or continued employment by **RENEO PHARMACEUTICALS, INC.**, its subsidiaries, parents, affiliates, successors and assigns (together "***Company***"), and the compensation paid to me now and during my employment with Company, I hereby enter into this Employee Confidential Information and Invention Assignment Agreement (the "***Agreement***") and agree as follows:

1. CONFIDENTIAL INFORMATION PROTECTIONS.

1.1 Recognition of Company's Rights; Nondisclosure. I understand and acknowledge that my employment by Company creates a relationship of confidence and trust with respect to Company's Confidential Information (as defined below) and that Company has a protectable interest therein. At all times during and after my employment, I will hold in confidence and will not disclose, use, lecture upon, or publish any of Company's Confidential Information, except as such disclosure, use or publication may be required in connection with my work for Company, or unless an officer of Company expressly authorizes such disclosure. I will obtain Company's written approval before publishing or submitting for publication any material (written, oral, or otherwise) that discloses and/or incorporates any Confidential Information. I hereby assign to Company any rights I may have or acquire in such Confidential Information and recognize that all Confidential Information shall be the sole and exclusive property of Company and its assigns. I will take all reasonable precautions to prevent the inadvertent accidental disclosure of Confidential Information. Notwithstanding the foregoing, pursuant to 18 U.S.C. Section 1833(b), I shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that: (1) is made in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney, and solely for the purpose of reporting or investigating a suspected violation of law; or (2) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.

1.2 Confidential Information. The term "***Confidential Information***" shall mean any and all confidential knowledge, data or information of Company. By way of illustration but not limitation, "***Confidential Information***" includes (a) trade secrets, inventions, mask works, ideas, processes, formulas, software in source or object code, data, programs, other works of authorship, know-how, improvements, discoveries, developments, designs and techniques and any other proprietary technology and all Intellectual Property Rights (as defined below) therein (collectively, "***Inventions***"); (b) information regarding research, development, new products, marketing and selling, business plans, budgets and unpublished financial statements, licenses, prices and costs, margins, discounts, credit terms, pricing and billing policies, quoting procedures, methods of obtaining business, forecasts, future plans and potential strategies, financial projections and business strategies, operational plans, financing and capital-raising plans, activities and agreements, internal services and operational manuals, methods of conducting Company business, suppliers and supplier information, and purchasing; (c) information regarding customers and potential customers of Company, including customer lists, names, representatives, their needs or desires with respect to the types of products or services offered by Company, proposals, bids,

contracts and their contents and parties, the type and quantity of products and services provided or sought to be provided to customers and potential customers of Company and other non-public information relating to customers and potential customers; (d) information regarding any of Company's business partners and their services, including names, representatives, proposals, bids, contracts and their contents and parties, the type and quantity of products and services received by Company, and other non-public information relating to business partners; (e) information regarding personnel, employee lists, compensation, and employee skills; and (f) any other non-public information which a competitor of Company could use to the competitive disadvantage of Company. Notwithstanding the foregoing, it is understood that, at all such times, I am free to use information which was known to me prior to my employment with Company or which is generally known in the trade or industry through no breach of this Agreement or other act or omission by me. Notwithstanding the foregoing or anything to the contrary in this Agreement or any other agreement between the Company and me, nothing in this Agreement shall limit my right to discuss my employment or report possible violations of law or regulation with the Equal Employment Opportunity Commission, United States Department of Labor, the National Labor Relations Board, the Securities and Exchange Commission, or other federal government agency or similar state or local agency or to discuss the terms and conditions of my employment with others to the extent expressly permitted by Section 7 of the National Labor Relations Act or to the extent that such disclosure is protected under the applicable provisions of law or regulation, including but not limited to "whistleblower" statutes or other similar provisions that protect such disclosure.

1.3 Third Party Information. I understand, in addition, that Company has received and in the future will receive from third parties their confidential and/or proprietary knowledge, data or information (***"Third Party Information"***) subject to a duty on Company's part to maintain the confidentiality of such information and to use it only for certain limited purposes. During the term of my employment and thereafter, I will hold Third Party Information in confidence and will not disclose to anyone (other than Company personnel who need to know such information in connection with their work for Company) or use, except in connection with my work for Company, Third Party Information or unless expressly authorized by an officer of Company in writing.

1.4 Term of Nondisclosure Restrictions. I understand that Confidential Information and Third Party Information is never to be used or disclosed by me, as provided in this Section 1 If a temporal limitation on my obligation not to use or disclose such information is required under applicable law, and the Agreement or its restriction(s) cannot otherwise be enforced, I agree and Company agrees that the two year period after the date my employment ends will be the temporal limitation relevant to the contested restriction; ***provided, however,*** that this sentence will not apply to trade secrets protected without temporal limitation under applicable law.

1.5 No Improper Use of Information of Prior Employers and Others. During my employment by Company, I will not improperly use or disclose confidential information or trade secrets, if any, of any former employer or any other person to whom I have an obligation of confidentiality, and I will not bring onto the premises of Company any unpublished documents or any property belonging to any former employer or any other person to whom I have an obligation of confidentiality unless consented to in writing by that former employer or person.

2. ASSIGNMENTS OF INVENTIONS.

2.1 Definitions. As used in this Agreement, the term ***"Intellectual Property Rights"*** means all trade secrets, Copyrights, trademarks, mask work rights, patents and other intellectual property rights recognized by the laws of any jurisdiction or country; the term "***Copyright***" means the exclusive legal right to reproduce, perform, display, distribute and make derivative works of a work of authorship (as a literary, musical, or artistic work) recognized by the laws of any jurisdiction or country; and the term

"***Moral Rights***" means all paternity, integrity, disclosure, withdrawal, special and any other similar rights recognized by the laws of any jurisdiction or country.

2.2 Excluded Inventions and Other Inventions. Attached hereto as **Exhibit A** is a list describing all existing Inventions, if any, (a) that are owned by me or in which I have an interest and were made or acquired by me prior to my date of first employment by Company, (b) that may relate to Company's business or actual or demonstrably anticipated research or development, and (c)that are not to be assigned to Company ("***Excluded Inventions***"). If no such list is attached, I represent and agree that it is because I have no Excluded Inventions. For purposes of this Agreement, "***Other Inventions***" means Inventions in which I have or may have an interest, as of the commencement of my employment or thereafter, other than Company Inventions (as defined below) and Excluded Inventions. I acknowledge and agree that if I use any Excluded Inventions or any Other Inventions in the scope of my employment, or if I include any Excluded Inventions or Other Inventions in any product or service of Company, or if my rights in any Excluded Inventions or Other Inventions may block or interfere with, or may otherwise be required for, the exercise by Company of any rights assigned to Company under this Agreement, I will immediately so notify Company in writing. Unless Company and I agree otherwise in writing as to particular Excluded Inventions or Other Inventions, I hereby grant to Company, in such circumstances (whether or not I give Company notice as required above), a non-exclusive, perpetual, transferable, fully-paid and royalty-free, irrevocable and worldwide license, with rights to sublicense through multiple levels of sublicensees, to reproduce, make derivative works of, distribute, publicly perform, and publicly display in any form or medium, whether now known or later developed, make, have made, use, sell, import, offer for sale, and exercise any and all present or future rights in, such Excluded Inventions and Other Inventions. To the extent that any third parties have rights in any such Other Inventions, I hereby represent and warrant that such third party or parties have validly and irrevocably granted to me the right to grant the license stated above.

2.3 Assignment of Company Inventions. Inventions assigned to Company or to a third party as directed by Company pursuant to Section 2.6are referred to in this Agreement as "***Company Inventions***." Subject to Section 2.4and except for Excluded Inventions set forth in **Exhibit A** and Other Inventions, I hereby assign to Company all my right, title, and interest in and to any and all Inventions (and all Intellectual Property Rights with respect thereto) made, conceived, reduced to practice, or learned by me, either alone or with others, during the period of my employment by Company. To the extent required by applicable Copyright laws, I agree to assign in the future (when any copyrightable Inventions are first fixed in a tangible medium of expression) my Copyright rights in and to such Inventions. Any assignment of Company Inventions (and all Intellectual Property Rights with respect thereto) hereunder includes an assignment of all Moral Rights. To the extent such Moral Rights cannot be assigned to Company and to the extent the following is allowed by the laws in any country where Moral Rights exist, I hereby unconditionally and irrevocably waive the enforcement of such Moral Rights, and all claims and causes of action of any kind against Company or related to Company's customers, with respect to such rights. I further acknowledge and agree that neither my successors-in-interest nor legal heirs retain any Moral Rights in any Company Inventions (and any Intellectual Property Rights with respect thereto).

2.4 Unassigned or Nonassignable Inventions. I recognize that this Agreement will not be deemed to require assignment of any Invention that is covered under California Labor Code section 2870(a) (the "***Specific Inventions Law***") except for those Inventions that are covered by a contract between Company and the United States or any of its agencies that require full title to such patent or Invention to be in the United States.

2.5 Obligation to Keep Company Informed. During the period of my employment, I will promptly and fully disclose to Company in writing all

Inventions authored, conceived, or reduced to practice by me, either alone or jointly with others. At the time of each such disclosure, I will advise Company in writing of any Inventions that I believe fully qualify for protection under the provisions of the Specific Inventions Law; and I will at that time provide to Company in writing all evidence necessary to substantiate that belief. Company will keep in confidence and will not use for any purpose or disclose to third parties without my consent any confidential information disclosed in writing to Company pursuant to this Agreement relating to Inventions that qualify fully for protection under the Specific Inventions Law. I will preserve the confidentiality of any Invention that does not fully qualify for protection under the Specific Inventions Law.

2.6 Government or Third Party. I agree that, as directed by Company, I will assign to a third party, including without limitation the United States, all my right, title, and interest in and to any particular Company Invention.

2.7 Ownership of Work Product.

(a) I acknowledge that all original works of authorship which are made by me (solely or jointly with others) within the scope of my employment and which are protectable by Copyright are "works made for hire," pursuant to United States Copyright Act (17 U.S.C., Section 101).

(b) I agree that Company will exclusively own all work product that is made by me (solely or jointly with others) within the scope of my employment, and I hereby irrevocably and unconditionally assign to Company all right, title, and interest worldwide in and to such work product. I understand and agree that I have no right to publish on, submit for publishing, or use for any publication any work product protected by this Section, except as necessary to perform services for Company.

2.8 Enforcement of Intellectual Property Rights and Assistance. I will assist Company in every proper way to obtain, and from time to time enforce, United States and foreign Intellectual Property Rights and Moral Rights relating to Company Inventions in any and all countries. To that end I will execute, verify and deliver such documents and perform such other acts (including appearances as a witness) as Company may reasonably request for use in applying for, obtaining, perfecting, evidencing, sustaining and enforcing such Intellectual Property Rights and the assignment thereof. In addition, I will execute, verify and deliver assignments of such Intellectual Property Rights to Company or its designee, including the United States or any third party designated by Company. My obligation to assist Company with respect to Intellectual Property Rights relating to such Company Inventions in any and all countries will continue beyond the termination of my employment, but Company will compensate me at a reasonable rate after my termination for the time actually spent by me at Company's request on such assistance. In the event Company is unable for any reason, after reasonable effort, to secure my signature on any document needed in connection with the actions specified in this paragraph, I hereby irrevocably designate and appoint Company and its duly authorized officers and agents as my agent and attorney in fact, which appointment is coupled with an interest, to act for and on my behalf to execute, verify and file any such documents and to do all other lawfully permitted acts to further the purposes of the preceding paragraph with the same legal force and effect as if executed by me. I hereby waive and quitclaim to Company any and all claims, of any nature whatsoever, which I now or may hereafter have for infringement of any Intellectual Property Rights assigned under this Agreement to Company.

2.9 Incorporation of Software Code. I agree that I will not incorporate into any Company software or otherwise deliver to Company any software code licensed under the GNU General Public License or Lesser General Public License or any other license that, by its terms, requires or conditions the use or distribution of such code on the disclosure, licensing, or distribution of any source code owned or licensed by Company **except** in strict compliance with Company's policies regarding the use of such software.

3. Records. I agree to keep and maintain adequate and current records (in the form of notes, sketches, drawings and in any other form that is required by Company) of all Confidential Information developed by me and all Company Inventions made by me during the period of my employment at Company, which records will be available to and remain the sole property of Company at all times.

4. Duty Of Loyalty During Employment. I agree that during the period of my employment by Company, I will not, without Company's express written consent, directly or indirectly engage in any employment or business activity which is directly or indirectly competitive with, or would otherwise conflict with, my employment by Company.

5. No Solicitation Of Employees, Consultants Or Contractors. I agree that during the period of my employment and for the one year period after the date my employment ends for any reason, including but not limited to voluntary termination by me or involuntary termination by Company, I will not, as an officer, director, employee, consultant, owner, partner, or in any other capacity, either directly or through others, except on behalf of Company, solicit, induce, encourage, or participate in soliciting, inducing or encouraging any person known to me to be an employee, consultant, or independent contractor of Company to terminate his or her relationship with Company, even if I did not initiate the discussion or seek out the contact.

6. Reasonableness Of Restrictions.

6.1 I agree that I have read this entire Agreement and understand it. I agree that this Agreement does not prevent me from earning a living or pursuing my career. I agree that the restrictions contained in this Agreement are reasonable, proper, and necessitated by Company's legitimate business interests. I represent and agree that I am entering into this Agreement freely and with knowledge of its contents with the intent to be bound by the Agreement and the restrictions contained in it.

6.2 In the event that a court finds this Agreement, or any of its restrictions, to be ambiguous, unenforceable, or invalid, I and Company agree that the court will read the Agreement as a whole and interpret the restriction(s) at issue to be enforceable and valid to the maximum extent allowed by law.

6.3 If the court declines to enforce this Agreement in the manner provided in subsection 6.2, Company and I agree that this Agreement will be automatically modified to provide Company with the maximum protection of its business interests allowed by law and I agree to be bound by this Agreement as modified.

7. No Conflicting Agreement Or Obligation. I represent that my performance of all the terms of this Agreement and as an employee of Company does not and will not breach any agreement to keep in confidence information acquired by me in confidence or in trust prior to my employment by Company. I have not entered into, and I agree I will not enter into, any agreement either written or oral in conflict with this Agreement.

8. Return Of Company Property. When I leave the employ of Company, I will deliver to Company any and all drawings, notes, memoranda, specifications, devices, formulas and documents, together with all copies thereof, and any other material containing or disclosing any Company Inventions, Third Party Information or Confidential Information of Company. I agree that I will not copy, delete, or alter any information contained upon my Company computer or Company equipment before I return it to Company. In addition, if I have used any personal computer, server, or e-mail system to receive, store, review, prepare or transmit any Company information, including but not limited to, Confidential Information, I agree to provide Company with a computer- useable copy of all such Confidential Information and then permanently delete and expunge such Confidential Information from those systems; and I agree to provide Company access to my system as reasonably requested to verify that the necessary copying and/or deletion is completed. I further agree that any property situated on Company's premises and owned by Company, including disks and other storage media, filing cabinets or other work areas, is subject to inspection by Company's personnel at any

time with or without notice. Prior to leaving, I will cooperate with Company in attending an exit interview and completing and signing Company's termination statementif required to do so by Company.

9. Legal And Equitable Remedies.

9.1 I agree that it may be impossible to assess the damages caused by my violation of this Agreement or any of its terms. I agree that any threatened or actual violation of this Agreement or any of its terms will constitute immediate and irreparable injury to Company, and Company will have the right to enforce this Agreement and any of its provisions by injunction, specific performance or other equitable relief, without bond and without prejudice to any other rights and remedies that Company may have for a breach or threatened breach of this Agreement.

9.2 In the event Company enforces this Agreement through a court order, I agree that the restrictions of Section 5will remain in effect for a period of 12 months from the effective date of the Order enforcingthe Agreement.

10. Notices. Any notices required or permitted under this Agreement will be given to Company at its headquarters location at the time notice is given, labeled "Attention Chief Executive Officer," and to me at my address as listed on Company payroll, or at such other address as Company or I may designate by written notice to the other. Notice will be effective upon receipt or refusalof delivery. If delivered by certified or registered mail, notice will be considered to have been given five business days after it was mailed, as evidenced by the postmark. If delivered by courier or express mail service, notice will be considered to have been given on the delivery date reflected by the courier or express mail service receipt.

11. Publication Of This Agreement To Subsequent Employer Or Business Associates Of Employee.

11.1 If I am offered employment or the opportunity to enter into any business venture as owner, partner, consultant or other capacity while the restrictions described in Section 5 of this Agreement are in effect I agree to inform my potential employer, partner, co-owner and/or others involved in managing the business with which I have an opportunity to be associated of my obligations under this Agreement and also agree to provide such person or persons with a copy of this Agreement.

11.2 I agree to inform Company of all employment and business ventures which I enter into while the restrictions described in Section 5of this Agreement are in effect and I also authorize Company to provide copies of this Agreement to my employer, partner, co- owner and/or others involved in managing the business with which I am employed or associated and to make such persons aware of my obligations under this Agreement.

12. General Provisions.

12.1 Governing Law; Consent To Personal Jurisdiction. This Agreement will be governed by and construed according to the laws of the State of California as such laws are applied to agreements entered into and to be performed entirely within California between residents of California. I hereby expressly consent to the personal jurisdiction and venue of the state and federal courts located in California for any lawsuit filed there against me by Company arising from or related to this Agreement.

12.2 Severability. In case any one or more of the provisions, subsections, or sentences contained in this Agreement will, for any reason, be held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability will not affect the other provisions of this Agreement, and this Agreement will be construed as if such invalid, illegal or unenforceable provision had never been contained in this Agreement. If moreover, any one or more of the provisions contained in this Agreement will for any reason be held to be excessively broad as to duration, geographical scope, activity or subject, it will be construed by limiting and reducing it, so as to be enforceable to the extent compatible with the applicable law as it will then appear.

12.3 Successors and Assigns. This Agreement is for my benefit and the benefit of Company, its successors, assigns, parent corporations,

subsidiaries, affiliates, and purchasers, and will be binding upon my heirs, executors, administrators and other legal representatives.

12.4 Survival. This Agreement shall survive the termination of my employment, regardless of the reason, and the assignment of this Agreement by Company to anysuccessor in interest or other assignee.

12.5 Employment At-Will. I agree and understand that nothing in this Agreement will change my at-will employment status or confer any right with respect to continuation of employment by Company, nor will it interfere in any way with my right or Company's right to terminate my employment at any time, with or without cause or advance notice.

12.6 Waiver. No waiver by Company of any breach of this Agreement will be a waiver of any preceding or succeeding breach. No waiver by Company of any right under this Agreement will be construed as a waiver of any other right. Company will not be required to give notice toenforce strict adherence to all terms of this Agreement.

12.7 Export. I agree not to export, reexport, or transfer, directly or indirectly, any U.S. technical data acquired from Company or any products utilizing such data, in violation of the United States export laws orregulations.

12.8 Counterparts. This Agreement may be executed in two or more counterparts, each of which shallbe deemed an original, but all of which together shall constitute one and the same instrument. Counterparts maybe delivered via facsimile, electronic mail (including pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, Uniform Electronic Transactions Act or other applicable law) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for allpurposes.

12.9 Advice of Counsel. I ACKNOWLEDGE THAT, IN EXECUTING THIS AGREEMENT, I HAVE HAD THE OPPORTUNITY TO SEEK THE ADVICE OF INDEPENDENT LEGAL COUNSEL, AND I HAVE READ AND UNDERSTOOD ALL OF THE TERMS AND PROVISIONS OF THIS AGREEMENT. THIS AGREEMENT WILL NOT BE CONSTRUED AGAINST ANY PARTY BY REASON OF THE DRAFTING OR PREPARATION OF THIS AGREEMENT.

12.10 Entire Agreement. The obligations pursuant to Sections 1and 2 (except Subsection 2.4and Subsection 2.7(a)) of this Agreement will apply to any time during which I was previously engaged, or am in the future engaged, by Company as a consultant if no other agreement governs nondisclosure and assignment of inventions during such period. This Agreement is the final, complete and exclusive agreement of the parties with respect to the subject matter of this Agreement and supersedes and merges all prior discussions between us. No modification of or amendment to this Agreement will be effective unless in writing and signed by the party to be charged. Any subsequent change or changes in my duties, salary or compensation will not affect the validity or scopeof this Agreement.

[signatures to follow on next page]

This Agreement will be effective as of Feb 1, 2018.

EMPLOYEE:

I HAVE READ THIS AGREEMENT CAREFULLY AND UNDERSTAND ITS TERMS. I HAVE COMPLETELY FILLED OUT EXHIBIT A TO THIS AGREEMENT.

/s/ Wendy Johnson

Wendy Johnson

2/6/18

Date

wjohnson@reneopharma.com

COMPANY:

ACCEPTED AND AGREED

RENEO PHARMACEUTICALS, INC.

By: /s/ Niall O'Donnel

Name: Niall O'Donnel
Title: President & CEO

Email: nodonnell@reneopharma.com

EXHIBIT A

EXCLUDED INVENTIONS

TO: **Reneo Pharmaceuticals, Inc.**

FROM: _____

DATE: _____

1. **Excluded Inventions Disclosure**. Except as listed in Section 2 below, the following is a complete list of all Excluded Inventions:

☒ No Excluded Inventions.

☐ See below:

_____

_____

_____

_____

_____

_____

☐ Additional sheets attached.

2. Due to a prior confidentiality agreement, I cannot complete the disclosure under Section 1 above with respect to the Excluded Inventions generally listed below, the intellectual property rights and duty of confidentiality with respect to which I owe to the following party(ies):

	Excluded Invention	**Party(ies)**	**Relationship**
1.			
2.			
3.			

☐ Additional sheets attached.

3. Limited Exclusion Notification.

This is to notify you in accordance with Section 2872 of the California Labor Code that the foregoing Agreement between you and Company does not require you to assign or offer to assign to Company any Invention that you develop entirely on your own time without using Company's equipment, supplies, facilities or trade secret information, except for those Inventions that either:

a. Relate at the time of conception or reduction to practice to Company's business, or actual or demonstrably anticipated research or development; or

b. Result from any work performed by you for Company.

To the extent a provision in the foregoing Agreement purports to require you to assign an Invention otherwise excluded from the preceding paragraph, the provision is against the public policy of this state and is unenforceable.

This limited exclusion does not apply to any patent or Invention covered by a contract between Company and the United States or any of its agencies requiring full title to such patent or Invention to be in the United States.

EXHIBIT B

SEPARATION DATE RELEASE

(to be signed and returned to the Company on or within twenty-one (21) days after the Separation Date)

In exchange for the severance benefits to be provided to me by Reneo Pharmaceuticals, Inc. (the "**Company**") pursuant to that certain transition, separation and consulting letter agreement with the Company dated February 21, 2021 (the "**Agreement**"), I hereby provide the following Separation Date Release (the "**Release**"). Capitalized terms used but not defined herein shall have the meanings ascribed to them in the Agreement.

I hereby represent that I have been paid all compensation owed and for all hours worked through the date I sign this Release, have received all the leave and leave benefits and protections for which I am eligible pursuant to the Family and Medical Leave Act, or otherwise, and have not suffered any on-the-job injury for which I have not already filed a workers' compensation claim. I acknowledge that, other than the severance benefits to be provided to me pursuant to the Agreement upon satisfaction of the Severance Preconditions, Ihave not earned and will not receive from the Company any additional compensation (including base salary, bonus, incentive compensation, or equity), severance, or benefits, with the exception of any vested right I may have under the express terms of a written ERISA-qualified benefit plan (e.g., 401(k) account) or any vested options or vested restrictedstock units.

I hereby generally and completely release the Company, and its affiliated, related, parent and subsidiary entities, and its and their current and former directors, officers, employees, shareholders, partners, agents, attorneys, predecessors, successors, insurers, affiliates, and assigns from any and all claims, liabilities, demands, causes of action, and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring at any time prior to and including the date I sign this Release. This general release includes, but is not limited to: (a) all claims arising out of or in any way related to my employment with the Company or the termination of that employment; (b) all claims related to my compensation or benefits from the Company, including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, restricted stock units, or any other ownership, equity, or profits interests in the Company; (c) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (d) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (e) all federal, state, and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys' fees, or other claims arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990, the California LaborCode (as amended), the California Family Rights Act, the Age Discrimination in Employment Act ("**ADEA**"), the California Fair Employment and Housing Act (as amended), the Texas Labor Code, including Chapter 21 of the Texas Labor Code (as amended), the Texas Payday Law (as amended), the Texas Anti-Retaliation Act (as amended), and the Texas Whistleblower Act (as amended). Notwithstanding the foregoing, I am not releasing the Company hereby from any obligation to indemnify me pursuant to the Certificate of Incorporation and

Bylaws of the Company, any valid fully executed indemnification agreement with the Company, applicable law, or applicable directors and officers liability insurance. Also, excluded from this Release are any claims that cannot be waived by law.

ADEA Release. I acknowledge that I am knowingly and voluntarily waiving and releasing any rights I have under the ADEA, and that the consideration given for the waiver and releases I have given in this Release is in addition to anything of value to which I was already entitled. I further acknowledge that I have been advised, as required by the ADEA, that: (a) my waiver and release does not apply to any rights or claims that arise after the date I sign this Release; (b) I should consult with an attorney prior to signing this Release (although I may choose voluntarily not to do so); (c) I have twenty-one (21) days to consider this Release (although I may choose voluntarily to sign it sooner); (d) I have seven (7) days following the date I sign this Release to revoke this Release (in a written revocation sent to the Company); and (e) this Release will not be effective until the date upon which the revocation period has expired, which will be the eighth day after I sign this Release provided that I do not revoke it (the "**Effective Date**").

In giving the release herein, which includes claims which may be unknown to me at present, I acknowledge that I have read and understand Section 1542 of the California Civil Code, which reads as follows:

> **"A general release does not extend to claims that the creditor or releasing party does not know or suspect to exist in his or her favor at the time of executing the release and that, if known by him or her, would have materially affected his or her settlement with the debtor or released party."**

I hereby expressly waive and relinquish all rights and benefits under that section and any law of any other jurisdiction of similar effect with respect to my release of claims herein, including but not limited to my release of unknown claims.

I understand that nothing in this Release limits my ability to file a charge or complaint with the Equal Employment Opportunity Commission, the Department of Labor, the National Labor Relations Board, the Occupational Safety and Health Administration, the Texas Workforce Commission, the Securities and Exchange Commission or any other federal, state or local governmental agency or commission ("**Government Agencies**"). I further understand this Release does not limit my ability to communicate with any Government Agencies or otherwise participate in any investigation or proceeding that may be conducted by any Government Agency, including providing documents or other information, without notice to the Company. While this Release does not limit my right to receive an award for information provided to the Securities and Exchange Commission, I understand and agree that, to maximum extent permitted by law, I am otherwise waiving any and all rights I may have to individual relief based on any claims that I have released and any rights I have waived by signing this Release.

[Signature page to follow]

This Release, together with the Agreement (and its exhibits) constitutes the entire agreement between me and the Company with respect to the subject matter hereof. I am not relying on any representation not contained herein or in the Agreement.

UNDERSTOOD, ACCEPTED, AND AGREED:

_____
Wendy Johnson

_____
Date

EXHIBIT C

INDEMNIFICATION AGREEMENT

THIS INDEMNIFICATION AGREEMENT (the "**Agreement**") is made and entered into as of December 22, 2017 between Reneo Pharmaceuticals, Inc, a Delaware corporation (the "**Company**"), and indemnitee whose signature appears below ("**Indemnitee**").

WITNESSETH THAT:

WHEREAS, high competent persons have become more reluctant to serve corporations as directors, officers or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporations;

WHEREAS, the Board of Directors of the Company (the "**Board**") has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries form certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance maybe available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Bylaws and Certificate of Incorporation Law of the State of Delaware ("**DGCL**"). The Bylaws and Certificate of Incorporation of the Company and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contract may be entered into between the Company and members of the Board, officers and other persons with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS, the Board has determined that the increased difficulty in attracting and retaining such person is detrimental to the best interests of the Company's stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of, such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the Bylaws and Certificate of Incorporation of the Company and any resolutions adopted pursuant thereto, and

shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder, and

WHEREAS, Indemnitee does not regard the protection available under the Company's Bylaws and Certificate of Incorporation and insurance as adequate in the present circumstances, and may not be willing to serve as an officer or director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified; and

WHEREAS, Indemnitee has certain rights to indemnification and/or insurance provided by other entities and/or organizations which Indemnitee and such other entities and/or organizations intend to be secondary to the primary obligation of the Company to indemnify Indemnitee as provided herein, with the Company's acknowledgement and agreement to the foregoing being a material condition to Indemnitee's willingness to serve on the Board.

NOW, THEREFORE, in consideration of Indemnitee's agreement to serve as an officer or director from and after the date hereof, the parties hereto agree as follows

1. Indemnity of Indemnitee. The Company hereby agrees to hold harmless and indemnify Indemnitee to the fullest extent permitted by law, as such may be amended from time to time. In furtherance of the foregoing indemnification, and without limiting the generality thereof.

(a) Proceedings Other Than Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(a) if, by reason of his Corporate Status (as hereinafter defined), the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding (as hereinafter defined) other than a Proceeding by or in the right of the Company. Pursuant to this Section 1(a), Indemnitee shall be indemnified against all Expenses (as hereinafter defined), judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him, or on his behalf, in connection with such Proceeding or any claim, issue or matter therein, if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, and with respect to any criminal Proceeding, had no reasonable cause to believe the Indemnitee's conduct was unlawful

(b) Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(b) if, by reason of his Corporate Status, the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding brought by or in the right of the Company. Pursuant to this Section 1(b), Indemnitee shall be indemnified against all Expenses actually and reasonably incurred by the Indemnitee, or on the Indemnitee's behalf, in connection with such Proceeding if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company; provided, however, if applicable law so provides, no indemnification against such Expenses shall be made in respect of any claim, issue or matter in such Proceeding as to which Indemnitee shall

have been adjudged to be liable to the Company unless and to the extent that the Court of Chancery of the State of Delaware shall determine that such indemnification may be made

(c) Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a party to and is successful, on the merits or otherwise, in any Proceeding, he shall be indemnified to the maximum extent permitted by law, as such may be amended from time to time, against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith, if Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with each successfully resolved claim, issue or matter. For purposes of this Section and without limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter

(d) Indemnification of Appointing Stockholder. If (i) Indemnitee is or was affiliated with one or more venture capital funds that has invested in the Company (an "**Appointing Stockholder**"), (ii) the Appointing Stockholder is, or is threatened to be made, a party to or a participant in any Proceeding, and (iii) the Appointing Stockholder's involvement in the Proceeding results from any claim based on the Indemnitee's service to the Company as a director or other fiduciary of the Company, the Appointing Stockholder will be entitled to indemnification hereunder for Expenses to the same extent as Indemnitee, and the terms of this Agreement as they relate to procedures for indemnification of Indemnitee and advancement of Expenses shall apply to any such indemnification of Appointing Stockholder

2. Additional Indemnity. In addition to, and without regard to any limitations on, the indemnification provided for in Section 1 of this Agreement, the Company shall and hereby does indemnify and hold harmless Indemnitee against all Expenses, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf if, by reason of his Corporate Status, he is, or is threatened to be made, a party to or participant in any Proceeding (including a Proceeding by or in the right of the Company), including, without limitation, all liability arising out of the negligence or active or passive wrongdoing of Indemnitee. The only limitation that shall exist upon the Company's obligations pursuant to this Agreement shall be that the Company shall not be obligated to make any payment to Indemnitee that is finally determined (under the procedures, and subject to the presumptions, set forth in Sections 6 and 7 hereof) to be unlawful.

3. Contribution.

(a) Whether or not the indemnification provided in Sections 1 and 2 hereof is available, in respect of any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall pay, in the first instance, the entire amount of any judgment or settlement of such action, suit or proceeding without requiring Indemnitee to contribute to such payment and the Company hereby waives and relinquishes any right of contribution it may have

against Indemnitee. The Company shall not enter into any settlement of any action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding) unless such settlement provides for a full and final release of all claims asserted against Indemnitee

(b) Without diminishing or impairing the obligations of the Company set forth in the preceding subparagraph, if, for any reason, Indemnitee shall elect or be required to pay all or any portion of any judgment or settlement in any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall contribute to the amount of Expenses, judgments, fines and amounts paid in settlement actually and reasonably incurred and paid or payable by Indemnitee in proportion to the relative benefits received by the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, from the transaction or events from which such action, suit or proceeding arose; provided, however, that the proportion determined on the basis of relative benefit may, to the extent necessary to conform to law, be further adjusted by reference to the relative fault of the Company and all officers, directors or employees of the Company other than Indemnitee who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, in connection with the transaction or events that resulted in such expenses, judgments, fines or settlement amounts, as well as any other equitable considerations which applicable law may require to be considered. The relative fault of the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, shall be determined by reference to, among other things, the degree to which their actions were motivated by intent to gain personal profit or advantage, the degree to which their liability is primary or secondary and the degree to which their conduct is active or passive

(c) The Company hereby agrees to fully indemnify and hold Indemnitee harmless from any claims of contribution which may be brought by officers, directors, or employees of the Company, other than Indemnitee, who may be jointly liable with Indemnitee

(d) To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the event(s) and/or transaction(s) giving cause to such Proceeding and/or (ii) the relative fault of the Company (and its directors, officers, employees and agents) and Indemnitee in connection with such event(s) and/or transaction(s)

4. Indemnification for Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a witness, or is made (or asked) to respond to discovery requests, in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith

5. Advancement of Expenses. Notwithstanding any other provision of this Agreement, the Company shall advance all Expenses incurred by or on behalf of Indemnitee in connection with any Proceeding by reason of Indemnitee's Corporate Status within thirty (30) days after the receipt by the Company of a statement or statements from Indemnitee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by Indemnitee and shall include or be preceded or accompanied by a written undertaking by or on behalf of Indemnitee to repay any Expenses advanced if it shall ultimately be determined that Indemnitee is not entitled to be indemnified against such Expenses. Any advances and undertakings to repay pursuant to this Sec土ion5 shall be unsecured and interest free.

6. Procedures and Presumptions for Determination of Entitlement to Indemnification. It is the intent of this Agreement to secure for Indemnitee rights of indemnity that are as favorable as may be permitted under the DGCL and public policy of the State of Delaware. Accordingly, the parties agree that the following procedures and presumptions shall apply in the event of any question as to whether Indemnitee is entitled to indemnification under this Agreement

(a) To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board in writing that Indemnitee has requested indemnification. Notwithstanding the foregoing, any failure of Indemnitee to provide such a request to the Company, or to provide such a request in a timely fashion, shall not relieve the Company of any liability that it may have to Indemnitee unless, and to the extent that, such failure actually and materially prejudices the interests of the Company

(b) Upon written request by Indemnitee for indemnification pursuant to the first sentence of Section 6(a) hereof, a determination with respect to Indemnitee's entitlement thereto shall be made in the specific case by one of the following four methods, which shall be at the election of the Board (1) by a majority vote of the disinterested directors, even though less than a quorum, (2) by a committee of disinterested directors designated by a majority vote of the disinterested directors, even though less than a quorum, (3) if there are no disinterested directors or if the disinterested directors so direct, by Independent Counsel in a written opinion to the Board, a copy of which shall be delivered to the Indemnitee, or (4) if so directed by the Board, by the stockholders of the Company. For purposes hereof, disinterested directors are those members of the Board who are not parties to the action, suit or proceeding in respect of which indemnification is sought by Indemnitee

(c) If the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 6(b) hereof, the Independent Counsel shall be selected as provided in this Section 6(c) . The Independent Counsel shall be selected by the Board. Indemnitee may, within ten (10) days after such written notice of selection shall have been given, deliver to the Company a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of "**Independent Counsel**" as defined in Section 13 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel, if a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within twenty (20) days after submission by Indemnitee of a written request for indemnification pursuant to Section 6(a) hereof, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Court of Chancery of the State of Delaware or other court of competent jurisdiction for resolution of any objection which shall have been made by the Indemnitee to the Company's selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 6(b) hereof. The Company shall pay any and all reasonable fees and expenses of Independent Counsel incurred by such Independent Counsel in connection with acting pursuant to Section 6(b) hereof, and the Company shall pay all reasonable fees and expenses incident to the procedures of this Section 6(c), regardless of the manner in which such Independent Counsel was selected or appointed.

(d) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall presume that Indemnitee is entitled to indemnification under this Agreement. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence. Neither the failure of the Company (including by its directors or Independent Counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or Independent Counsel) that Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(e) Indemnitee shall be deemed to have acted in good faith if Indemnitee's action is based on the records or books of account of the Enterprise (as hereinafter defined), including financial statements, or on information supplied to Indemnitee by the officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with reasonable care by the Enterprise. In addition, the knowledge and/or actions, or failure to act, of any director, officer, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement. Whether or not the foregoing provisions of this Section 6

(e) are satisfied, it shall in any event be presumed that Indemnitee has at all times acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(f) If the person, persons or entity empowered or selected under Section 6 to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall be deemed to have been made and Indemnitee shall be entitled to such indemnification absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such sixty (60) day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making such determination with respect to entitlement to indemnification in good faith requires such additional time to obtain or evaluate documentation and/or information relating thereto; and provided further, that the foregoing provisions of this Section 6(f) shall not apply if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 6(b) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request for such determination, the Board or the Disinterested Directors, if appropriate, resolve to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat.

(g) Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee's entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any Independent Counsel, member of the Board or stockholder of the Company shall act reasonably and in good faith in making a determination regarding the Indemnitee's entitlement to indemnification under this Agreement. Any costs or expenses (including attorneys' fees and disbursements) incurred by Indemnitee in so cooperating with the person, persons or entity making such determination shall be borne by the Company (irrespective of the determination as to Indemnitee's entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom

(h) The Company acknowledges that a settlement or other disposition short of final judgment may be successful if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any action, claim or proceeding to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such action, claim or proceeding with or without payment of money or other consideration) it shall be presumed that Indemnitee has been successful on the merits or otherwise in such action, suit or proceeding. Anyone seeking to overcome this

presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence

(i) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nob0 contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.

7. Remedies of Indemnitee.

(a) In the event that (i) a determination is made pursuant to Section 6 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 5 of this Agreement, (iii) no determination of entitlement to indemnification is made pursuant to Section 6(b) of this Agreement within ninety (90) days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to this Agreement within ten (10) days after receipt by the Company of a written request therefor, or (v) payment of indemnification is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification or such determination is deemed to have been made pursuant to Section 6 of this Agreement, Indemnitee shall be entitled to an adjudication in an appropriate court of the State of Delaware, or in any other court of competent jurisdiction, of Indemnitee's entitlement to such indemnification. Indemnitee shall commence such proceeding seeking an adjudication within one hundred eighty (180) days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 7(a). The Company shall not oppose Indemnitee's right to seek any such adjudication

(b) In the event that a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding commenced pursuant to this Section 7 shall be conducted in all respects as a de novo trial on the merits, and Indemnitee shall not be prejudiced by reason of the adverse determination under Section 6(b).

(c) If a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding commenced pursuant to this Section 7 , absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's misstatement not materially misleading in connection with the application for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) In the event that Indemnitee, pursuant to this Section 7 , seeks a judicial adjudication of his rights under, or to recover damages for breach of, this Agreement, or to recover under any directors' and officers' liability insurance policies maintained by the Company, the Company shall pay on his behalf, in advance, any and all Expenses (as defined below) actually

and reasonably incurred by him in such judicial adjudication, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of expenses or insurance recovery

(e) The Company shall be precluded from asserting in any judicial proceeding commenced pursuant to this Section 7 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court that the Company is bound by all the provisions of this Agreement. The Company shall indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefore) advance, to the extent not prohibited by law, such expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of Expenses or insurance recovery, as the case may be

(f) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

8. Non-Exclusivity; Survival of Rights; Insurance; Primacy of Indemnification; Subrogation.

(a) The rights of indemnification as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the Certificate of Incorporation, the By-laws, any agreement, a vote of stockholders, a resolution of directors of the Company, or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in the DGCL, whether by statute or judicial decision, permits greater indemnification than would be afforded currently under the Certificate of Incorporation, By-laws and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy

(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents or fiduciaries of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person serves at the request of the Company, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any director, officer, employee, agent or fiduciary under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the

Company has directors' and officers' liability insurance in effect, the Company shall give prompt notice of the commencement of such proceeding to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such proceeding in accordance with the terms of such policies

(c) The Company hereby acknowledges that Indemnitee has certain rights to indemnification, advancement of expenses and/or insurance provided by other entities and/or organizations (collectively, the "**Fund Indemnitors**"). The Company hereby agrees (i) that it is the indemnitor of first resort (i.e., its obligations to Indemnitee are primary and any obligation of the Fund Indemnitors to advance expenses or to provide indemnification for the same expenses or liabilities incurred by Indemnitee are secondary), (ii) that it shall be required to advance the full amount of expenses incurred by Indemnitee and shall be liable for the full amount of all Expenses, judgments, penalties, fines and amounts paid in settlement to the extent legally permitted and as required by the terms of this Agreement and the Certificate of Incorporation or Bylaws of the Company (or any other agreement between the Company and Indemnitee), without regard to any rights Indemnitee may have against the Fund Indemnitors, and (iii) that it irrevocably waives, relinquishes and releases the Fund Indemnitors from any and all claims against the Fund Indemnitors for contribution, subrogation or any other recovery of any kind in respect thereof The Company further agrees that no advancement or payment by the Fund Indemnitors on behalf of Indemnitee with respect to any claim for which Indemnitee has sought indemnification from the Company shall affect the foregoing and the Fund Indemnitors shall have a right of contribution and/or be subrogated to the extent of such advancement or payment to all of the rights of recovery of Indemnitee against the Company. The Company and Indemnitee agree that the Fund Indemnitors are express third party beneficiaries of the terms of this Section 8(c).

(d) Except as provided in paragraph (c) above, in the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee (other than against the Fund Indemnitors), who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

(e) Except as provided in paragraph (c) above, the Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise

(f) Except as provided in paragraph (c) above, the Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, employee or agent of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount Indemnitee has actually received as indemnification or advancement of expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise

9. Exception to Right of Indemnification. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnity in connection with any claim made against Indemnitee

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision, provided, that the foregoing shall not affect the rights of Indemnitee or the Fund Indemnitors set forth in Section 8(c) above; or

(b) for an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Securities Exchange Act of 1934, as amended, or similar provisions of state statutory law or common law; or

(c) in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board authorized the Proceeding (or any part of any Proceeding) prior to its initiation, or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law

10. Duration of Agreement. All agreements and obligations of the Company contained herein shall continue during the period Indemnitee is an officer or director of the Company (or is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise) and shall continue thereafter for six (6) years or so long as Indemnitee shall be subject to any Proceeding (or any proceeding commenced under Section 7 hereof by reason of his Corporate Status, whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement. This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives

11. Security To the extent requested by Indemnitee and approved by the Board, the Company may at any time and from time to time provide security to Indemnitee for the Company's obligations hereunder through an irrevocable bank line of credit, funded trust or other collateral. Any such security, once provided to Indemnitee, may not be revoked or released without the prior written consent of the Indemnitee

12. Enforcement.

(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumes the obligations imposed on it hereby in order to induce Indemnitee to

serve as an officer or director of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as an officer or director of the Company

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof

(c) The Company shall not seek from a court, or agree to, a "bar order" which would have the effect of prohibiting or limiting the Indemnitee's rights to receive advancement of expenses under this Agreement.

13. Definitions. For purposes of this Agreement:

(a) "**Corporate Status**" describes the status of a person who is or was a director, officer, employee, agent or fiduciary of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person is or was serving at the express written request of the Company

(b) "**Disinterested Director**" means a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(c) "**Enterprise**" shall mean the Company and any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that Indemnitee is or was serving at the express written request of the Company as a director, officer, employee, agent or fiduciary.

(d) "**Expenses**" shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, duplicating costs, printing and binding costs, telephone charges, postage, delivery service fees and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, participating, or being or preparing to be a witness in a Proceeding, or responding to, or objecting to, a request to provide discovery in any Proceeding. Expenses also shall include Expenses incurred in connection with any appeal resulting from any Proceeding and any federal, state, local or foreign taxes imposed on the Indemnitee as a result of the actual or deemed receipt of any payments under this Agreement, including without limitation the premium, security for, and other costs relating to any cost bond, supersede as bond, or other appeal bond or its equivalent. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee

(e) "**Independent Counsel**" means a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning Indemnitee under this Agreement, or of other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" shall not include any person who, under the applicable standards of

professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement. The Company agrees to pay the reasonable fees of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses, claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.

(f) "**Proceeding**" includes any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought by or in the right of the Company or otherwise and whether civil, criminal, administrative or investigative, in which Indemnitee was, is or will be involved as a party or otherwise, by reason of his or her Corporate Status, by reason of any action taken by him or of any inaction on his part while acting in his or her Corporate Status; in each case whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement; including one pending on or before the date of this Agreement, but excluding one initiated by an Indemnitee pursuant to Section 7 of this Agreement to enforce his rights under this Agreement.

14. Severability. The invalidity or unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision. Further, the invalidity or unenforceability of any provision hereof as to either Indemnitee or Appointing Stockholder shall in no way affect the validity or enforceability of any provision hereof as to the other. Without limiting the generality of the foregoing, this Agreement is intended to confer upon Indemnitee and Appointing Stockholder indemnification rights to the fullest extent permitted by applicable laws. In the event any provision hereof conflicts with any applicable law, such provision shall be deemed modified, consistent with the aforementioned intent, to the extent necessary to resolve such conflict.

15. Modification and Waiver. No supplement, modification, termination or amendment of this Agreement shall be binding unless executed in writing by both of the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar) nor shall such waiver constitute a continuing waiver

16. Notice By Indemnitee. Indemnitee agrees promptly to notify the Company in writing upon being served with or otherwise receiving any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification covered hereunder. The failure to so notify the Company shall not relieve the Company of any obligation which it may have to Indemnitee under this Agreement or otherwise unless and only to the extent that such failure or delay materially prejudices the Company.

17. Notices. All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day, (c)

five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent

(a) To Indemnitee at the address set forth below Indemnitee signature hereto.

(b) To the Company at

Reneo Pharmaceuticals, Inc
12730 High Bluff Drive, Suite 160
San Diego, California 92130
Attention: Chief Executive Officer

or to such other address as may have been furnished to Indemnitee by the Company or to the Company by Indemnitee, as the case may be

18. Counterparts. This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same the same instrument. Counterparts may be delivered via facsimile, electronic mail (including pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, e.g., www.docusign.com) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

19. Headings. The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

20. Governing Law and Consent to Jurisdiction. This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. The Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Chancery Court of the State of Delaware (the "**Delaware Court**"), and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) appoint, to the extent such party is not otherwise subject to service of process in the State of Delaware, an agent in the State of Delaware as such party's agent for acceptance of legal process in connection with any such action or proceeding against such party with the same legal force and validity as if served upon such party personally within the State of Delaware, (iv) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (v) waive, and agree not to plead or to make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

SIGNATURE PAGE TO FOLLOW

265478460 v1

IN WITNESS WHEREOF, the parties hereto have executed this Indemnification Agreement on and as of the day and year first above written.

RENEO PHARMACEUTICALS, INC.

By: */s/ Niall O'Donnell*
Name: Niall O'Donnell
Title:: President and Chief Executive Officer

INDEMNITEE

/s/ Wendy Johnson
Name: Wendy Johnson

Address:

Exhibit 10.13

January 20, 2022

Paul W. Hoelscher

RE: Member of the Reneo Board of Directors

Dear Paul:

This letter confirms our understanding regarding the terms of your appointment as a member of the Board of Directors (the "Board") of Reneo Pharmaceuticals, Inc., a Delaware corporation (the "Company"), contingent and effective upon your execution of this letter. In addition, you will also initially serve as a member and as the chair of the Audit Committee of the Board. Nothing in this is meant, or shall be construed in any way or manner, to create between you and the Company a relationship of employer and employee.

In consideration of your services to the Company as a member of the Board and as a member or chair of any of the committees of the Board, you will receive compensation for such services, as applicable, pursuant to the Company's Non-Employee Director Compensation Policy, as it may be in effect from time to time.

As a member of the Board, pursuant to the Delaware General Corporation Law ("DGCL") and related case law you will owe fiduciary duties to the Company and its stockholders, including the duty of care (directors must act in good faith, with the care of a prudent person, and in the best interest of the corporation), duty of loyalty (directors must refrain from self-dealing, usurping corporate opportunities and receiving improper personal benefits) and the duty of disclosure (directors must disclose all material information to their fellow directors and, when stockholder action is sought, to the corporation's stockholders). Our amended and restated certificate of incorporation and amended and restated bylaws provide that, as a director, you will be entitled to indemnification to the fullest extent permitted by the DGCL, and, upon your becoming a member of the Board, we will enter into the Company's standard form of indemnification agreement with you. We would be happy to arrange a conference with our outside counsel, Cooley LLP, if you have any questions about the indemnification agreement or your duties in general under Delaware law.

As a member of the Board, you will be reimbursed for any reasonable travel and other out-of-pocket expenses incurred in connection with your services on the Board. Please keep copies of all bills, receipts, or other written documentation of such reimbursable expenses and submit such documentation with your requests for reimbursement.

We look forward with enthusiasm to your service as a member of theBoard. If the foregoing terms are acceptable to you, please sign this letter and return it to me.

Sincerely,

/s/ Gregory J. Flesher
Gregory J. Flesher

President and Chief Executive Officer

AGREED TO AND ACCEPTED:

Signature: /s/ Paul W. Hoelscher
Paul W. Hoelscher

Date: 1/20/2022

February 2, 2022

Vineet R. Jindal 5521 Linmore Lane
Plano, TX 75093

Re: Transition, Separation and Consulting Agreement

Dear Vinny:

This letter sets forth the substance of the transition, separation and consulting agreement (the "**Agreement**") that Reneo Pharmaceuticals, Inc. (the "**Company**") is offering to you to aid in your employment transition.

1. Separation. Your last day of work with the Company and your employment termination date will be March 31, 2022 (the "**Separation Date**"), unless your employment terminates sooner pursuant to Section 3(c) below. If termination occurs earlier or later than March 31, 2022, the actual date of termination shall become the Separation Date for purposes of this Agreement. As of the Separation Date, you hereby resign as Chief Financial Officer and from any other officer or director roles you may hold with the Company and its subsidiaries.

2. Accrued Salary and Paid Time Off. On or promptly following the Separation Date, the Company will pay you all accrued salary and all accrued and unused paid time off earned through the Separation Date, subject to standard payroll deductions and withholdings. You are entitled to this payment by law.

3. Transition Period.

a. Duties. Between now and the Separation Date (the "**Transition Period**"), you will remain in your current role and will continue to perform your regular duties, including signing and certifying as to the Company's 2021 Annual Report on Form 10-K as the principal financial officer of the Company. During the Transition Period, you agree to transition your duties and responsibilities and perform other tasks as requested by the Company. During the Transition Period, you will be allowed a reasonable amount of time to pursue outside professional opportunities and to conduct job search efforts, subject to your satisfying all reasonable Company work deadlines and performing all transition and other tasks as requested of you by the Company. You agree to perform your Transition Period services in good faith and to the best of your abilities. During the Transition Period, you must continue to comply with all of the Company's policies and procedures and with all of your statutory and contractual obligations to the Company, including, without limitation, your obligations under your Employee Confidential Information and Inventions

Assignment Agreement (a copy of which is attached hereto as **Exhibit A**), which you acknowledge and agree are contractual commitments that remain binding upon you, both during and after the Transition Period.

b. Compensation/Benefits. During the Transition Period, your base salary of $385,000 per year will remain the same, and you will continue to be eligible for the Company's standard benefits, subject to the terms and conditions applicable to such plans and programs. During the Transition Period, your outstanding equity awards (the "**Equity Awards**") will continue to vest under the existing terms and conditions set forth in the Company's 2014 Equity Incentive Plan and 2021 Equity Incentive Plan (together, each as amended from time to time, the "**Equity Plans**"), as applicable, and your applicable grant documents (the "**Equity Documents**").

c. Termination. Nothing in this Agreement alters your employment at will status. Accordingly, during the Transition Period you are entitled to resign your employment with or without cause or advance notice, and the Company may terminate your employment with or without Cause (as defined below) or advance notice. If prior to March 31, 2022, you resign your employment for any reason or the Company terminates your employment with Cause, then you will no longer be eligible for participation in any Company benefit plans, and you will not be entitled to the severance benefits specified in Sections 4 through 6 below or the Consulting Agreement specified in Section 7 below.

d. Definition of Cause. For purposes of this Agreement, "***Cause***" for termination will mean any one or more of the following: (i) commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) the attempted commission of, or participation in, a fraud or act of dishonesty against the Company; (iii) the intentional or material violation of any contract or agreement between you and the Company or of any statutory duty owed to the Company (including violation of any provision or obligation under this Agreement); (iv) the unauthorized use or disclosure of the Company's confidential information or trade secrets; or (v) your gross misconduct.

4. Severance Payment. If you timely sign this Agreement, allow it to become effective, comply with your obligations under this Agreement (including without limitation satisfactorily transitioning your duties during the Transition Period, and, on or after the Separation Date, timely sign and return the Separation Date Release attached hereto as **Exhibit B** (collectively, the "**Severance Preconditions**"), and allow it to become effective, then the Company will pay you, as severance, regular payments based on your base salary in effect as of the Separation Date, subject to standard payroll deductions and withholdings, for a period of nine (9) months. Such payments shall be made on the Company's regularly-scheduled payroll dates commencing on the first payroll period following the Effective Date (as defined below) of the Separation Date Release.

5. Acceleration Benefit. Upon satisfaction of the Severance Preconditions, the Company shall accelerate the vesting of your outstanding Equity Awards that are subject to time-based vesting requirements as if you had completed an additional twelve (12) months of service with the Company following the Separation Date (the "**Acceleration Benefit**"). For clarity, the restricted stock units granted to you on December 1, 2021 will not be subject to the Acceleration Benefit. Your rights to exercise or otherwise acquire any vested shares shall be governed and controlled by the applicable Equity Documents, as modified by Section 7 below. All terms,

conditions and limitations applicable to the Equity Awards will continue to be governed by the applicable Equity Documents, subject to the provisions hereof.

6. Health Insurance. Your participation in the Company's group health insurance plan will end on the last day of the month in which the Separation Date occurs (i.e. if the Separation Date occurs on March 25, 2022, your participation in the Company's group health insurance plan will end on March 31, 2022). To the extent provided under the Consolidated Omnibus Budget Reconciliation Act of 1985 ("**COBRA**") or, if applicable, state insurance laws, and by the Company's current group health insurance policies, you will be eligible to continue your group health insurance benefits at your own expense following the Separation Date. Later, you may be able to convert to an individual policy through the provider of the Company's health insurance, if you wish. You will be provided with a separate notice describing your rights and obligations under COBRA. As an additional severance benefit under this Agreement, provided that you satisfy the Severance Preconditions set forth above and timely elect continued coverage under COBRA, then the Company shall pay directly to the carrier on your behalf the full amount of the COBRA premiums to continue your health insurance coverage (including coverage for eligible dependents, if applicable) through the period (the "**COBRA Premium Period**") starting on the Separation Date and ending on the earliest to occur of: (i) twelve (12) months following the Separation Date; (ii) the date you become eligible for group health insurance coverage through a new employer; or (iii) the date you cease to be eligible for COBRA coverage for any reason. Upon the conclusion of the COBRA Premium Period, you will be responsible for the entire payment of premiums (or payment for the cost of coverage) required under COBRA for the duration of your eligible COBRA coverage period, if any. For purposes of this Section, (1) references to COBRA shall be deemed to refer also to analogous provisions of state law and (2) any applicable insurance premiums that are paid by the Company shall not include any amounts payable by you under an Internal Revenue Code Section 125 health care reimbursementplan, which amounts, if any, are your sole responsibility. In the event you become covered underanother employer's group health plan or otherwise cease to be eligible for COBRA during the COBRA Premium Period, you must immediately notify the Company in writing of such event.

Notwithstanding the foregoing, if at any time the Company determines, in its sole discretion, thatit cannot provide the COBRA premium benefits without potentially incurring financial costs or penalties under applicable law (including, without limitation, Section 2716 of the Public Health Service Act), then in lieu of paying COBRA premiums directly to the carrier on your behalf, the Company will instead pay you on the last day of each remaining month of the COBRA Premium Period a fully taxable cash payment equal to the value of your monthly COBRA premium for the first month of COBRA coverage, subject to applicable tax withholding (each such amount, a "**COBRA Severance Payment**"), such COBRA Severance Payment to be made without regard to your election of COBRA coverage or payment of COBRA premiums and without regard to your continued eligibility for COBRA coverage during the COBRA Premium Period. No further COBRA Severance Payments shall be made following the conclusion of the COBRA Premium Period.

7. Consulting Agreement. As part of this Agreement, and subject to your fulfillment of the Severance Preconditions, the Company agrees to engage you as a consultant, pursuant to the following terms and conditions (the "**Consulting Relationship**"):

a. Consulting Period. The Consulting Relationship will be deemed to have commenced on the Separation Date and will continue for twelve (12) months thereafter, unless terminated earlier pursuant to the terms below (the "**Consulting Period**"). The Consulting Period can only be extended by a writing signed by you and an authorized representative of the Company.

b. Consulting Services. You agree to provide consulting services at mutually agreeable times to the Company in any area of your expertise, including but not limited to general transition support on investor relations, corporate communications related matters and other assignments as requested by the Chief Executive Officer (the "**Consulting Services**"). You agree to make yourself available to the Company for Consulting Services for no more than an average of eight (8) hours per week for the duration of the Consulting Period. You agree to make yourself available to perform such Consulting Services throughout the Consulting Period, on an as needed basis. You agree to exercise the highest degree of professionalism and utilize your expertise and talents in performing these services. When providing such services, you shall abide by the Company's policies and procedures.

c. Independent Contractor Relationship. Your relationship with the Company during the Consulting Period will be that of an independent contractor, and nothing in this Agreement is intended to, or should be construed to, create a partnership, agency, joint venture or employment relationship after the Separation Date. Other than your COBRA rights, you will not be entitled to any of the benefits that the Company may make available to its employees, including but not limited to, group health or life insurance, profit-sharing or retirement benefits, and you acknowledge and agree that your relationship with the Company during the Consulting Period will not be subject to the Fair Labor Standards Act or other laws or regulations governing employment relationships.

d. Consideration for Consulting Services. During the Consulting Period, you will be eligible for the following consideration:

(i) Consulting Fees. During the Consulting Period, you will receive cash compensation at the rate of $375.00 per hour for your Consulting Services (the "**Consulting Fees**"). You will submit detailed invoices of your Consulting Services on a monthly basis, and the Company will provide payment of any owed Consulting Fees within thirty (30) days after receipt of such invoices. The Company will not withhold from the Consulting Fees any amount for taxes, social security or other payroll deductions. The Company will report your Consulting Fees on an IRS Form 1099. You acknowledge that you will be entirely responsible for payment of any taxes that may be due with regard to the Consulting Fees, and you hereby indemnify, defend and save harmless the Company, and its officers and directors in their individual capacities, from any liability for any taxes, penalties or interest that may be assessed by any taxing authority with respect to the Consulting Fees (with the exception of the employer's share of social security, if any). The Company encourages you to obtain professional advice from an advisor of your choice with respect to the tax treatment of, and any and all tax issues with respect to, the Consulting Fees.

(ii) Cessation of Vesting; Extended Post-Termination Exercise Period. Notwithstanding anything in any Equity Document evidencing an Equity Award to the contrary, you agree that as of the Separation Date you will cease to vest in any then-remaining unvested and outstanding Equity Awards. However, as additional consideration for the Consulting

Services, the Company will extend the period of time during which you may exercise any vested, outstanding and unexercised stock options as of the Separation Date to the earliest of (i) three (3) months following the termination of the Consulting Period, (ii) the applicable expiration date of your stock options, and (iii) such earlier date as provided or permitted under the Equity Plans. Note that any unexercised "incentive stock options" under Section 422 of the Internal Revenue Code that you hold will convert into "non-qualified stock options" upon the three (3) month anniversary of the Separation Date, and by signing this Agreement, you acknowledge and agree to such change. Your rights to exercise or otherwise acquire any vested shares shall be governed and controlled by the Equity Documents. All terms, conditions and limitations applicable to the Equity Awards will continue to be subject to the applicable Equity Documents, subject to the provisions hereof. For the avoidance of doubt, if you do not enter into the Consulting Relationship, the exercisability of the Equity Awards will terminate three (3) months from the Separation Date pursuant to the applicable Equity Documents.

e. Limitations on Authority. You will have no responsibilities or authority as a consultant to the Company other than as provided above. You will have no authority to bind the Company to any contractual obligations, whether written, oral or implied, except with the authorization of the Company's Chief Executive Officer. Further, except as part of your Consulting Services, you agree not to represent or purport to represent the Company in any manner whatsoever to any third party (including but not limited to customers, potential customers, investors, business partners or vendors), unless authorized by the Company's Chief Executive Officer to do so.

f. Confidential Information and Inventions. You agree that, during the Consulting Period and thereafter, you will not use or disclose, other than in furtherance of the Consulting Services, any confidential or proprietary information or materials of the Company, including any confidential or proprietary information that you obtain or develop in the course of performing the Consulting Services. Any and all work product you create in the course of performing the Consulting Services will be the sole and exclusive property of the Company. You hereby assign to the Company all right, title, and interest in all inventions, techniques, processes, materials, and other intellectual property developed in the course of performing the Consulting Services. Notwithstanding the foregoing nondisclosure obligations, pursuant to 18 U.S.C. Section 1833(b), you will not be held criminally or civilly liable under any federal or state trade secret law for the disclosure of a trade secret that is made: (i) in confidence to a federal, state, or local government official, either directly or indirectly, or to an attorney, and solely for the purpose of reporting or investigating a suspected violation of law; or (ii) in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.

g. Early Termination of Consulting Period. Without waiving any other rights or remedies, the Company has the immediate right to terminate the Consulting Relationship if the Company determines that you have breached this Agreement (including any breach of any of the representations, warranties or Consulting Service commitments made by you in this Agreement) or your continuing obligations owed to the Company (including, but not limited to, the Employee Confidential Information and Inventions Assignment Agreement). Additionally, each of you and the Company have the right to terminate the Consulting Relationship at any time and for any reason, upon thirty (30) days' advance written notice to the other party.

h. Other Work Activities / Representations. Throughout the Consulting Period, you retain the right to engage in employment, consulting, or other work relationships in addition to your Consulting Services for the Company, so long as such activities do not present a conflict of interest with the Company's business, or interfere with your continuing obligations owed to the Company. In the event that it is unclear to you whether a particular activity would breach this commitment, you agree to contact the Company's Chief Executive Officer to seek clarification. You represent and warrant that you are self-employed in an independently established trade, occupation, or business, maintain and operate a business that is separate and independent from the Company's business, hold yourself out to the public as independently competent and available to provide applicable services similar to the Consulting Services, have obtained and/or expect to obtain clients or customers other than the Company for whom you will perform services, and will perform work for the Company that you understand is outside the usual course of the Company's business.

8. No Other Compensation or Benefits. You acknowledge that, except as expressly provided in this Agreement, you have not earned and will not receive from the Company any additional compensation (including base salary, bonus, incentive compensation, or equity), severance, or benefits before or after the Separation Date, with the exception of any vested right you may have under the express terms of a written ERISA-qualified benefit plan (e.g., 401(k) account) or any vested options or vested restricted stock units.

9. Expense Reimbursements. You agree that, within thirty (30) days after the Separation Date, you will submit your final documented expense reimbursement statement reflecting all business expenses you incurred through the Separation Date, if any, for which you seek reimbursement. The Company will reimburse you for these expenses pursuant to its regular business practice.

10. Return of Company Property. By the Separation Date, or earlier if requested by the Company, you agree to return to the Company all Company documents (and all copies thereof) and other Company property which you have in your possession or control, including, but not limited to, Company files, notes, drawings, records, plans, forecasts, reports, studies, analyses, proposals, agreements, financial information, research and development information, sales and marketing information, customer lists, prospect information, pipeline reports, sales reports, operational and personnel information, specifications, code, software, databases, computer-recorded information, tangible property and equipment (including, but not limited to, computers, facsimile machines, mobile telephones, servers), credit cards, entry cards, identification badges and keys; and any materials of any kind which contain or embody any proprietary or confidential information of the Company (and all reproductions thereof in whole or in part). You agree that you will make a diligent search to locate any such documents, property and information by the close of business on the Separation Date. If you have used any personally owned computer, server, or e-mail system to receive, store, review, prepare or transmit any Company confidential or proprietary data, materials or information, within five (5) days after the Separation Date, you shall provide the Company with a computer-useable copy of such information and then permanently delete and expunge such Company confidential or proprietary information from those systems; and you agree to provide the Company access to your system as requested to verify that the necessary copying and/or deletion is done. **Your timely compliance with this paragraph is a condition to your receipt of the consideration provided under this Agreement.** Following your

return of Company property pursuant to this Section, the Company may permit you to receive and/or use certain documents, equipment, and/or information reasonably necessary to perform the Consulting Services, all of which you shall return to the Company by the last day of the Consulting Period, or earlier upon the Company's request, without retaining any copies or embodiments (in whole or in part).

11. Confidentiality. The provisions of this Agreement will be held in strictest confidence by you and will not be publicized or disclosed by you in any manner whatsoever; *provided, however,* that: (a) you may disclose this Agreement in confidence to your immediate family and to your attorneys, accountants, tax preparers and financial advisors; and (b) you may disclose this Agreement insofar as such disclosure may be necessary to enforce its terms or as otherwise required by law. In particular, and without limitation, you agree not to disclose the terms of this Agreement to any current or former Company employee or independent contractor.

12. Nondisparagement. You agree not to disparage the Company, its officers, directors, employees, shareholders, parents, subsidiaries, affiliates, and agents, in any manner likely to be harmful to its or their business, business reputation, or personal reputation; provided that you may respond accurately and fully to any question, inquiry, or request for information if required by legal process or in connection with a government investigation. In addition, nothing in this provision or this Agreement is intended to prohibit or restrain you in any manner from making disclosures that are protected under the whistleblower provisions of federal or state law or regulation or under other applicable law or regulation, nor prevent you from disclosing information about unlawful acts in the workplace, including, but not limited to, sexual harassment.

13. References. In response to any reference request from a prospective employer, the Company will only confirm your dates of employment and last job title.

14. No Voluntary Adverse Action. You agree that you will not voluntarily (except in response to legal compulsion or as permitted under the Protected Rights section below) assist any person in bringing or pursuing any proposed or pending litigation, arbitration, administrative claim or other formal proceeding against the Company, its parent or subsidiary entities, affiliates, officers, directors, employees or agents.

15. Cooperation. You agree to cooperate fully with the Company in connection with its actual or contemplated defense, prosecution, or investigation of any claims or demands by or against third parties, or other matters arising from events, acts, or failures to act that occurred during the period of your employment by the Company. Such cooperation includes, without limitation, making yourself available to the Company upon reasonable notice, without subpoena, to provide complete, truthful and accurate information in witness interviews, depositions, and trial testimony. The Company will reimburse you for reasonable out-of-pocket expenses you incur in connection with any such cooperation (excluding foregone wages) and will make reasonable efforts to accommodate your scheduling needs.

16. No Admissions. You understand and agree that the promises and payments in consideration of this Agreement shall not be construed to be an admission of any liability or obligation by the Company to you or to any other person, and that the Company makes no such admission.

17. Release of Claims. In exchange for the consideration provided to you under this Agreement to which you would not otherwise be entitled, you hereby generally and completely release the Company, and its affiliated, related, parent and subsidiary entities, and its and their current and former directors, officers, employees, shareholders, partners, agents, attorneys, predecessors, successors, insurers, affiliates, and assigns from any and all claims, liabilities, demands, causes of action, and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring at any time prior to and including the date you sign this Agreement. This general release includes, but is not limited to: (a) all claims arising out of or in any way related to your employment with the Company or the termination of that employment; (b) all claims related to your compensation or benefits from the Company, including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, restricted stock units, or any other ownership, equity, or profits interests in the Company; (c) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (d) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (e) all federal, state, and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys' fees, or other claims arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990, the California Labor Code (as amended), the California Family Rights Act, the Age Discriminationin Employment Act ("**ADEA**"), the California Fair Employment and Housing Act (as amended), the Texas Labor Code, including Chapter 21 of the Texas Labor Code (as amended), the Texas Payday Law (as amended), the Texas Anti-Retaliation Act (as amended), and the Texas Whistleblower Act (as amended). Notwithstanding the foregoing, you are not releasing the Company hereby from any obligation to indemnify you pursuant to the Certificate of Incorporation and Bylaws of the Company, any valid fully executed indemnification agreement with the Company, applicable law, or applicable directors and officers liability insurance. Also, excluded from this Agreement are any claims that cannot be waived by law.

18. ADEA Release. You acknowledge that you are knowingly and voluntarily waiving and releasing any rights you have under the ADEA, and that the consideration given for the waiver and releases you have given in this Agreement is in addition to anything of value to which you were already entitled. You further acknowledge that you have been advised, as required by the ADEA, that: (a) your waiver and release does not apply to any rights or claims that arise after the date you sign this Agreement; (b) you should consult with an attorney prior to signing this Agreement (although you may choose voluntarily not to do so); (c) you have twenty-one (21) days to consider this Agreement (although you may choose voluntarily to sign it sooner); (d) you have seven (7) days following the date you sign this Agreement to revoke this Agreement (in a written revocation sent to the Company); and (e) this Agreement will not be effective until the date upon which the revocation period has expired, which will be the eighth day after you sign this Agreement provided that you do not revoke it (the "**Effective Date**").

19. Section 1542 Waiver. In giving the release herein, which includes claims which may be unknown to you at present, you acknowledge that you have read and understand Section 1542 of the California Civil Code, which reads as follows:

> **"A general release does not extend to claims that the creditor or releasing party does not know or suspect to exist in his or her favor at the time of**

executing the release and that, if known by him or her, would have materially affected his or her settlement with the debtor or released party."

You hereby expressly waive and relinquish all rights and benefits under that section and any law of any other jurisdiction of similar effect with respect to your release of claims herein, including but not limited to your release of unknown claims.

20. Protected Rights. You understand that nothing in this Agreement limits your ability to file a charge or complaint with the Equal Employment Opportunity Commission, the Department of Labor, the National Labor Relations Board, the Occupational Safety and Health Administration, the Texas Workforce Commission, the Securities and Exchange Commission or any other federal, state or local governmental agency or commission ("**Government Agencies**"). You further understand this Agreement does not limit your ability to communicate with any Government Agencies or otherwise participate in any investigation or proceeding that may be conducted by any Government Agency, including providing documents or other information, without notice to the Company. While this Agreement does not limit your right to receive an award for information provided to the Securities and Exchange Commission, you understand andagree that, to maximum extent permitted by law, you are otherwise waiving any and all rights you may have to individual relief based on any claims that you have released and any rights you have waived by signing this Agreement.

21. Representations. You hereby represent that you have been paid all compensation owed and for all hours worked through the date you sign this Agreement, have received all the leave and leave benefits and protections for which you are eligible pursuant to the Family and Medical Leave Act, or otherwise, and have not suffered any on-the-job injury for which you have not already filed a workers' compensation claim.

22. Miscellaneous. This Agreement, including its Exhibits, constitutes the complete, final and exclusive embodiment of the entire agreement between you and the Company with regard to its subject matter. It is entered into without reliance on any promise or representation, written or oral, other than those expressly contained herein, and it supersedes any other promises,warranties, representations or agreements relating to the subject matter hereof, including that certain Amended Participation Agreement under the Severance Benefit Plan by and between youand the Company, dated April 8, 2021. This Agreement may not be modified or amended except in a writing signed by both you and a duly authorized officer of the Company. This Agreement will bind the heirs, personal representatives, successors and assigns of both you and the Company, and inure to the benefit of both you and the Company, their heirs, successors and assigns. If any provision of this Agreement is determined to be invalid or unenforceable, in whole or in part, this determination will not affect any other provision of this Agreement and the provision in question will be modified by the court so as to be rendered enforceable to the fullest extent permitted by law, consistent with the intent of the parties. This Agreement will be deemedto have been entered into and will be construed and enforced in accordance with the laws of the State of Texas without regard to conflict of laws principles. Any ambiguity in this Agreement shall not be construed against either party as the drafter. Any waiver of a breach of thisAgreement shall be in writing and shall not be deemed to be a waiver of any successive breach. This Agreement may be executed in counterparts and facsimile signatures will suffice as originalsignatures.

[Signature page to follow]

If this Agreement is acceptable to you, please sign below and return the original to me. You have twenty-one (21) calendar days to decide whether you would like to accept this Agreement, and the Company's offer contained herein will automatically expire if you do not sign and return it within this timeframe.

We wish you the best in your future endeavors.

Sincerely,

By: /s/ Gregory J. Flesher
Gregory J. Flesher
Chief Executive Officer

I HAVE READ, UNDERSTAND AND AGREE FULLY TO THE FOREGOING AGREEMENT:

/s/ Vineet R. Jindal
Vineet R. Jindal

February 2, 2022
Date

EXHIBIT A

EMPLOYEE CONFIDENTIAL INFORMATION AND INVENTIONS ASSIGNMENT AGREEMENT

RENEO PHARMACEUTICALS, INC.

EMPLOYEE CONFIDENTIAL INFORMATION AND INVENTION ASSIGNMENT AGREEMENT

In consideration of my employment or continued employment by **RENEO PHARMACEUTICALS, INC.**, its subsidiaries, parents, affiliates, successors and assigns (together "***Company***"), and the compensation paid to me now and during my employment with Company, I hereby enter into this Employee Confidential Information and Invention Assignment Agreement (the "***Agreement***") and agree as follows:

1. CONFIDENTIAL INFORMATION PROTECTIONS.

1.1 Recognition of Company's Rights; Nondisclosure. I understand and acknowledge that my employment by Company creates a relationship of confidence and trust with respect to Company's Confidential Information (as defined below) and that Company has a protectable interest therein. At all times during and after my employment, I will hold in confidence and will not disclose, use, lecture upon, or publish any of Company's Confidential Information, except as such disclosure, use or publication may be required in connection with my work for Company, or unless an officer of Company expressly authorizes such disclosure. I will obtain Company's written approval before publishing or submitting for publication any material (written, oral, or otherwise) that discloses and/or incorporates any Confidential Information. I hereby assign to Company any rights I may have or acquire in such Confidential Information and recognize that all Confidential Information shall be the sole and exclusive property of Company and its assigns. I will take allreasonable precautions to prevent the inadvertent accidental disclosure of Confidential Information. Notwithstanding the foregoing, pursuant to 18 U.S.C. Section 1833(b), I shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that: (1) is made in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney, and solely for the purpose of reporting or investigating a suspected violation of law; or (2) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.

1.2 Confidential Information. The term "***Confidential Information***" shall mean any and all confidential knowledge, data or information of Company. By way of illustration but not limitation, "***Confidential Information***" includes (a) trade secrets, inventions, mask works, ideas, processes, formulas, software in source or object code, data, programs, other works of authorship, know-how, improvements, discoveries, developments, designs and techniques and any other proprietary technology and all Intellectual Property Rights (as defined below) therein (collectively, "***Inventions***"); (b) information regarding research, development, new products, marketing and selling, business plans, budgets and unpublished financial statements, licenses, prices and costs, margins, discounts, credit terms, pricing and billing policies, quoting procedures, methods of obtaining business, forecasts, future plans and potential strategies, financial projections and business strategies, operational plans, financing and capital-raising plans, activities and agreements, internal services and operational manuals, methods of conducting Company business, suppliers and supplier information, and purchasing; (c) information regarding customers and potential customers of Company, including customer lists, names, representatives, their needs or desires with respect to the types of products or services offered by Company, proposals, bids, contracts and their contents and parties, the type and quantity of products and services provided or sought to be provided to customers and potential customers of Company and other non-public information relating to customers and potential customers; (d) information regarding any of Company's business partners and their services, including names, representatives, proposals, bids, contracts and their contents and parties, the type and quantity of products and services received by Company, and other non-public information relating to business partners; (e) information regarding personnel, employee lists,

compensation, and employee skills; and (f) any other non-public information which a competitor of Company could use to the competitive disadvantage of Company. Notwithstanding the foregoing, it is understood that, at all such times, I am free to use information which was known to me prior to my employment with Company or which is generally known in the trade or industry through no breach of this Agreement or other act or omission by me. Notwithstanding the foregoing or anything to the contrary in this Agreement or any other agreement between the Company and me, nothing in this Agreement shall limit my right to discuss my employment or report possible violations of law or regulation with the Equal Employment Opportunity Commission, United States Department of Labor, the National Labor Relations Board, the Securities and Exchange Commission, or other federal government agency or similar state or local agency or to discuss the terms and conditions of my employment with others to the extent expressly permitted by Section 7 of the National Labor Relations Act or to the extent that such disclosure is protected under the applicable provisions of law or regulation, including but not limited to "whistleblower" statutes or other similar provisions that protect such disclosure.

1.3 Third Party Information. I understand, in addition, that Company has received and in the future will receive from third parties their confidential and/or proprietary knowledge, data or information (***"Third Party Information"***) subject to a duty on Company's part to maintain the confidentiality of such information and to use it only for certain limited purposes. During the term of my employment and thereafter, I will hold Third Party Information in confidence and will not disclose to anyone (other than Company personnel who need to know such information in connection with their work for Company) or use, except in connection with my work for Company, Third Party Information or unless expressly authorized by an officer of Company in writing.

1.4 Term of Nondisclosure Restrictions. I understand that Confidential Information and Third Party Information is never to be used or disclosed by me, as provided in this Section 1. If a temporal limitation on my obligation not to use or disclose such information is required under applicable law, and the Agreement or its restriction(s) cannot otherwise be enforced, I agree and Company agrees that the two year period after the date my employment ends will be the temporal limitation relevant to the contested restriction; ***provided, however,*** that this sentence will not apply to trade secrets protected without temporal limitation under applicable law.

1.5 No Improper Use of Information of Prior Employers and Others. During my employment by Company, I will not improperly use or disclose confidential information or trade secrets, if any, of any former employer or any other person to whom I have an obligation of confidentiality, and I will not bring onto the premises of Company any unpublished documents or any property belonging to any former employer or any other person to whom I have an obligation of confidentiality unless consented to in writing by that former employer or person.

2. Assignments Of Inventions.

2.1 Definitions. As used in this Agreement, the term ***"Intellectual Property Rights"*** means all trade secrets, Copyrights, trademarks, mask work rights, patents and other intellectual property rights recognized by the laws of any jurisdiction or country; the term "***Copyright***" means the exclusive legal right to reproduce, perform, display, distribute and make derivative works of a work of authorship (as a literary, musical, or artistic work) recognized by the laws of any jurisdiction or country; and the term "***Moral Rights***" means all paternity, integrity, disclosure, withdrawal, special and any other similar rights recognized by the laws of any jurisdiction or country.

2.2 Excluded Inventions and Other Inventions. Attached hereto as **Exhibit A** is a list describing all existing Inventions, if any, (a) that are owned by me or in which I have an interest and were made or acquired by me prior to my date of first employment by Company, (b) that may relate to Company's business or actual or demonstrably

anticipated research or development, and (c) that are not to be assigned to Company ("***Excluded Inventions***"). If no such list is attached, I represent and agree that it is because I have no Excluded Inventions. For purposes of this Agreement, "***Other Inventions***" means Inventions in which I have or may have an interest, as of the commencement of my employment or thereafter, other than Company Inventions (as defined below) and Excluded Inventions. I acknowledge and agree that if I use any Excluded Inventions or any Other Inventions in the scope of my employment, or if I include any Excluded Inventions or Other Inventions in any product or service of Company, or if my rights in any Excluded Inventions or Other Inventions may block or interfere with, or may otherwise be required for, the exercise by Company of any rights assigned to Company under this Agreement, I will immediately so notify Company in writing. Unless Company and I agree otherwise in writing as to particular Excluded Inventions or Other Inventions, I hereby grant to Company, in such circumstances (whether or not I give Company notice as required above), a non-exclusive, perpetual, transferable, fully-paid and royalty-free, irrevocable and worldwide license, with rights to sublicense through multiple levels of sublicensees, to reproduce, make derivative works of, distribute, publicly perform, and publicly display in any form or medium, whether now known or later developed, make, have made, use, sell, import, offer for sale, and exercise any and all present or future rights in, such Excluded Inventions and Other Inventions. To the extent that any third parties have rights in any such Other Inventions, I hereby represent and warrant that such third party or parties have validly and irrevocably granted to me the right to grant the license stated above.

2.3 Assignment of Company Inventions. Inventions assigned to Company or to a third party as directed by Company pursuant to Section 2.6 are referred to in this Agreement as "***Company Inventions***." Subject to Section 2.4 and except for Excluded Inventions set forth in **Exhibit A** and Other Inventions, I hereby assign to Company all my right, title, and interest in and to any and all Inventions (and all Intellectual Property Rights with respect thereto) made, conceived, reduced to practice, or learned by me, either alone or with others, during the period of my employment by Company. To the extent required by applicable Copyright laws, I agree to assign in the future (when any copyrightable Inventions are first fixed in a tangible medium of expression) my Copyright rights in and to such Inventions. Any assignment of Company Inventions (and all Intellectual Property Rights with respect thereto) hereunder includes an assignment of all Moral Rights. To the extent such Moral Rights cannot be assigned to Company and to the extent the following is allowed by the laws in any country where Moral Rights exist, I hereby unconditionally and irrevocably waive the enforcement of such Moral Rights, and all claims and causes of action of any kind against Company or related to Company's customers, with respect to such rights. I further acknowledge and agree that neither my successors-in-interest nor legal heirs retain any Moral Rights in any Company Inventions (and any Intellectual Property Rights with respect thereto).

2.4 Unassigned or Nonassignable Inventions. I recognize that this Agreement will not be deemed to require assignment of any Invention that is covered under California Labor Code section 2870(a) (the "***Specific Inventions Law***") except for those Inventions that are covered by a contract between Company and the United States or any of its agencies that require full title to such patent or Invention to be in the United States.

2.5 Obligation to Keep Company Informed. During the period of my employment, I will promptly and fully disclose to Company in writing all Inventions authored, conceived, or reduced to practice by me, either alone or jointly with others. At the time of each such disclosure, I will advise Company in writing of any Inventions that I believe fully qualify for protection under the provisions of the Specific Inventions Law; and I will at that time provide to Company in writing all evidence necessary to substantiate that belief. Company will keep in confidence and will not use for any purpose or disclose to third parties without my consent any confidential information disclosed in writing to Company pursuant to this Agreement relating to Inventions that qualify fully for protection under the Specific Inventions Law. I will preserve the confidentiality of any Invention that

does not fully qualify for protection under the Specific Inventions Law.

2.6 Government or Third Party. I agree that, as directed by Company, I will assign to a third party, including without limitation the United States, all my right, title, and interest in and to any particular Company Invention.

2.7 Ownership of Work Product.

(a) I acknowledge that all original works of authorship which are made by me (solely or jointly with others) within the scope of my employment and which are protectable by Copyright are "works made for hire," pursuant to United States Copyright Act (17 U.S.C., Section 101).

(b) I agree that Company will exclusively own all work product that is made by me (solely or jointly with others) within the scope of my employment, and I hereby irrevocably and unconditionally assign to Company all right, title, and interest worldwide in and to such work product. I understand and agree that Ihave no right to publish on, submit for publishing, or use for any publication any work product protected by this Section, except as necessary to perform services for Company.

2.8 Enforcement of Intellectual Property Rights and Assistance. I will assist Company in every proper way to obtain, and from time to time enforce, United States and foreign Intellectual Property Rights and Moral Rights relating to Company Inventions in any and all countries. To that end I will execute, verify and deliver such documents and perform such other acts (including appearances as a witness) as Company may reasonably request for use in applying for, obtaining, perfecting, evidencing, sustaining and enforcing such Intellectual Property Rights and the assignment thereof. In addition, I will execute, verify and deliver assignments of such Intellectual Property Rights to Company or its designee, including the United States or any third party designated by Company. My obligation to assist Company with respect to Intellectual Property Rights relating to such Company Inventions in any and all countries will continue beyond the termination of my employment, but Company will compensate me at a reasonable rate after my termination for the time actually spent by me at Company's request on such assistance. In the event Company is unable for any reason, after reasonable effort, to secure my signature on any document needed in connection with the actions specified in this paragraph, I hereby irrevocably designate and appoint Company and its duly authorized officers and agents as my agent and attorney in fact, which appointment is coupled with an interest, to act for and on my behalf to execute, verify and file any such documents and to do all other lawfully permitted acts to further the purposes of the preceding paragraph with the same legal force and effect as if executed by me. I hereby waive and quitclaim to Company any and all claims, of any nature whatsoever, which I now or may hereafter have for infringement of any Intellectual Property Rights assigned under this Agreement to Company.

2.9 Incorporation of Software Code. I agree that I will not incorporate into any Company software or otherwise deliver to Company any software code licensed under the GNU General Public License or Lesser General Public License or any other license that, by its terms, requires or conditions the use or distribution of such code on the disclosure, licensing, or distribution of any source code owned or licensed by Company **except** in strict compliance with Company's policies regarding the use of such software.

3. Records. I agree to keep and maintain adequate and current records (in the form of notes, sketches, drawings and in any other form that is required by Company) of all Confidential Information developed by me and all Company Inventions made by me during the period of my employment at Company, which records will be available to and remain the sole property of Company at all times.

4. Duty Of Loyalty During Employment. I agree that during the period of my employment by Company, I will not, without Company's express written consent, directly or indirectly engage in any employment or business activity which is directly or

indirectly competitivewith, or would otherwise conflict with, my employment byCompany.

5. No Solicitation Of Employees, Consultants Or Contractors. I agree that during the period of my employment and for the one year period after the date my employment ends for any reason, including but not limited to voluntary termination by me or involuntary termination by Company, I will not, as an officer, director, employee, consultant, owner, partner, or in any other capacity, either directly or through others, except on behalf of Company, solicit, induce, encourage, or participate in soliciting, inducing or encouraging any person known to me to be an employee, consultant, or independent contractor of Company to terminate his or her relationship with Company, even if I did not initiate the discussion or seek out the contact.

6. Reasonableness Of Restrictions.

6.1 I agree that I have read this entire Agreement and understand it. I agree that this Agreement does not prevent me from earning a living or pursuing my career. I agree that the restrictions contained in this Agreement are reasonable, proper, and necessitated by Company's legitimate business interests. I represent and agree that I am entering into this Agreement freely and with knowledge of its contents with the intent to be bound by the Agreement and the restrictions contained in it.

6.2 In the event that a court finds this Agreement, or any of its restrictions, to be ambiguous, unenforceable, or invalid, I and Company agree that the court will read the Agreement as a whole and interpret therestriction(s) at issue to be enforceable and valid to the maximum extent allowed by law.

6.3 If the court declines to enforce this Agreement in the manner provided in subsection 6.2, Company and I agree that this Agreement will be automatically modified to provide Company with the maximum protection of its business interests allowed by law and I agree to be bound by this Agreement as modified.

7. No Conflicting Agreement Or Obligation. I represent that my performance of all the terms of this Agreement and as an employee of Company does not and will not breach any agreement to keep in confidence information acquired by me in confidence or in trust priorto my employment by Company. I have not entered into, and I agree I will not enter into, any agreement either written or oral in conflict with this Agreement.

8. Return Of Company Property. When I leave the employ of Company, I will deliver to Company any and all drawings, notes, memoranda, specifications, devices, formulas and documents, together with all copies thereof, and any other material containing or disclosing any Company Inventions, Third Party Information orConfidential Information of Company. I agree that I will not copy, delete, or alter any information contained upon my Company computer or Company equipment before I return it to Company. In addition, if I have used any personal computer, server, or e-mail system to receive, store, review, prepare or transmit any Company information, including but not limited to, Confidential Information, I agree to provide Company with a computer- useable copy of all such Confidential Information and then permanently delete and expunge such Confidential Information from those systems; and I agree to provide Company access to my system as reasonably requested to verify that the necessary copying and/or deletion is completed. I further agree that any property situated on Company's premises and owned by Company, including disks and other storage media, filing cabinets or other work areas, is subject to inspection by Company's personnel at any time with or without notice. Prior to leaving, I will cooperate with Company in attending an exit interview and completing and signing Company's termination statementif required to do so by Company.

9. Legal And Equitable Remedies.

9.1 I agree that it may be impossible to assess the damages caused by my violation of this Agreement or any of its terms. I agree that any threatened or actual violation of this Agreement or any of its terms will constitute immediate and irreparable injury to Company, and Company will have the right to

enforce this Agreement and any of its provisions by injunction, specific performance or other equitable relief, without bond and without prejudice to any other rights and remedies that Company may have for a breach or threatened breach of this Agreement.

9.2 In the event Company enforces this Agreement through a court order, I agree that the restrictions of Section 5 will remain in effect for a period of 12 months from the effective date of the Order enforcingthe Agreement.

10. Notices. Any notices required or permitted under this Agreement will be given to Company at its headquarters location at the time notice is given, labeled "Attention Chief Executive Officer," and to me at my address as listed on Company payroll, or at such other address as Company or I may designate by written notice to the other. Notice will be effective upon receipt or refusalof delivery. If delivered by certified or registered mail, notice will be considered to have been given five business days after it was mailed, as evidenced by the postmark. If delivered by courier or express mail service, notice will be considered to have been given on the delivery date reflected by the courier or express mail service receipt.

11. Publication Of This Agreement To Subsequent Employer Or Business Associates Of Employee.

11.1 If I am offered employment or the opportunity to enter into any business venture as owner, partner, consultant or other capacity while the restrictions described in Section 5 of this Agreement are in effect I agree to inform my potential employer, partner, co-owner and/or others involved in managing the business with which I have an opportunity to be associated of my obligations under this Agreement and also agree to provide such person or persons with a copy of this Agreement.

11.2 I agree to inform Company of all employment and business ventures which I enter into while the restrictions described in Section 5 of this Agreement are in effect and I also authorize Company to provide copies of this Agreement to my employer, partner, co- owner and/or others involved in managing the business with which I am employed or associated and to make such persons aware of my obligations under this Agreement.

12. General Provisions.

12.1 Governing Law; Consent To Personal Jurisdiction. This Agreement will be governed by and construed according to the laws of the State of California as such laws are applied to agreements entered into and to be performed entirely within California between residents of California. I hereby expressly consent to the personal jurisdiction and venue of the state and federal courts located in California for any lawsuit filed there against me by Company arising from or related to this Agreement.

12.2 Severability. In case any one or more of the provisions, subsections, or sentences contained in this Agreement will, for any reason, be held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability will not affect the other provisions of this Agreement, and this Agreement will be construed as if such invalid, illegal or unenforceable provision had never been contained in this Agreement. If moreover, any one or more of the provisions contained in this Agreement will for any reason be held to be excessively broad as to duration, geographical scope, activity or subject, it will be construed by limiting and reducing it, so as to be enforceable to the extent compatible with the applicable law as it will then appear.

12.3 Successors and Assigns. This Agreement is for my benefit and the benefit of Company, its successors, assigns, parent corporations, subsidiaries, affiliates, and purchasers, and will be binding upon my heirs, executors, administrators and other legal representatives.

12.4 Survival. This Agreement shall survive the termination of my employment, regardless of the reason, and the assignment of this Agreement by Company to anysuccessor in interest or other assignee.

12.5 Employment At-Will. I agree and understand that nothing in this Agreement will change my at-will employment status or confer any right with respect to continuation of employment by Company, nor will it interfere in any way with my right or Company's right to terminate my employment at any time, with or without cause or advance notice.

12.6 Waiver. No waiver by Company of any breach of this Agreement will be a waiver of any preceding or succeeding breach. No waiver by Company of any right under this Agreement will be construed as a waiver of any other right. Company will not be required to give notice toenforce strict adherence to all terms of this Agreement.

12.7 Export. I agree not to export, reexport, or transfer, directly or indirectly, any U.S. technical data acquired from Company or any products utilizing such data, in violation of the United States export laws orregulations.

12.8 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts maybe delivered via facsimile, electronic mail (including pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, Uniform Electronic Transactions Act or other applicable law) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for allpurposes.

12.9 Advice of Counsel. **I ACKNOWLEDGE THAT, IN EXECUTING THIS AGREEMENT, I HAVE HAD THE OPPORTUNITY TO SEEK THE ADVICE OF INDEPENDENT LEGAL COUNSEL, AND I HAVE READ AND UNDERSTOOD ALL OF THE TERMS AND PROVISIONS OF THIS AGREEMENT. THIS AGREEMENT WILL NOT BE CONSTRUED AGAINST ANY PARTY BY REASON OF THE DRAFTING OR PREPARATION OF THIS AGREEMENT.**

12.10 Entire Agreement. The obligations pursuant to Sections 1 and 2 (except Subsection 2.4 and Subsection 2.7(a)) of this Agreement will apply to any timeduring which I was previously engaged, or am in the futureengaged, by Company as a consultant if no other agreement governs nondisclosure and assignment of inventions during such period. This Agreement is the final, complete and exclusive agreement of the parties with respect to the subject matter of this Agreement and supersedes and merges all prior discussions between us. No modification of or amendment to this Agreement will be effective unless in writing and signed by the party to be charged. Any subsequent change or changes in my duties, salary or compensation will not affect the validity or scopeof this Agreement.

[signatures to follow on next page]

This Agreement will be effective as of March 16, 2021.

EMPLOYEE:

I HAVE READ THIS AGREEMENT CAREFULLY AND UNDERSTAND ITS TERMS. I HAVE COMPLETELY FILLED OUT EXHIBIT A TO THIS AGREEMENT.

/s/ Vinny Jindal

(Signature)

Vinny Jindal

Name

22 December 2021

Date

vjindal@reneopharma.com

Email

COMPANY:

ACCEPTED AND AGREED

RENEO PHARMACEUTICALS, INC.

By: /s/ Michael P. Cruse
Name: Michael P. Cruse
Title: Sr. Vice President Corporate Operations
Email: mcruse@reneopharma.com
Phone: +1 858.283.0287

EXHIBIT A

EXCLUDED INVENTIONS

TO: **Reneo Pharmaceuticals, Inc.**

FROM: Vinny Jindal

DATE: 22 December 2021

1. **Excluded Inventions Disclosure**. Except as listed in Section 2 below, the following is a complete list of allExcluded Inventions:

☐ No Excluded Inventions.

☒ See below:

_____

_____

_____

_____

_____

_____

☐ Additional sheets attached.

2. Due to a prior confidentiality agreement, I cannot complete the disclosure under Section 1 above with respect to the Excluded Inventions generally listed below, the intellectual property rights and duty of confidentiality with respect to which I owe to the following party(ies):

	Excluded Invention	**Party(ies)**	**Relationship**
1.			
2.			
3.			

☐ Additional sheets attached.

3. Limited Exclusion Notification.

This is to notify you in accordance with Section 2872 of the California Labor Code that the foregoing Agreement between you and Company does not require you to assign or offer to assign to Company any Invention that you develop entirely on your own time without using Company's equipment, supplies, facilities or trade secret information, except for those Inventions that either:

a. Relate at the time of conception or reduction to practice to Company's business, or actual or demonstrably anticipated research or development; or

b. Result from any work performed by you for Company.

To the extent a provision in the foregoing Agreement purports to require you to assign an Invention otherwise excluded from the preceding paragraph, the provision is against the public policy of this state and is unenforceable.

This limited exclusion does not apply to any patent or Invention covered by a contract between Company and the United States or any of its agencies requiring full title to such patent or Invention to be in the United States.

EXHIBIT B

SEPARATION DATE RELEASE

(to be signed and returned to the Company on or within twenty-one (21) days after the Separation Date)

In exchange for the severance benefits to be provided to me by Reneo Pharmaceuticals, Inc. (the "**Company**") pursuant to that certain transition, separation and consulting letter agreement with the Company dated February 2, 2022 (the "**Agreement**"), I hereby provide the following Separation Date Release (the "**Release**"). Capitalized terms used but not defined herein shall have the meanings ascribed to them in the Agreement.

I hereby represent that I have been paid all compensation owed and for all hours worked through the date I sign this Release, have received all the leave and leave benefits and protections for which I am eligible pursuant to the Family and Medical Leave Act, or otherwise, and have not suffered any on-the-job injury for which I have not already filed a workers' compensation claim. I acknowledge that, other than the severance benefits to be provided to me pursuant to the Agreement upon satisfaction of the Severance Preconditions, Ihave not earned and will not receive from the Company any additional compensation (including base salary, bonus, incentive compensation, or equity), severance, or benefits, with the exception of any vested right I may have under the express terms of a written ERISA-qualified benefit plan (e.g., 401(k) account) or any vested options or vested restrictedstock units.

I hereby generally and completely release the Company, and its affiliated, related, parent and subsidiary entities, and its and their current and former directors, officers, employees, shareholders, partners, agents, attorneys, predecessors, successors, insurers, affiliates, and assigns from any and all claims, liabilities, demands, causes of action, and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring at any time prior to and including the date I sign this Release. This general release includes, but is not limited to: (a) all claims arising out of or in any way related to my employment with the Company or the termination of that employment; (b) all claims related to my compensation or benefits from the Company, including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, restricted stock units, or any other ownership, equity, or profits interests in the Company; (c) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (d) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (e) all federal, state, and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys' fees, or other claims arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990, the California LaborCode (as amended), the California Family Rights Act, the Age Discrimination in Employment Act ("**ADEA**"), the California Fair Employment and Housing Act (as amended), the Texas Labor Code, including Chapter 21 of the Texas Labor Code (as amended), the Texas Payday Law (as amended), the Texas Anti-Retaliation Act (as amended), and the Texas Whistleblower Act (as amended). Notwithstanding the foregoing, I am not releasing the Company hereby from any obligation to indemnify me pursuant to the Certificate of Incorporation and Bylaws of the Company, any valid fully executed indemnification agreement with the Company, applicable law, or applicable directors and officers liability insurance. Also, excluded from this Release are any claims that cannot be waived by law.

ADEA Release. I acknowledge that I am knowingly and voluntarily waiving and releasing any rights I have under the ADEA, and that the consideration given for the waiver and releases I have given in this Release is in addition to anything of value to which I was already entitled. I further acknowledge that I have been advised, as required by the ADEA, that: (a) my waiver and release does not apply to any rights or claims that arise after the date I sign this Release; (b) I should consult with an attorney prior to signing this Release (although I may choose voluntarily not to do so); (c) I have twenty-one (21) days to consider this Release (although I may choose voluntarily to sign it sooner); (d) I have seven (7) days following the date I sign this Release to revoke this Release (in a written revocation sent to the Company); and (e) this Release will not be effective until the date upon which the revocation period has expired, which will be the eighth day after I sign this Release provided that I do not revoke it (the "**Effective Date**").

In giving the release herein, which includes claims which may be unknown to me at present, I acknowledge that I have read and understand Section 1542 of the California Civil Code, which reads as follows:

> **"A general release does not extend to claims that the creditor or releasingparty does not know or suspect to exist in his or her favor at the time of executing the release and that, if known by him or her, would havematerially affected his or her settlement with the debtor or releasedparty."**

I hereby expressly waive and relinquish all rights and benefits under that section and any law of any other jurisdiction of similar effect with respect to my release of claims herein, including but not limited to my release of unknown claims.

I understand that nothing in this Release limits my ability to file a charge or complaint with the Equal Employment Opportunity Commission, the Department of Labor, the National Labor Relations Board, the Occupational Safety and Health Administration, the Texas Workforce Commission, the Securities and Exchange Commission or any other federal, state or local governmental agency or commission ("**Government Agencies**"). I further understand this Release does not limit my ability to communicate with any Government Agencies or otherwise participate in any investigation or proceeding that may be conducted by any Government Agency, including providing documents or other information, without notice to the Company. While this Release does not limit my right to receive an award for information provided to the Securities and Exchange Commission, I understand and agree that, to maximum extent permitted by law, I am otherwise waiving any and all rights I may have to individual relief based on any claims that I have released and any rights I have waived by signing this Release.

[Signature page to follow]

This Release, together with the Agreement (and its exhibits) constitutes the entire agreement between me and the Company with respect to the subject matter hereof. I am not relying on any representation not contained herein or in the Agreement.

UNDERSTOOD, ACCEPTED, AND AGREED:

_____

Vineet R. Jindal

_____

Date

EXHIBIT 21.1

SUBSIDIARIES OF RENEO PHARMACEUTICALS, INC.

Name of Subsidiary	Jurisdiction of Incorporation
Reneo Pharma Ltd	United Kingdom

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-255140) pertaining to the 2014 Equity Incentive Plan, the 2021 Equity Incentive Plan, and the 2021 Employee Stock Purchase Plan of Reneo Pharmaceuticals, Inc. of our report dated March 23, 2022, with respect to the consolidated financial statements of Reneo Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2021.

/s/ Ernst & Young LLP

San Diego, California
March 23, 2022

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER

PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Gregory J. Flesher, certify that:

1. I have reviewed this Annual Report on Form 10-K of Reneo Pharmaceuticals, Inc. (the "registrant");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respects to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize, and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2022

/s/ Gregory J. Flesher
Gregory J. Flesher
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER

PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Vineet R. Jindal, certify that:

1. I have reviewed this Annual Report on Form 10-K of Reneo Pharmaceuticals, Inc. (the "registrant");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations, and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize, and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2022

/s/ Vineet R. Jindal
Vineet R. Jindal
Chief Financial Officer
(Principal Financial and Accounting Officer)

STATEMENT PURSUANT TO
18 U.S.C. SECTION 1350
AS REQUIRED BY
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Gregory J. Flesher, Chief Executive Officer of Reneo Pharmaceuticals, Inc. (the "Company"), and Vinnet R. Jindal, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2021, to which this Certification is attached as Exhibit 32.1 (the "Annual Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

March 23, 2022 /s/ Gregory J. Flesher
Gregory J. Flesher
Chief Executive Officer
(Principal Executive Officer

March 23, 2022 /s/ Vineet R. Jindal
Vineet R. Jindal
Chief Financial Officer
(Principal Accounting Officer)

This certification accompanies the Annual Report to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Annual Report), irrespective of any general incorporation language contained in such filing.