Filed Pursuant to Rule 424(b)(4)
Registration No. 333-254534

**PROSPECTUS**

# 6,250,000 Shares


## Common Stock

We are offering 6,250,000 shares of common stock. This is our initial public offering. Prior to this offering, there has been no public market for our common stock. The initial public offering price is $15.00 per share. Our common stock has been approved for listing on the Nasdaq Global Market under the symbol “RPHM.”

We are an “emerging growth company” under applicable Securities and Exchange Commission rules and have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

**Our business and an investment in our common stock involve significant risks. These risks are described under the caption “Risk Factors” beginning on page 11 of this prospectus.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.**

| | PER SHARE | TOTAL |
|---|---|---|
| Initial Public Offering Price | $ 15.00 | $93,750,000 |
| Underwriting Discounts and Commissions (1) | $ 1.05 | $ 6,562,500 |
| Proceeds, Before Expenses, to Reneo Pharmaceuticals, Inc. | $ 13.95 | $87,187,500 |

(1) See the section titled “Underwriting” for additional information regarding compensation payable to the underwriters.

Delivery of the shares of common stock is expected to be made on or about April 13, 2021. We have granted the underwriters an option for a period of 30 days to purchase an additional 937,500 shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $7,546,875, and the total proceeds to us, before expenses, will be $100,265,625.

**Jefferies** **SVB Leerink** **Piper Sandler**

April 8, 2021

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**Through and including May 3, 2021 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.**

We are responsible for the information contained in this prospectus and in any free-writing prospectus we prepare or authorize. We have not, and the underwriters have not, authorized anyone to provide you with different information, and we take no, and the underwriters take no, responsibility for any other information others may give you. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front of this prospectus.

For investors outside of the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

This prospectus includes our trademarks which are our property and are protected under applicable intellectual property laws. This prospectus also includes trademarks and trade names that are the property of other organizations. Solely for convenience, trademarks and trade names referred to in this prospectus appear without the ® and ™ symbols, but those references are not intended to indicate that we will not assert, to the fullest extent under applicable law, our rights, or that the applicable owner will not assert its rights, to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

## PROSPECTUS SUMMARY

*This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, including the sections in this prospectus titled "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations," and our consolidated financial statements and the related notes included elsewhere in this prospectus, before making an investment decision. Unless otherwise indicated, all references in this prospectus to "Reneo," the "company," "we," "our," "us" or similar terms refer to Reneo Pharmaceuticals, Inc. and its subsidiary.*

### Overview

Reneo is a clinical stage pharmaceutical company focused on the development of therapies for patients with rare genetic mitochondrial diseases, which are often associated with the inability of mitochondria to produce adenosine triphosphate (ATP). We are developing REN001 to modulate genes critical to metabolism and generation of ATP, which is the primary source of energy for cellular processes. REN001 is a selective peroxisome proliferator-activated receptor delta (PPARd) agonist that has been shown to increase transcription of genes involved in mitochondrial function and increase fatty acid oxidation (FAO), and may increase production of new mitochondria.

We believe REN001 could benefit patients with genetic mitochondrial myopathies who experience weakness, fatigue, cramping, and wasting of muscle due to the mitochondria's inability to produce adequate levels of ATP. These patients often struggle to perform everyday activities, and over time, are at risk of experiencing cardiac and multisystem morbidities and have reduced life expectancy.

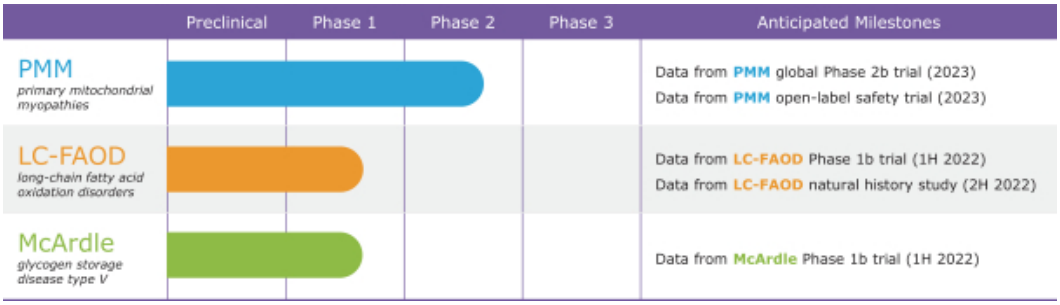
We are initially developing REN001 in three rare genetic diseases that typically present with myopathy and have high unmet medical needs: primary mitochondrial myopathies (PMM), long-chain fatty acid oxidation disorders (LC-FAOD), and glycogen storage disease type V (McArdle disease).

We completed an open-label Phase 1b clinical trial in patients with PMM to assess the safety and tolerability of REN001, and to 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 in this trial. Compared to baseline, patients receiving REN001 once-daily for 12 weeks experienced an average increase in distance of 104 meters in the 12-minute walk test (12MWT) and an average increase of 1.7mL/kg/min in peak oxygen consumption (peak $VO_2$) as well as a reduction in patient-reported fatigue and pain.

Based on these results, we initiated a global, randomized, double-blind, placebo-controlled Phase 2b clinical trial in patients with PMM and plan to begin enrollment in the first half of 2021. We also plan to conduct an open-label, long-term safety trial outside the United States in a subset of patients from the Phase 2b clinical trial. We anticipate results from these clinical trials in 2023. Following our interactions with the U.S. Food and Drug Administration (FDA) 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 are also conducting two open-label Phase 1b clinical trials of REN001 in patients with LC-FAOD and with McArdle disease. Both Phase 1b clinical trials are currently enrolling and we anticipate results in the first half of 2022. We also plan to explore the potential of REN001 in other rare diseases, such as Duchenne muscular dystrophy and Alport syndrome, where we have supportive preclinical data.

The following table summarizes our pipeline for REN001.




**Background and Disease Overview**

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

- PMM: This rare 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 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.
- McArdle disease: This rare disease has an estimated prevalence of 2:100,000, representing at least 6,000 patients in the United States and 8,000 in Europe. Patients with McArdle disease have a specific inability to break down glycogen to glucose as a source of energy for mitochondria. Patients with McArdle disease experience muscle damage with severe acute fatigue and muscle pain. Breakdown of muscle tissue can also cause kidney damage. We are initially targeting adult patients with McArdle disease.

Muscle cells mainly rely on three sources to generate energy: phosphocreatine, carbohydrates (glycogen), and fatty acids. At the onset of exertion, muscle cells use readily available sources of energy such as phosphocreatine and carbohydrates (glycogen). As these sources of energy become depleted with continued exertion, muscle cells turn to fatty acids as the primary source to generate 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, and 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 management 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.

Patients with McArdle disease are unable to break down glycogen in the muscle. Patients with McArdle disease present with severe acute pain and difficulty moving their muscles after the first few minutes of muscle activity. An increase in fatty acid metabolism may allow patients to overcome the deficiency in glycogen, thereby minimizing the lack of energy associated with their disease.

**REN001 Overview**

REN001 is designed to selectively activate PPARd receptors found in the nuclear membrane of muscle and other cells. PPARd 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). PPARd is highly expressed in muscle cells and activation of PPARd 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 in study animals. We believe these are the mechanisms by which REN001 will act to help patients with mitochondrial diseases.

We completed an open-label Phase 1b clinical trial in patients with PMM to assess the safety and tolerability of REN001, and to 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 in this trial. Compared to baseline, patients receiving REN001 once-daily for 12 weeks experienced an average increase of 104 meters in the 12MWT and an average increase of 1.7mL/kg/min in peak $VO_2$ as well as a reduction in patient-reported fatigue and pain.

Based on these results, we initiated a global randomized, double-blind, placebo-controlled Phase 2b clinical trial in patients with PMM and plan to begin enrollment in the first half of 2021. We also plan to conduct an open-label, long-term safety trial outside the United States in a subset of patients from the Phase 2b clinical trial. We anticipate results from these clinical trials in 2023. Following our interactions with the FDA 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 are also conducting open-label Phase 1b clinical trials of REN001 in patients with LC-FAOD and with McArdle disease. Available results from the first six patients in the LC-FAOD trial showed an improvement in multiple measures, including the 12MWT and patient-reported outcome questionnaires in some patients compared to baseline. Both trials are currently enrolling patients, and we anticipate results from these two Phase 1b clinical trials in the first half of 2022.

As of January 31, 2021, REN001 has been dosed in 112 individuals across multiple clinical trials and was well tolerated, with no drug-related serious adverse events (SAE) reported.

We licensed exclusive, worldwide rights to develop and commercialize REN001 and other related compounds from vTv Therapeutics LLC (vTv Therapeutics) in December 2017.

**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, LC-FAOD, and McArdle disease, 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 patients with PMM;
- Advance REN001 clinical development in patients with LC-FAOD and with McArdle disease;
- Maximize the commercial potential of REN001 in additional rare disease indications;

- Commercialize REN001 in the United States and key European markets and establish REN001 as standard of care; and
- Expand our rare disease pipeline through acquisitions and/or licensing of complementary programs.

**Our Team**

Our experienced management team is led by our President and Chief Executive Officer, Gregory J. Flesher, who has more than 25 years of biopharmaceutical industry experience and has been closely involved with the successful development and commercialization of multiple novel drugs. Mr. Flesher previously served as Chief Executive Officer of Novus Therapeutics, Inc., and has held additional leadership roles at Avanir Pharmaceuticals, Inc. (acquired by Otsuka Pharmaceutical Co., Ltd.), InterMune, Inc. (acquired by Roche Holding AG), Amgen Inc. and Eli Lilly and Company. Our Chief Medical Officer, Alejandro Dorenbaum, M.D., has extensive experience in the development of drugs for rare diseases such as Kuvan, Naglazyme, and Palynziq. Dr. Dorenbaum previously served as Chief Medical Officer at Allakos Inc. and Lumena Pharmaceuticals, Inc. and held other leadership roles at Genentech and BioMarin Pharmaceuticals Inc. Our Chief Financial Officer, Vineet R. Jindal, has extensive experience in the biotechnology public markets, including senior positions at ThinkEquity Partners LLC and Wedbush Morgan Securities Inc. Mr. Jindal oversaw Strategy, Business Development, Corporate Communications and Investor Relations at Reata Pharmaceuticals, Inc. Our Chief Development Officer, Wendy Johnson, has over 30 years of pharmaceutical industry experience, including development of the rare disease drug, Treanda. Ms. Johnson held previous leadership positions at AmpliPhi Biosciences Corporation, Aires Pharmaceuticals, Inc. (acquired by Mast Therapeutics, Inc.), and Salmedix, Inc. (acquired by Cephalon, Inc.).

**Our Investors**

We are supported by leading life sciences investors, including Novo Holdings A/S, Abingworth, New Enterprise Associates, RiverVest Venture Partners, Pappas Capital, Lundbeckfond Ventures, Rock Springs Capital, Aisling Capital, and Amzak Health.

**Risks Associated with Our Business**

Investing in our common stock involves substantial risk. The risks described under the heading “Risk Factors” immediately following this summary may cause us to not realize the full benefits of our strengths or may cause us to be unable to successfully execute all or part of our strategy. Some of the more significant challenges include the following:

- We have incurred significant net losses since our inception 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.
- 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, 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, 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.
- 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 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.
- 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.
- 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.

**Implications of Being an Emerging Growth Company and Smaller Reporting 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 the last day of the fiscal year ending after the fifth anniversary of this offering 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 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 particular, in this prospectus, we have provided only two years of audited consolidated financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company, and we may elect to take advantage of other reduced reporting requirements in

future filings. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

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.

### Corporate Information

We were incorporated under the laws of the State of Delaware in September 2014 as Reneo Pharmaceuticals, Inc. Our principal executive offices are located at 12230 El Camino Real, Suite 230, San Diego, California 92130, and our telephone number is (858) 283-0280. We also occupy offices in Sandwich, United Kingdom. Our website address is www.reneopharma.com. Information contained in, or that can be accessed through, our website is not incorporated by reference into this prospectus.

**THE OFFERING**

| | |
|---|---|
| Common stock offered by us | 6,250,000 shares. |
| Option to purchase additional shares | We have granted the underwriters the option to purchase up to 937,500 additional shares of our common stock. The underwriters can exercise this option at any time within 30 days after the date of this prospectus. |
| Common stock to be outstanding after this offering | 24,210,699 shares (or 25,148,199 shares if the underwriters' option to purchase additional shares of our common stock from us is exercised in full). |
| Use of proceeds | We estimate that the net proceeds from this offering will be approximately $84.2 million (or approximately $97.3 million if the underwriters' option to purchase up to 937,500 additional shares of our common stock from us is exercised in full), based on the initial public offering price of $15.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.<br><br>We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, to fund the research and development of REN001, for commercial readiness preparations, for other research and development activities, and for working capital and general corporate purposes. See the section titled "Use of Proceeds" for additional information. |
| Risk factors | See the section titled "Risk Factors" and other information included in this prospectus for a discussion of factors you should consider carefully before deciding to invest in our common stock. |
| Nasdaq Global Market symbol | "RPHM." |

The number of shares of our common stock to be outstanding after this offering is based on 17,960,699 shares of common stock outstanding as of December 31, 2020, after giving effect to the issuance and sale of 23,440,514 shares of our Series B convertible preferred stock in March 2021 and the conversion of all outstanding shares of our convertible preferred stock into 15,907,629 shares of common stock in connection with the closing of this offering, and excludes:

- 935,478 shares of our common stock issuable upon the exercise of outstanding stock options as of December 31, 2020, with a weighted-average exercise price of $2.56 per share;
- 2,273,285 shares of our common stock issuable upon the exercise of outstanding stock options granted from January 1, 2021 through April 8, 2021, with a weighted-average exercise price of $5.06 per share;
- 2,187,524 shares of our common stock reserved for future issuance under our 2021 Equity Incentive Plan (2021 Plan) which became effective immediately prior to the execution of the underwriting agreement in connection with this offering, as well as any automatic annual increases in the number of shares of common stock reserved for future issuance under our 2021 Plan and plus (i) the number of shares that remained available for future issuance under our 2014 Equity Incentive Plan, as amended (2014 Plan), at the time our 2021 Plan became effective and (ii) any shares subject to

outstanding stock options or stock awards that were granted under our 2014 Plan that expire or are repurchased, forfeited, cancelled or withheld, as more fully described in the section titled "Executive Compensation—Employee Benefit Plans";

- 243,058 shares of our common stock reserved for future issuance under our 2021 Employee Stock Purchase Plan (ESPP) which became effective immediately prior to the execution of the underwriting agreement in connection with this offering, and any automatic annual increases in the number of shares of common stock reserved for future issuance under our ESPP; and
- 98,000 shares of our common stock issuable upon the exercise of stock options granted to certain of our directors and employees under our 2021 Plan, effective immediately prior to the execution of the underwriting agreement in connection with this offering, with an exercise price per share that is equal to the price per share at which our common stock is first sold to the public in this offering.

In addition, unless we specifically state otherwise, the information in this prospectus assumes or gives effect to:

- the issuance and sale of an aggregate of 23,440,514 shares of our Series B convertible preferred stock in March 2021 with aggregate net proceeds of $47.3 million;
- the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 15,907,629 shares of our common stock in connection with the closing of this offering;
- no exercise of the outstanding options described above;
- no exercise of the underwriters' option to purchase up to an additional 937,500 shares of common stock from us in this offering;
- a 1-for-4.4748 reverse stock split of our common stock effected on April 5, 2021; and
- the filing and effectiveness of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws in connection with the closing of this offering.

## SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables set forth our summary consolidated financial data for the periods and as of the dates indicated. We derived our summary consolidated statements of operations and comprehensive loss data for the years ended December 31, 2019 and December 31, 2020 and the summary consolidated balance sheet data as of December 31, 2020 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future. You should read the following summary consolidated financial data in conjunction with our consolidated financial statements and related notes included elsewhere in this prospectus and the information in the sections titled "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

| Consolidated Statements of Operations and Comprehensive Loss Data: | YEAR ENDED DECEMBER 31, 2019 | 2020 |
|---|---|---|
| | (in thousands, except share and per share amounts) | |
| Operating expenses: | | |
| Research and development | $ 13,097 | $ 15,944 |
| General and administrative | 2,376 | 3,608 |
| Total operating expenses | 15,473 | 19,552 |
| Loss from operations | (15,473) | (19,552) |
| Other income: | | |
| Change in fair value of Series A convertible preferred stock purchase right liability | 2,581 | — |
| Other income | 456 | 87 |
| Net loss | $ (12,436) | $ (19,465) |
| Net loss per share attributable to common stockholders, basic and diluted (1) | $ (6.38) | $ (9.60) |
| Weighted-average shares of common stock outstanding, basic and diluted (1) | 1,948,170 | 2,028,198 |
| Pro forma net loss per share, basic and diluted (unaudited)(2) | | $ (2.50) |
| Pro forma weighted-average shares of common stock outstanding, basic and diluted (unaudited) (2) | | 7,788,340 |

(1) See Note 2 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate historical net loss per share, basic and diluted, and the weighted-average number of shares of common stock used in the computation of the per share amounts.

(2) Unaudited pro forma net loss per share, basic and diluted, attributable to common stockholders, is calculated giving effect to the conversion of the convertible preferred stock into shares of common stock. Unaudited pro forma net loss per share attributable to common stockholders does not include the shares expected to be sold and related proceeds to be received in this offering. Unaudited pro forma net loss per share attributable to common stockholders for the year ended December 31, 2020 was calculated using the weighted-average number of shares of common stock outstanding, including the pro forma effect of the conversion of all outstanding shares of convertible preferred stock into shares of common stock, as if such conversion had occurred at the beginning of the period, or their issuance dates if later.

| | AS OF DECEMBER 31, 2020 | | |
|---|---|---|---|
| | ACTUAL | PRO FORMA (1) | PRO FORMA AS ADJUSTED (2) |
| | (in thousands) (unaudited) | | |
| **Consolidated Balance Sheet Data:** | | | |
| Cash and cash equivalents | $ 53,613 | $100,898 | $ 185,086 |
| Working capital (3) | 50,445 | 97,730 | 181,918 |
| Total assets | 55,221 | 102,506 | 186,694 |
| Total liabilities | 4,616 | 4,616 | 4,616 |
| Convertible preferred stock | 92,720 | — | — |
| Accumulated deficit | (44,958) | (44,958) | (44,958) |
| Total stockholders' (deficit) equity | (42,115) | 97,890 | 182,078 |

(1) Gives effect to (i) the issuance and sale of an aggregate of 23,440,514 shares of our Series B convertible preferred stock in March 2021 and our receipt of approximately $47.3 million in aggregate net proceeds therefrom, (ii) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 15,907,629 shares of common stock and the related reclassification of the carrying value of our convertible preferred stock to permanent equity in connection with the closing of this offering and (iii) the filing and effectiveness of our amended and restated certificate of incorporation in connection with the closing of this offering.

(2) Gives effect to (i) the items described in footnote (1) above and (ii) the issuance and sale of 6,250,000 shares of our common stock in this offering at the initial public offering price of $15.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

(3) We define working capital as current assets less current liabilities. See our consolidated financial statements and related notes included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

# RISK FACTORS

*Investing in 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 prospectus, 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 invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.*

## Risks Related to Our Business and Industry

***We have incurred significant net losses since our inception 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, 2019 and 2020, we reported a net loss of $12.4 million and $19.5 million, respectively. As of December 31, 2020, we had an accumulated deficit of $45.0 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.

We estimate that the net proceeds from this offering will be approximately $84.2 million, based on the initial public offering price of $15.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We believe, based on our current operating plan, that such proceeds, together with our existing cash and cash equivalents, will be sufficient to fund our operations for at least the next 24 months. 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 the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. 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, patients with LC-FAOD and patients with McArdle disease. 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 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 clinical trial of REN001 of PMM, such as the Modified Fatigue Impact Scale, the Brief Pain Inventory assessment, and a short form health survey 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 1b clinical trial of REN001 in patients with PMM and our Phase 1b clinical trial 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.

***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.***

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. A failure of one or more 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 indication for which we are evaluating REN001 is a rare genetic disease with limited patient populations from which to draw participants in clinical trials. For example, we estimate that PPM, LC-FAOD and McArdle disease have a prevalence of at least 148,000 patients, 11,000 patients and 14,000 patients, respectively, in the United States and Europe combined. 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 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 IND or similar regulatory filing under which we must receive authorization to proceed with clinical development. While we have already submitted the INDs for our clinical trials of REN001 in PMM and LC-FAOD, if our clinical trial of REN001 in McArdle disease, which is currently being conducted outside of the United States, is instead conducted within the United States, we will need to submit an IND with the FDA prior to initiating such trial.

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 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 clinical trial 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. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. For example, in 2005, the FDA published data from two-year mouse and rat carcinogenicity studies that showed correlations between tissue distribution and rodent tumor development in 11 PPAR agonists (five gamma (g) and six alpha/gamma (a/g)). Although PPAR agonists are not considered genotoxic, tissue-specific distribution of PPAR receptors appear to correlate with tumor incidence in rodent models. PPAR alpha (PPARa) mediated activation of genes involved in peroxisome oxidation and biogenesis is known to be carcinogenic in rodents, an effect that has not been observed in humans. FDA placed a class-wide partial clinical hold on all PPAR agonists, requiring 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. 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. For example, we observed an incipient cataract in one patient in the McArdle Phase 1b study and if this adverse event is observed disproportionately in placebo-controlled studies, the FDA or comparable foreign agencies may determine that the risk-benefit profile is not favorable and may not approve REN001, and even if REN001 is approved, such findings may lead to a more limited label, including warnings and precautions, or a risk evaluation and mitigation strategy or other risk minimization tools available to FDA. 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.

While to date we have not seen any drug-related serious adverse effects, only 112 subjects have been treated with REN001, and the safety profile in a broader number of patients with genetic mitochondrial myopathies is unknown and may be different than that observed in previous clinical trials. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects.

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 clinical trial of REN001 in PMM patients was closed early and we temporarily paused enrollment in our Phase 1b clinical trials of LC-FAOD and McArdle disease, which enrollment has now recommenced in certain countries. 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 United Kingdom (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. For example, we have been delayed in finalizing a clinical study report for our Phase 1b clinical trial of REN001 in PMM, as a result of COVID-19 site restrictions that have prevented study monitors from our CRO from timely completing an in-person audit of trial site source documentation. While virtual monitoring visits have occurred and now monitoring visits have resumed at some trial sites, onsite visits have been limited to certain times of the month thus delaying our site close out activities. 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 clinical trials 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. From time to time, we may also disclose interim data from our clinical trials. Interim, topline, and preliminary data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary, interim, or topline data and final data could significantly harm our business prospects.

We have been delayed in finalizing a clinical study report for our Phase 1b clinical trial of REN001 in PMM, as a result of COVID-19 site restrictions that have prevented study monitors from our CRO from timely completing an in-person audit of trial site source documentation. Further, while virtual monitoring visits have occurred and now monitoring visits have resumed at some trial sites, onsite visits have been limited to certain times of the month thus delaying our site close out activities.

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, 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. For example, while the path to accurately diagnose patients with primary mitochondrial diseases is well known, physician lack of awareness about McArdle disease may result in the condition being significantly under diagnosed and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. In addition, the potentially addressable patient population for PMM, LC-FAOD and McArdle disease 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, LC-FAOD or McArdle disease, 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, LC-FAOD and McArdle disease, 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 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 CHMP, is a similarly lengthy and expensive process and the EMA has its own procedures for approval for product candidates. 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 Europe.

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. For instance, the EU has adopted Regulation (EU) No 536/2014 (Clinical Trials Regulation (CTR)) in April 2014, which is expected to come into application in 2022. The CTR will be directly applicable in all the EU member states, repealing the current Clinical Trials Directive. Conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new CTR becomes applicable. The extent to which ongoing clinical trials will be governed by the CTR will depend on when the CTR becomes applicable and on the duration of the

individual clinical trial. If a clinical trial continues for more than three years from the day on which the CTR becomes applicable the CTR will at that time begin to apply to the clinical trial. The CTR harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which will notably contain a centralized EU portal and database. 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.

Separately, in response to the global COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most foreign and domestic manufacturing facility inspections and in July 2020, resumed routine surveillance inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States have adopted similar restrictions and other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities 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 other 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.

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. 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 December 14, 2018, a Texas U.S. District Court Judge ruled that the Affordable Care Act is unconstitutional in its entirety because the “individual mandate” was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. The United States Supreme Court is currently reviewing this case, but it is unclear when or how the Supreme Court will rule. Although the U.S. Supreme Court has yet ruled on the constitutionality of the Affordable Care Act, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructs 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 also unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the Affordable Care Act or 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, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, unless additional Congressional action is taken. Legislation is currently pending in Congress that would further extend the suspension through December 31, 2021. In addition, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Such scrutiny has resulted in several recent congressional inquiries 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 released a final rule on September 24, 2020, effective November 30, 2020, providing guidance 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. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives.

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 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 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 PPARd agonist for PMM and has announced that it is initiating a Phase 2/3 trial in the first quarter of 2021. Other companies are developing therapies for mitochondrial diseases, including 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 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. However, Dojolvi has not demonstrated clear functional benefits on endurance in clinical trials. There are no approved therapies indicated for the treatment of McArdle disease in any country. We are not aware of any drug interventional studies underway or currently announced for LC-FAOD or for McArdle disease.

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 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 European Union (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 EMA from approving another marketing application for the same drug for the same drug 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 disease or condition. In addition, even after a drug is granted orphan exclusivity and approved, the FDA and the EMA can subsequently approve another drug for the same condition before the expiration of the seven-year (or ten-year in the EU) exclusivity period if the FDA or EMA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the EU, the EMA may deny marketing approval for a product candidate if it determines such product candidate is structurally similar to an approved product for the same indication. 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 long chain acyl-CoA dehydrogenase (LCHAD) and mitochondrial encephalomyopathy, lactic acidosis, and neurological stroke-like episodes (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 San Diego, California and Sandwich, United Kingdom. These regions serve as the headquarters to many other 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. The value to employees of stock options that vest over time 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, 2020, we had 23 employees, 12 of whom are full-time. As our development and commercialization plans and strategies develop, and as we transition into operating as a public company, 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) and teaching hospitals, as well as ownership and investment interests held by such physicians and their immediate family members. Beginning in 2022, such obligations will include payments and other transfers of value provided in the previous year to certain other healthcare professionals, including physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified nurse anesthetists, and certified nurse-midwives.

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.

***Failure to comply with data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.***

We and our partners may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). 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 collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. In addition, we may obtain health information from third parties that are subject to privacy and security requirements under HIPAA. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), and regulations promulgated thereunder, imposes requirements relating to the privacy, security and transmission of individually identifiable health information on certain health care providers, health plans and health care

clearinghouses, known as covered entities and their business associates that perform certain services that involve creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities as well as their covered subcontractors. Depending on the facts and circumstances, we could be subject to penalties if we violate HIPAA.

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

In addition to, California recently enacted the California Consumer Privacy Act (CCPA) which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling certain personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA became effective January 1, 2020, and the California Attorney General may bring enforcement actions for violations beginning July 1, 2020. The CCPA has been amended from time to time, and it remains unclear what, if any, further modifications will be made to this legislation or how it will be interpreted. The CCPA, California Privacy Rights Act (CPRA), Consumer Data Protection Act (CDPA) and other similar laws pending in several states, as currently written, may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. Further, the CPRA was recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. In addition, a similar law, the CDPA, was recently passed in Virginia. It goes into effect on January 1, 2023.

Foreign data protection laws, including the GDPR, which became effective on May 25, 2018, may also apply to our processing of health-related and other personal data of data subjects within the European Economic Area (EEA) regardless of where the processing in question is carried out. The GDPR applies to processing operations carried out in the context of an establishment in the EEA and any processing relating to the offering of goods or services to individuals in the EEA and/or the monitoring of their behavior in the EEA. Also, notwithstanding the UK's withdrawal from the EU, by operation of the so-called UK GDPR, the GDPR continues to apply in substantially equivalent form to processing operations carried out in the context of an establishment in the UK and any processing relating to the offering of goods or services to individuals in the UK and/or monitoring of their behavior in the UK—so, when we refer to the GDPR in this section, we are also making reference to the UK GDPR in the context of the UK, unless the context requires otherwise.

The GDPR also provides that EEA Member States may make their own further laws and regulations to introduce specific requirements related to the processing of "special categories of personal data", including personal data related to health, biometric data used for unique identification purposes and genetic information as well as personal data related to criminal offences or convictions. In the UK the Data Protection Act 2018 complements the UK GDPR in this regard. This may lead to greater divergence on the law that applies to the processing of such data types across the EEA and/or UK, compliance with which, as and where applicable, may increase our costs and could increase our overall compliance risk. Such country-specific regulations could also limit our ability to collect, use and share data in the context of our EEA and/or UK operations, and/or could cause our compliance costs to increase, ultimately having an adverse impact on our business and harming our business and financial condition.

The GDPR imposes stringent requirements for controllers and processors of personal data. Further, the UK's vote in favor of exiting the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation

in the UK and in respect of transfers of personal data from the EEA to the UK. A summary of each of these matters is detailed in the "Business—Government Regulation and Product Approval—Data Privacy and Security," below.

A particular issue presented by certain European data protection laws, including the GDPR, is that they generally restrict transfers of personal data from Europe, including the EEA, United Kingdom and Switzerland, to the United States and most other countries unless the parties to the transfer have implemented specific safeguards to protect the transferred personal data; and certain previously available safeguards have been invalidated, and reliance on alternative safeguards may be complex or not possible in certain circumstances—an overview of this area is summarized in "Business—Government Regulation and Product Approval—Data Privacy and Security," below. If we are unable to implement a valid solution for personal data transfers from Europe, including, for example, obtaining individuals' explicit consent to transfer their personal data from Europe to the United States or other countries, we will face increased exposure to regulatory actions, substantial fines and injunctions against processing personal data from Europe. Inability to import personal data from Europe, including the EEA, United Kingdom or Switzerland, may also (i) restrict our activities in Europe; (ii) limit our ability to collaborate with partners as well as other service providers, contractors and other companies subject to European data protection laws; and (iii) require us to increase our data processing capabilities in Europe at significant expense or otherwise cause us to change the geographical location or segregation of our relevant systems and operations—any or all of which could adversely affect our financial results. Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of delivering our services and operating our business. The type of challenges we face in Europe will likely also arise in other jurisdictions that adopt laws similar in construction to the GDPR or regulatory frameworks of equivalent complexity.

The GDPR also provides for more robust regulatory enforcement and greater penalties for noncompliance than previously applicable data protection laws, including fines of up to €20 million or 4% of an undertaking's total worldwide annual turnover for the preceding financial year, whichever is higher. In addition to administrative fines, a wide variety of other potential enforcement powers are available to competent supervisory authorities in respect of potential and suspected violations of the GDPR, including extensive audit and inspection rights, and powers to order temporary or permanent bans on all or some processing of personal data carried out by noncompliant actors. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. Additionally, as noted above, the UK has transposed the GDPR into the laws of the United Kingdom by way of the UK GDPR, which could expose us to two parallel regimes, each of which potentially authorizes similar fines, with the UK GDPR permitting fines of up to the higher of £17.5 million or 4% of global annual revenue of any noncompliant organizations for the preceding financial year; as well as other potentially divergent enforcement actions for certain violations. Implementing mechanisms to endeavor to ensure compliance with the GDPR and relevant local legislation in EEA Member States and the UK may be onerous and may interrupt or delay our development activities, and adversely affect our business, financial condition, results of operations and prospects. In addition to the foregoing, a breach of the GDPR or other applicable privacy and data protection laws and regulations could result in regulatory investigations, reputational damage, orders to cease/change our use of data, enforcement notices, or potential civil claims including class action-type litigation. While we have taken steps to comply with the GDPR where applicable, including by reviewing our security procedures, engaging data protection personnel, and entering into data processing agreements with relevant contractors, our efforts to achieve and remain in compliance may not be fully successful.

Compliance with U.S. and foreign privacy and security laws, rules and regulations could require us to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Each of these constantly evolving laws can be subject to varying interpretations. Failure to comply with U.S. and foreign data protection laws and regulations could result in government investigations and enforcement actions (which could include civil or criminal penalties), fines, private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, patients about whom we or our partners obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data

protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

***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. Since the expiry of the Transition Period, the United Kingdom operates under a distinct regulatory regime. EU pharmaceutical laws only apply to the United Kingdom 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 closely align with EU laws, detailed proposals are yet to be published. Significant political and economic uncertainty therefore remains about how much the relationship between the United Kingdom and EU will differ as a result of the United Kingdom’s withdrawal.

Since a significant proportion of the regulatory framework in the UK applicable to our business and our product candidates is derived from EU directives and regulations, Brexit, has had, and may continue to have, a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the UK or the EU. For example, Great Britain (GB) is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization (MA) from the European Medicines Agency (EMA) and a separate process for authorization of drug products, including REN001 and any future product candidates, will be required to market our product candidates in GB. It is currently unclear whether the Medicines & Healthcare products Regulatory Agency (MHRA) in the UK is sufficiently prepared to handle the increased volume of MAAs that it is likely to receive. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing REN001 in the UK or the EU 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 United Kingdom 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 impacted nations 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). At December 31, 2020, we had NOL carryforwards of approximately $27.1 million and $1.6 million for federal and state, respectively. The federal NOL carryforwards arising in taxable years beginning prior to 2018 will begin to expire in 2034, unless previously utilized. At December 31, 2020, we also had UK NOLs of $4.1 million which carryforward indefinitely. As of December 31, 2020, we also have federal and state research and development credit carryforwards totaling $0.7 million and $0.2 million, respectively. The federal research and development credit carryforwards will begin to expire in 2034, unless previously utilized. The state research and development credits will not expire.

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, including potential changes in connection with this offering. 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 this offering or future offerings and/or subsequent changes in our stock ownership (some of which shifts 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 to offset California taxable income in tax years beginning after 2019 and before 2023.

***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. 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’ PPARd agonist program, to develop, manufacture and commercialize PPARd agonists and products containing such PPARd 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. See “Business—License Agreement with vTv Therapeutics LLC” for a description of our license agreement, which includes a description of the termination provision of this agreement.

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 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 United States Patent and Trademark Office (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 patent extension term (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 or 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 United States Patent and Trademark Office (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 have 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 rule-making, 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. See "Business—License Agreement with vTv Therapeutics LLC" for a description of our license agreement with vTv Therapeutics.

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 prospectus, 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 This Offering and Ownership of Our Common Stock

***We do not know whether an active, liquid and orderly trading market will develop for our common stock or what the market price of our common stock will be and as a result it may be difficult for you to sell your shares of our common stock.***

Prior to this offering there has been no public market for shares of our common stock. Although our common stock has been approved for listing on the Nasdaq Global Market (Nasdaq), an active trading market for our shares may never develop or be sustained following this offering. 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. The initial public offering price for our common stock was determined through negotiations with the underwriters, and the negotiated price may not be indicative of the market price of our common stock after the offering. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the initial public offering price. 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 following this offering 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 prospectus, 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 clinical trial 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, LC-FAOD and McArdle disease, 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. If the market price of our common stock after this offering does not exceed the initial public offering price, you may not realize any return on your investment in us and may lose some or all of your investment.

***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.***

Prior to this offering, our executive officers, directors, greater than 5% holders, and their affiliates beneficially owned approximately 79.5% of our voting stock as of March 31, 2021, and, upon the closing of this offering, that same group will hold approximately 60.9% of our outstanding voting stock (assuming no exercise of the underwriters' option to purchase additional shares and no purchases by such holders in this offering). In addition, if any of our executive officers, directors and greater than 5% stockholders purchase shares in this offering, or if any of our other current investors purchase shares in this offering and become greater than 5% stockholders as a result, the ability of such persons, acting together, to control or significantly influence such matters may increase. Therefore, even after this offering, 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.

***If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.***

The initial public offering price is substantially higher than the net tangible book value per share of our common stock. Investors purchasing common stock in this offering will pay a price per share that substantially exceeds the book value of our tangible assets after subtracting our liabilities. As a result, investors purchasing common stock in this offering will incur immediate dilution of $7.48 per share, based on the initial public offering price of $15.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Further, investors purchasing common stock in this offering will contribute approximately 39.0% of the total amount invested by stockholders since our inception, but will own only approximately 25.8% of the shares of common stock outstanding after giving effect to this offering.

This dilution is due to our investors who purchased shares prior to this offering having paid substantially less when they purchased their shares than the price offered to the public in this offering and the exercise of stock options granted to our employees. To the extent outstanding options are exercised, there will be further dilution to new investors. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. For a further description of the dilution that you will experience immediately after this offering, see the section titled "Dilution."

***We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.***

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section titled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. We intend to use the net proceeds from this offering, together with

our existing cash and cash equivalents, to fund the clinical development of REN001, for commercial readiness preparations, for other research and development activities, and for working capital and general corporate purposes. We may also use a portion of the remaining net proceeds we receive from this offering, together with our existing cash and cash equivalents, to in-license, acquire, or invest in complementary businesses, technologies, products, or assets. However, we have no current commitments or obligations to do so. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing instruments. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

***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 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 prospectus, 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, reduced disclosure obligations regarding executive compensation in this prospectus and 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 the last day of the fiscal year ending after the fifth anniversary of this offering 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 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. Prior to this offering, we have never been required to test our internal controls within a specified period, and, as a result, 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 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.***

As a public company, we will incur significant legal, accounting, and other expenses that we did not incur as a private company. We will be subject to the reporting requirements of the Exchange Act, which will require, among other things, that we file with the SEC annual, quarterly, and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and 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 by our existing stockholders in the public market could cause our stock price to fall.***

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the trading price of our common stock could decline. Upon the closing of this offering, we will have outstanding a total of 24,305,822 shares of common stock. Of these shares, only the shares of common stock sold in this offering by us, other than to our affiliates plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable without restriction in the public market immediately following this offering.

We expect that the lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. After the lock-up agreements expire, up to an additional 18,055,822 shares of common stock will be eligible for sale in the public market, of which 13,873,829 shares are held by directors, executive officers, and other affiliates and will be subject to volume limitations under Rule 144 under the Securities Act of 1933, as amended (the Securities Act). In addition, shares of common stock that are either subject to outstanding options 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, the lock-up agreements, and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

After this offering, the holders of 16,819,282 shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the 180-day lock-up agreements described above. See the section titled “Description of Capital Stock—Registration Rights.” 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.

***Participation in this offering by our directors, officers or affiliates would reduce the available public float of our shares.***

If any of our directors, officers or affiliates purchase shares in this offering, such purchases would reduce the available public float of our common stock because such purchasers would be restricted from selling such shares during the 180-day period following this offering and thereafter would be subject to volume limitations pursuant to restrictions under applicable securities laws. As a result, any purchase of shares by our directors, officers or affiliates in this offering will reduce the liquidity of our common stock relative to what it would have been had these shares been purchased by investors that were not directors, officers or our affiliates.

***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, including shares of common stock sold in this offering.

Pursuant to our 2021 Plan, our management is authorized to grant stock options 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, beginning on January 1, 2022 and continuing 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 ESPP, the number of shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year, beginning on January 1, 2022 through 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, which are to become effective in connection with the closing of this offering, 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 current amended and restated certificate of incorporation provides, and our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective in connection with the closing of this offering, will 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 current amended and restated certificate of incorporation provides, and our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective in connection with the closing of this offering, will provide, that the Court of Chancery of the State of Delaware will 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 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 current amended and restated certificate of incorporation provides, and our amended and restated certificate of incorporation and our amended and restated bylaws, which will become effective in connection with the closing of this offering, will 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, 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, 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 current amended and restated certificate of incorporation, and our amended and restated certificate of incorporation and our amended and restated bylaws, which will become effective in connection with the closing of this offering. This may require significant additional costs associated with resolving such action in other jurisdictions and the provisions may not be enforced by a court in those other jurisdictions.

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. If a court were to find either exclusive forum provision contained in our current amended and restated certificate of incorporation, or our amended and restated certificate of incorporation or amended and restated bylaws, which will become effective in connection with the closing of this offering, to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action 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.

***Our internal computer systems, or those used by our third-party collaborators or other contractors or consultants, may fail or suffer security breaches.***

Despite the implementation of security and back-up measures, our internal computer, server, and other information technology systems as well as those of our third-party collaborators, consultants, contractors, suppliers, and service providers, may be vulnerable to damage from physical or electronic break-ins, computer viruses, malware, ransomware, natural disasters, terrorism, war, telecommunication and electrical failure, denial of service, and other cyberattacks or disruptive incidents that could result in unauthorized access to, use or disclosure of, corruption of, or loss of sensitive, and/or proprietary data, including personal information, including health-related information, and could subject us to significant liabilities and regulatory and enforcement actions, and reputational damage. For example, the loss of clinical trial data from completed or ongoing clinical trials could result in delays in 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. If we or our third-party collaborators, consultants, contractors, suppliers, or service providers were to suffer an attack or breach, for example, that resulted in the unauthorized access to or use or disclosure of personal or health information, we may have to notify consumers, partners, collaborators, government authorities, and the media, and may be subject to investigations, civil penalties, administrative and enforcement actions, and litigation, any of which could harm our business and reputation. 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.
The COVID-19 pandemic has generally increased the risk of cybersecurity intrusions. For example, there has been an increase in phishing and spam emails as well as social engineering attempts from “hackers” hoping to use the recent COVID-19 pandemic to their advantage. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate or unauthorized access to or disclosure or use of confidential, proprietary, or other sensitive, personal, or health information, we could incur liability and suffer reputational harm, and the development and commercialization of REN001 could be delayed.

***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 will depend in part on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements about us and our industry. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position; business strategy; research and development costs; the anticipated timing, costs and conduct of our clinical trials and preclinical studies for our only product candidate, REN001, including the timing and availability of data from such trials; our expectations regarding the potential market size and size of the potential patient populations for REN001, if approved; the impact of COVID-19 on our business; the timing and likelihood of regulatory filings and approvals for REN001; our ability to commercialize REN001, if approved; the pricing and reimbursement of REN001, if approved; the potential benefits of strategic collaborations and our ability to enter into strategic arrangements; the timing and likelihood of success, plans and objectives of management for future operations; the potential to develop future product candidates and future results of anticipated product development efforts; the scope of protection we are able to establish and maintain for intellectual property rights covering REN001, including the projected terms of patent protection; developments and projections relating to our competitors and our industry, including competing products; our expected future financing needs; and expected uses of the net proceeds from this offering, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described under the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we undertake no obligation to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this prospectus. See the section titled “Where You Can Find Additional Information.”

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this prospectus, and while we believe such information provides a reasonable basis for these statements, such information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to unduly rely on these statements.

## MARKET, INDUSTRY AND OTHER DATA

We obtained the industry, market, and competitive position data used throughout this prospectus from our own internal estimates and research, as well as from independent market research, industry, and general publications and surveys, governmental agencies, and publicly available information in addition to research, surveys, and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research, and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires. In addition, while we believe the industry, market, and competitive position data included in this prospectus is reliable and based on reasonable assumptions, such data involve risks and uncertainties and are subject to change based on various factors, including those discussed in the section titled “Risk Factors.” These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties or by us.

## USE OF PROCEEDS

We estimate that we will receive net proceeds from this offering of approximately $84.2 million (or approximately $97.3 million if the underwriters' option to purchase 937,500 additional shares of our common stock is exercised in full) based on the initial public offering price of $15.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to increase our financial flexibility, create a public market for our common stock, and facilitate our future access to capital markets. We currently intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately $20.0 million to fund the research and development of REN001 in PMM, including completion of our global Phase 2b clinical trial of REN001 in patients with PMM and our planned long-term safety trial of REN001 outside the United States in patients from the Phase 2b clinical trial;
- approximately $15.0 million to fund the research and development of REN001 in patients with LC-FAOD, including completion of our Phase 1b clinical trial;
- approximately $15.0 million to fund the research and development of REN001 in patients with McArdle disease, including completion of our Phase 1b clinical trial; and
- the remaining proceeds for commercial readiness preparations, for other research and development activities, and for working capital and general corporate purposes.

We may also use a portion of the remaining net proceeds and our existing cash and cash equivalents to in-license, acquire, or invest in complementary businesses, technologies, products, or assets. However, we have no current commitments or obligations to do so.

We believe, based on our current operating plan, that the net proceeds from this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operations for at least the next 24 months. However, our expected use of proceeds from this offering described above represents our current intentions based on our present plans and business condition. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the proceeds to be received upon the closing of this offering or the actual amounts that we will spend on the uses set forth above.

The amounts and timing of our actual expenditures will depend on numerous factors, including the time and cost necessary to conduct our clinical trials, the results of our clinical trials and preclinical studies and other factors described in the section titled "Risk Factors" in this prospectus, as well as the amount of cash used in our operations and any unforeseen cash needs. Therefore, our actual expenditures may differ materially from the estimates described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the use of the net proceeds from this offering as described above, we intend to invest the net proceeds in a variety of capital preservation instruments, including short-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

## DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and future earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. In addition, any future debt instruments may materially restrict our ability to pay dividends on our common stock. Any future determination regarding the declaration and payment of dividends, if any, will be 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.

## CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2020:

- on an actual basis;
- on a pro forma basis, giving effect to (i) the issuance and sale of an aggregate of 23,440,514 shares of our Series B convertible preferred stock in March 2021 and our receipt of approximately $47.3 million in aggregate net proceeds therefrom, (ii) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 15,907,629 shares of common stock and the related reclassification of the carrying value of our convertible preferred stock to permanent equity in connection with the closing of this offering and (iii) the filing and effectiveness of our amended and restated certificate of incorporation in connection with the closing of this offering; and
- on a pro forma as adjusted basis, giving effect to (i) the pro forma adjustments set forth above and (ii) our receipt of net proceeds from the sale of 6,250,000 shares of common stock in this offering at the initial public offering price of $15.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with the sections titled “Selected Consolidated Financial Data,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” and “Description of Capital Stock” and our consolidated financial statements and related notes included elsewhere in this prospectus.

| | AS OF DECEMBER 31, 2020 | | |
|---|---|---|---|
| | ACTUAL | PRO FORMA | PRO FORMA, AS ADJUSTED |
| | | (unaudited) | |
| | (in thousands, except share and par value amounts) | | |
| Cash and cash equivalents | $ 53,613 | $100,898 | $ 185,086 |
| Convertible preferred stock, $0.0001 par value; 71,183,500 shares authorized, 47,742,986 shares issued and outstanding, actual, and no shares authorized or outstanding, pro forma and pro forma as adjusted | $ 92,720 | $ — | $ — |
| Stockholders’ (deficit) equity: | | | |
| Preferred stock, $0.0001 par value; no shares authorized, issued and outstanding, actual, and 10,000,000 shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted | — | — | — |
| Common stock, $0.0001 par value; 105,000,000 shares authorized, 2,053,070 shares issued and outstanding, actual, 200,000,000 shares authorized, 17,960,699 shares issued and outstanding, pro forma; 200,000,000 shares authorized, 24,210,699 shares issued and outstanding, pro forma as adjusted | — | 2 | 2 |
| Additional paid-in capital | 2,843 | 142,846 | 227,034 |
| Accumulated deficit | (44,958) | (44,958) | (44,958) |
| Total stockholders’ (deficit) equity | $(42,115) | $ 97,890 | $ 182,078 |
| Total capitalization | $ 50,605 | $ 97,890 | $ 182,078 |

The number of shares of our common stock to be outstanding after this offering pro forma and pro forma as adjusted reflected in the table above is based on 17,960,699 shares of common stock outstanding as of December 31, 2020, after giving effect to the issuance and sale of 23,440,514 shares of our Series B convertible preferred stock in March 2021 and the conversion of all outstanding shares of our convertible preferred stock into 15,907,629 shares of common stock in connection with the closing of this offering, and excludes:

- 935,478 shares of our common stock issuable upon the exercise of outstanding stock options as of December 31, 2020, with a weighted-average exercise price of $2.56 per share;
- 2,273,285 shares of our common stock issuable upon the exercise of outstanding stock options granted from January 1, 2021 through April 8, 2021, with a weighted-average exercise price of $5.06 per share;
- 2,187,524 shares of our common stock reserved for future issuance under our 2021 Plan, which became effective immediately prior to the execution of the underwriting agreement in connection with this offering, as well as any automatic annual increases in the number of shares of common stock reserved for future issuance under our 2021 Plan and plus (i) the number of shares that remained available for future issuance under our 2014 Plan at the time our 2021 Plan became effective and (ii) any shares subject to outstanding stock options or stock awards that were granted under our 2014 Plan that expire or are repurchased, forfeited, cancelled or withheld, as more fully described in the section titled “Executive Compensation—Employee Benefit Plans”;
- 243,058 shares of our common stock reserved for future issuance under our ESPP, which became effective immediately prior to the execution of the underwriting agreement in connection with this offering, and any automatic annual increases in the number of shares of common stock reserved for future issuance under our ESPP; and
- 98,000 shares of our common stock issuable upon the exercise of stock options granted to certain of our directors and employees under our 2021 Plan, effective immediately prior to the execution of the underwriting agreement in connection with this offering, with an exercise price per share that is equal to the price per share at which our common stock is first sold to the public in this offering.

## DILUTION

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the initial public offering price per share of common stock and the pro forma as adjusted net tangible book value per share immediately after this offering.

As of December 31, 2020, we had a historical net tangible book deficit of $(42.1) million, or $(20.51) per share of common stock based on 2,053,070 shares of common stock outstanding as of such date. Our historical net tangible book value (deficit) per share represents total tangible assets less total liabilities and convertible preferred stock, which is not included within permanent equity, divided by the number of shares of common stock outstanding as of December 31, 2020.

Our pro forma net tangible book value as of December 31, 2020 was $97.9 million, or $5.45 per share. Pro forma net tangible book value per share represents the amount of our total tangible assets less our total liabilities, divided by 17,960,699 shares of common stock outstanding as of such date, after giving effect to (i) the issuance and sale of 23,440,514 shares of our Series B convertible preferred stock in March 2021 and our receipt of approximately $47.3 million in aggregate net proceeds therefrom, (ii) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 15,907,629 shares of common stock and the related reclassification of the carrying value of our convertible preferred stock to permanent equity in connection with the closing of this offering, and (iii) the filing and effectiveness of our amended and restated certificate of incorporation in connection with the closing of this offering.

After giving effect to the sale by us of 6,250,000 shares of common stock in this offering at the initial public offering price of $15.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2020 would have been $182.1 million, or $7.52 per share. This amount represents an immediate increase in pro forma as adjusted net tangible book value of $2.07 per share to our existing stockholders and an immediate dilution in pro forma as adjusted net tangible book value of $7.48 per share to new investors purchasing common stock in this offering. We determine dilution by subtracting the pro forma as adjusted net tangible book value per share after this offering from the amount of cash paid by an investor for a share of common stock in this offering. The following table illustrates this dilution on a per share basis:

| | | |
|---|---|---|
| Initial public offering price per share | | $15.00 |
| Historical net tangible book deficit per share as of December 31, 2020 | $(20.51) | |
| Pro forma increase in historical net tangible book value per share attributable to the pro forma transactions described in the preceding paragraphs | 25.96 | |
| Pro forma net tangible book value per share as of December 31, 2020 | 5.45 | |
| Increase in pro forma net tangible book value per share attributable to investors purchasing shares in this offering | 2.07 | |
| Pro forma as adjusted net tangible book value per share after this offering | | 7.52 |
| Dilution per share to new investors purchasing shares in this offering | | $ 7.48 |

If the underwriters exercise their option to purchase additional shares of common stock in full, the pro forma as adjusted net tangible book value per share would be $7.76 per share, and the dilution to new investors in this offering would be $7.24 per share.

The following table summarizes on the pro forma as adjusted basis described above, the differences between the number of shares purchased from us on an as converted basis, the total consideration paid and the weighted-average price per share paid to us by existing stockholders and by investors purchasing shares in this offering at the initial public offering price of $15.00 per share, before deducting the underwriting discounts and commissions and estimated offering expenses payable by us:

| | Total Shares | | Total Consideration | | Weighted-Average Price per Share |
|---|---|---|---|---|---|
| | Number | Percent | Amount | Percent | |
| Existing stockholders | 17,960,699 | 74.2% | $146,556,274 | 61.0% | $ 8.16 |
| New investors | 6,250,000 | 25.8% | $ 93,750,000 | 39.0% | $ 15.00 |
| Total | 24,210,699 | 100.0% | $240,306,274 | 100.0% | |

If the underwriters exercise their option to purchase additional shares of common stock in full, our existing stockholders would own 71.4% and our new investors would own 28.6% of the total number of shares of our common stock outstanding upon the completion of this offering.

The foregoing discussion and tables above (other than the historical net tangible book value (deficit) calculation) are based on 17,960,699 shares of common stock outstanding as of December 31, 2020, after giving effect to the issuance and sale of 23,440,514 shares of our Series B convertible preferred stock in March 2021 and the conversion of all outstanding shares of our convertible preferred stock into 15,907,629 shares of common stock in connection with the closing of this offering, and excludes:

- 935,478 shares of our common stock issuable upon the exercise of outstanding stock options as of December 31, 2020, with a weighted-average exercise price of $2.56 per share;
- 2,273,285 shares of our common stock issuable upon the exercise of outstanding stock options granted from January 1, 2021 through April 8, 2021, with a weighted-average exercise price of $5.06 per share;
- 2,187,524 shares of our common stock reserved for future issuance under our 2021 Plan, which became effective immediately prior to the execution of the underwriting agreement in connection with this offering, as well as any automatic annual increases in the number of shares of common stock reserved for future issuance under our 2021 Plan and plus (i) the number of shares that remained available for future issuance under our 2014 Plan at the time our 2021 Plan became effective and (ii) any shares subject to outstanding stock options or stock awards that were granted under our 2014 Plan that expire or are repurchased, forfeited, cancelled or withheld, as more fully described in the section titled “Executive Compensation—Employee Benefit Plans”;
- 243,058 shares of our common stock reserved for future issuance under our ESPP, which became effective immediately prior to the execution of the underwriting agreement in connection with this offering, and any automatic annual increases in the number of shares of common stock reserved for future issuance under our ESPP; and
- 98,000 shares of our common stock issuable upon the exercise of stock options granted to certain of our directors and employees under our 2021 Plan, effective immediately prior to the execution of the underwriting agreement in connection with this offering, with an exercise price per share that is equal to the price per share at which our common stock is first sold to the public in this offering.

To the extent that any outstanding options are exercised or new options or other equity awards are issued under our stock-based compensation plans, or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

## SELECTED CONSOLIDATED FINANCIAL DATA

The following tables set forth our selected consolidated financial data for the periods and as of the dates indicated. We derived our consolidated statements of operations and comprehensive loss data for the years ended December 31, 2019 and December 31, 2020 and our consolidated balance sheets data as of December 31, 2019 and December 31, 2020 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future. You should read the following selected consolidated financial data in conjunction with our consolidated financial statements and related notes included elsewhere in this prospectus and the information in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations."

| Consolidated Statements of Operations and Comprehensive Loss Data: | YEAR ENDED DECEMBER 31, 2019 | 2020 |
|---|---|---|
| | (in thousands, except share and per share amounts) | |
| Operating expenses: | | |
| Research and development | $ 13,097 | $ 15,944 |
| General and administrative | 2,376 | 3,608 |
| Total operating expenses | 15,473 | 19,552 |
| Loss from operations | (15,473) | (19,552) |
| Other income: | | |
| Change in fair value of Series A convertible preferred stock purchase right liability | 2,581 | - |
| Other income | 456 | 87 |
| Net loss | $ (12,436) | $ (19,465) |
| Net loss per share attributable to common stockholders, basic and diluted (1) | $ (6.38) | $ (9.60) |
| Weighted-average shares of common stock outstanding, basic and diluted (1) | 1,948,170 | 2,028,198 |
| Pro forma net loss per share, basic and diluted (unaudited)(2) | | $ (2.50) |
| Pro forma weighted-average shares of common stock outstanding, basic and diluted (unaudited) (2) | | 7,788,340 |

(1) See Note 2 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate historical net loss per share, basic and diluted, and the weighted-average number of shares of common stock used in the computation of the per share amounts.

(2) Unaudited pro forma net loss per share, basic and diluted, attributable to common stockholders, is calculated giving effect to the conversion of the convertible preferred stock into shares of common stock. Unaudited pro forma net loss per share attributable to common stockholders does not include the shares expected to be sold and related proceeds to be received in this offering. Unaudited pro forma net loss per share attributable to common stockholders for the year ended December 31, 2020 was calculated using the weighted-average number of shares of common stock outstanding, including the pro forma effect of the conversion of all outstanding shares of convertible preferred stock into shares of common stock, as if such conversion had occurred at the beginning of the period, or their issuance dates if later.

| | AS OF DECEMBER 31, | |
|---|---|---|
| | 2019 | 2020 |
| | (in thousands) | |
| **Consolidated Balance Sheets Data:** | | |
| Cash, cash equivalents and short-term investments | $ 24,887 | $ 53,613 |
| Working capital (1) | 22,467 | 50,445 |
| Total assets | 25,505 | 55,221 |
| Total liabilities | 2,980 | 4,616 |
| Convertible preferred stock | 45,652 | 92,720 |
| Accumulated deficit | (25,493) | (44,958) |
| Total stockholders' deficit | (23,127) | (42,115) |

(1) We define working capital as current assets less current liabilities. See our consolidated financial statements included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

## 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 the section titled "Selected Consolidated Financial Data" and our consolidated financial statements and related notes included elsewhere in this prospectus. This discussion contains forward-looking statements that involve risks and uncertainties, including those described in the section titled "Special Note Regarding Forward-Looking Statements." Our actual results and the timing of selected events could differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those set forth under the section titled "Risk Factors."*

### Overview

Reneo is a clinical stage pharmaceutical company focused on the development of therapies for patients with rare genetic mitochondrial diseases, which are often associated with the inability of mitochondria to produce ATP. We are developing REN001 to modulate genes critical to metabolism and generation of ATP, which is the primary source of energy for cellular processes. REN001 is a selective PPARd agonist that has been shown to increase transcription of genes involved in mitochondrial function and increase FAO, and may increase production of new mitochondria.

We believe REN001 could benefit patients with genetic mitochondrial myopathies who experience weakness, fatigue, cramping, and wasting of muscle due to the mitochondria's inability to produce adequate levels of ATP. These patients often struggle to perform everyday activities, and over time, are at risk of experiencing cardiac and multisystem morbidities and have reduced life expectancy. We are initially developing REN001 in three rare genetic diseases that typically present with myopathy and have high unmet medical needs: PMM, LC-FAOD, and McArdle disease.

We completed an open-label Phase 1b clinical trial 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 in this trial. Compared to baseline, patients receiving REN001 once-daily for 12 weeks experienced an average increase in distance of 104 meters in the 12MWT and an average increase of 1.7mL/kg/min in peak $VO_2$ as well as a reduction in patient-reported fatigue and pain.

Based on these results, we initiated a global, randomized, double-blind, placebo-controlled Phase 2b clinical trial in patients with PMM and plan to begin enrollment in the first half of 2021. We also plan to conduct an open-label, long-term safety trial outside the United States in a subset of patients from the Phase 2b clinical trial. We anticipate results from these clinical trials in 2023. Following our interactions with the FDA 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 are also conducting two open-label Phase 1b clinical trials of REN001 in patients with LC-FAOD and with McArdle disease. Both Phase 1b clinical trials are currently enrolling and we anticipate results in the first half of 2022. We also plan to explore the potential of REN001 in other rare diseases, such as Duchenne muscular dystrophy and Alport syndrome, where we have supportive preclinical data.

Since our inception in 2014, our operations have 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 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 several years, if ever. Since inception, we have incurred significant operating losses. Our net losses were $12.4 million and $19.5 million for the years ended December 31, 2019 and 2020, respectively. As of December 31, 2020, we had an accumulated deficit of $45.0 million, and cash and cash equivalents of $53.6 million. We have funded our operations primarily through the issuance and sale of equity securities. From our inception through December 31, 2020, we have raised an aggregate of $99.2 million in gross proceeds primarily from the sale of our convertible preferred stock and exercise of stock

options. In March 2021, we completed the second closing of a Series B convertible preferred stock issuance at $2.0215 per share. A total of 23,440,514 shares were issued for cash consideration of approximately $47.4 million.

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 the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. 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 the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements through at least the next 24 months.

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 manufacture 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 rapidly evolve, and we will continue to monitor the COVID-19 situation closely. The extent of the impact of the 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 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 clinical trial 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. Although the majority of our workforce now works remotely, there has been minimal disruption 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 a License Agreement with vTv Therapeutics (the vTv License Agreement), under which we obtained an exclusive, worldwide, sublicensable license under certain vTv Therapeutics intellectual

property to develop, manufacture and commercialize PPARd agonists and products containing such PPARd 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. For additional information regarding the vTv License Agreement, see “Business—License Agreement with vTv Therapeutics LLC.”

## Components of Our Results of Operations

### *Operating Expenses*

*Research and Development Expenses*

To date, our research and development expenses have related primarily 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;
- laboratory supplies 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, 2019 and 2020:

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2019 | 2020 |
| | (in thousands) | |
| Nonclinical | $ 2,623 | $ 4,026 |
| Contract manufacturing cost | 3,411 | 4,254 |
| Clinical and regulatory | 5,750 | 7,894 |
| Research and development-other | 1,313 | (230) |
| Total | $13,097 | $ 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. We also anticipate incurring additional expenses associated with operating as a public company, including increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with the rules and regulations of the SEC and standards applicable to companies listed on a national securities exchange, additional insurance expenses, investor relations activities and other administrative and professional services.

***Other Income***

Other income consists of interest income on our cash, cash equivalents and short-term investments. It also includes the change in fair value of the Series A convertible preferred stock purchase right liability that is marked-to-market at each measurement period with the change in fair value charged to earnings.

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2019 | 2020 |
| | (in thousands) | |
| Interest income | $ 456 | $ 87 |
| Change in fair value of Series A convertible preferred stock purchase right liability | 2,581 | - |
| Total | $3,037 | $ 87 |

## Results of Operations

### *Comparison of Years Ended December 31, 2019 and 2020*

The following table summarizes our results of operations for the years ended December 31, 2019 and 2020:

| | YEAR ENDED DECEMBER 31, | | |
|---|---|---|---|
| | 2019 | 2020 | CHANGE |
| | (in thousands) | | |
| Operating expenses: | | | |
| Research and development | $ 13,097 | $ 15,944 | $ 2,847 |
| General and administrative | 2,376 | 3,608 | 1,232 |
| Total operating expenses | 15,473 | 19,552 | 4,079 |
| Loss from operations | (15,473) | (19,552) | (4,079) |
| Change in fair value of Series A convertible preferred stock purchase right liability | 2,581 | - | (2,581) |
| Other income | 456 | 87 | (369) |
| Net loss | $(12,436) | $(19,465) | $ (7,029) |

### *Operating Expenses*

*Research and Development Expenses*

Research and development expenses for the year ended December 31, 2019 were $13.1 million, compared to $15.9 million for the year ended December 31, 2020. This increase of $2.8 million was primarily due to an increase of $4.3 million in clinical and regulatory, contract manufacturing and nonclinical activities and resources, partially offset by $1.5 million received from the UK's Research & Development tax relief program for research and development conducted through our UK subsidiary in 2018 and recorded in the financial statements in 2020.

*General and Administrative Expenses*

General and administrative expenses for the year ended December 31, 2019 were $2.4 million, compared to $3.6 million during the year ended December 31, 2020. This increase of $1.2 million was primarily attributable to increases in employee and employee related expenses of $0.8 million and market research and business development expenditures of $0.4 million.

### *Change in Fair Value of Series A Convertible Preferred Stock Purchase Right Liability*

Change in fair value of Series A convertible preferred stock purchase right liability for the year ended December 31, 2019 was $2.6 million compared to $0 during the year ended December 31, 2020. This decrease of $2.6 million is primarily attributable to the extinguishment of the Series A convertible preferred stock purchase right liability during the year ended December 31, 2019 with no such liability outstanding as of December 31, 2020 or amount recorded during the year ended December 31, 2020.

### *Other Income*

Other income for the year ended December 31, 2019 was $0.5 million compared to $0.1 million during the year ended December 31, 2020. This decrease of $0.4 million was primarily attributable to lower interest income earned on deposits in money market accounts indexed to the federal funds rates, which declined significantly during the year ended December 31, 2020.

## Liquidity and Capital Resources

### *Sources of Liquidity*

Since our inception, we have incurred significant operating losses. To date, we have funded our operations primarily through the issuance and sale of equity securities. From our inception through December 31, 2020, we have raised an aggregate of $99.2 million in gross proceeds primarily from the sale of our convertible preferred stock and exercises of stock options. As of December 31, 2020, we had $53.6 million in cash and cash equivalents and an accumulated deficit of $45.0 million. 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.

### *Cash Flows*

The following table summarizes our cash flows for the years ended December 31, 2019 and 2020:

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2019 | 2020 |
| | (in thousands) | |
| Net cash used in operating activities | $(12,510) | $(18,536) |
| Net cash (used in) provided by investing activities | (7,241) | 7,376 |
| Net cash provided by financing activities | 24,986 | 47,272 |
| Net increase in cash and cash equivalents | $ 5,235 | $ 36,112 |

*Operating Activities*

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 charges primarily consisting of stock-based compensation expense.

Net cash used in operating activities for the year ended December 31, 2019 was $12.5 million, consisting primarily of our net loss of $12.4 million and a $1.6 million net change in operating assets and liabilities, partially offset by $1.5 million in net non-cash gain. The net non-cash gain of $1.5 million consisted primarily of non-cash gain related to the change in fair value of the Series A convertible preferred stock purchase right liability offset by non-cash charges for stock-based compensation expense and non-cash expense associated with issuance of shares of our common stock in connection with the vTv License Agreement.

*Investing Activities*

Net cash provided by 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.

Net cash used in investing activities for the year ended December 31, 2019 was $7.2 million, consisting primarily of $19.8 million purchases of short-term investments partially offset by proceeds of $12.6 million on maturities of available-for-sale short-term investments.

*Financing Activities*

Net cash provided by financing activities in the year ended December 31, 2020 was $47.3 million, consisting primarily of $47.4 million of proceeds from the issuance of Series B convertible preferred stock, net of $0.2 million issuance costs and proceeds from the exercise of stock options of $0.1 million.

Net cash provided by financing activities in the year ended December 31, 2019 was $25.0 million, consisting primarily of $25.0 million in proceeds from the issuance and sale of Series A convertible preferred stock and Series A convertible preferred stock purchase right liabilities, net of issuance costs.

***Funding Requirements***

To date, we have not generated any revenue. We do not expect to generate revenue 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. In addition, upon the completion of this offering, we expect to incur 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 the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. 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 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 arrangement;
- 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.

Along with the closing of the first tranche of Series B convertible preferred stock, we issued rights to the purchasers for the purchase of an additional 23,440,514 shares of Series B convertible preferred stock under the same terms and conditions as the initial closing. Management's liquidity analysis includes the receipt of the additional funds associated with the purchase rights of the Series B convertible preferred stock as we received $47.4 million gross proceeds pursuant to the closing of the second tranche of the Series B convertible preferred stock in March 2021. We believe, based upon our current operating plan, that the net proceeds from this offering, together with our cash and cash equivalents as of December 31, 2020, and the net aggregate proceeds of approximately $47.3 million from the issuance and sale of an aggregate of 23,440,514 shares of our Series B convertible preferred stock in March 2021, will be sufficient to fund our operations for at least the next 24 months.

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.

### Contractual Obligations & Commitments

Under the vTv License Agreement, we may be required to make milestone payments and pay royalties on annual net sales. The amount, timing and likelihood of any contingent payment obligations, such as milestones or royalties, under the vTv License Agreement are not known. For additional information regarding the vTv License Agreement, see “Business—License Agreement with vTv Therapeutics LLC.”

We enter into contracts in the normal course of business with third-party contract manufacturing organizations and CROs for clinical trials, preclinical studies, and other services and products for operating purposes. These contracts generally provide for termination upon notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

### Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

### Critical Accounting Policies and Estimates

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

While our significant accounting policies are described in more detail in Note 2 to our consolidated financial statements included elsewhere in this prospectus, we believe that the following critical accounting policies are most important to understanding and evaluating our reported financial results.

#### *Accrued Research and Development Costs*

We record 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. We accrue 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, we adjust accrued expenses or prepaid expenses accordingly, which impact research and development expenses. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. We have not experienced any material differences between accrued or prepaid costs and actual costs incurred since inception. 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. 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. We have determined that technological feasibility for REN001 is reached when the requisite regulatory approvals are obtained to make the product candidate available for sale.

***Series A Convertible Preferred Stock Purchase Right Liability***

In connection with our Series A convertible preferred stock financing, in addition to the initial closings in December 2017 and January 2018, investors agreed to buy, and we agreed to sell, additional shares of Series A convertible preferred stock at a fixed price upon achievement of certain conditions. We evaluated this purchase right and concluded that it meets the definition of a freestanding instrument. Accordingly, we determined the fair value of the purchase right liability and recorded it on the balance sheet with the remainder of the proceeds raised being allocated to convertible preferred stock. The preferred stock purchase right liability was revalued at each reporting period with changes in the fair value of the liability recorded as change in fair value of preferred stock purchase right liability in the consolidated statements of operations and comprehensive loss. The preferred stock purchase right liability was revalued at settlement and the resultant fair value is then reclassified to convertible preferred stock at that time.

***Stock-Based Compensation***

We maintain a stock-based compensation plan as a long-term incentive for employees, non-employee directors and consultants. The plan allows for the issuance of incentive stock options, non-qualified stock options, restricted stock units and other forms of equity awards.

We measure and recognize compensation expense for all options based on the estimated fair value of the award on the grant date. We use the Black-Scholes option-pricing model to estimate the fair value of option awards. The fair value is recognized as expense over the requisite service period, which is generally the vesting period of the respective award, on a straight-line basis when the only condition to vesting is continued service. Forfeitures are recognized as a reduction of stock-based compensation expense as they occur. We have not issued awards where vesting is subject to a market or performance condition; however, if we were to grant such awards in the future, recognition would be based on the derived service period. Expense for awards with performance conditions would be estimated and adjusted on a quarterly basis based upon our assessment of the probability that the performance condition will be met.

The determination of the grant date fair value of options using an option pricing model is affected principally by our estimated fair value of our common stock and requires management to make a number of other assumptions, including the expected life of the option, the volatility of the underlying shares, the risk-free interest rate, and expected dividends. The assumptions used in our Black-Scholes option-pricing model represent management's best estimates at the time of grant. These estimates are complex, involve a number of variables, uncertainties and assumptions and the application of management's judgment, as they are inherently subjective. If any assumptions change, our stock-based compensation expense could be materially different in the future.

These assumptions include:

- *Fair Value of Common Stock*. As our common stock has not historically been publicly traded, we estimated the fair value of our common stock. See "—Fair Value of Common Stock."

- *Expected Term*. The expected term represents the period that our options are expected to be outstanding. We calculated the expected term using the simplified method based on the average of each option's vesting term and the contractual period during which the option can be exercised, which is typically 10 years following the date of grant.
- *Expected Volatility*. The expected volatility was based on the historical share volatility of several of our comparable publicly traded companies over a period of time equal to the expected term of the options, as we do not have any trading history to use the volatility of our own common stock.
- *Risk-Free Interest Rate*. The risk-free interest rate was based on the yields of U.S. Treasury zero-coupon bond securities with maturities appropriate for the term of the award.
- *Expected Dividend Yield*. We have not paid dividends on our common stock nor do we expect to pay dividends in the foreseeable future. Therefore, we used an expected dividend yield of zero.

See Note 8 to our audited consolidated financial statements included elsewhere in this prospectus for more information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options. Certain of such assumptions involve inherent uncertainties and the application of significant judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation could be materially different.

We recorded stock-based compensation expense of $0.4 million and $0.4 million for the years ended December 31, 2019 and 2020, respectively. As of December 31, 2020, we had $0.6 million of total unrecognized stock-based compensation cost which we expect to recognize over an estimated weighted-average period of 1.9 years. We expect to continue to grant stock options and other equity-based awards in the future, and to the extent that we do, our stock-based compensation expense recognized in future periods will likely increase.

The intrinsic value of all outstanding options as of December 31, 2020 was $11.6 million based on the initial public offering price of $15.00 per share, of which approximately $7.9 million is related to vested options and approximately $3.7 million is related to unvested options.

*Fair Value of Common Stock*

Historically, for all periods prior to this offering, the fair values of the common stock underlying our options were estimated on each grant date by our board of directors. In order to determine the fair value, our board of directors considered, among other things, contemporaneous valuations of our common stock prepared by unrelated third-party valuation firms in accordance with the guidance provided by the American Institute of Certified Public Accountants 2013 Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation* (the Practice Aid). Given the absence of a public trading market of our capital shares, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including, but not limited to:

- contemporaneous third-party valuations of our common stock;
- important developments in our business;
- sales of our convertible preferred stock;
- the prices, rights, preferences, and privileges of our preferred shares relative to our common stock;
- our business, financial condition, and results of operations, including related industry trends affecting our operations;
- the progress of clinical development;
- the likelihood of achieving a liquidity event, such as an initial public offering or sale of our company, given prevailing market conditions;
- the lack of marketability of our common stock;
- the market performance of comparable publicly traded companies; and
- U.S. and global economic and capital market conditions and outlook.

*Common Stock Valuation Methodology*

Our valuations were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for setting the value of an enterprise, such as the cost, income and market approaches, and various methodologies for allocating the value of an enterprise to its common stock. The cost approach establishes the value of an enterprise based on the cost of reproducing or replacing the property less depreciation and functional or economic obsolescence, if present. The income approach establishes the value of an enterprise based on the present value of future cash flows that are reasonably reflective of our company's future operations, discounting to the present value with an appropriate risk adjusted discount rate or capitalization rate. The market approach is based on the assumption that the value of an asset is equal to the value of a substitute asset with the same characteristics.

Each valuation methodology was considered in our valuations. In valuing our common stock for 2019 and 2020, we determined the equity value of our business using the back-solve method, a market approach that assigns an implied enterprise value based on the most recent round of funding or investment and allows for the incorporation of the implied future benefits and risks of the investment decision assigned by an outside investor. The back-solve method requires considering the rights and preferences of each class of equity and solving for the total market value of invested capital that is consistent with a recent transaction in the company's own securities, considering the rights and preferences of each class of equity.

In December 2020, in connection with our Series B convertible preferred stock financing with new and certain current investors, we applied a hybrid method of the probability weighted expected return method (PWERM), where the non-initial public offering scenario is modeled using an option pricing model to reflect the full distribution of possible non-initial public offering outcomes based on the value determined in the back-solve method. Under the option pricing model, common stock is valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of each class of equity are inferred by analyzing these options. In the initial public offering scenario, we used the fully-diluted shares outstanding to allocate value to each class of equity based on a market approach. The hybrid method is useful when certain discrete future outcomes can be predicted, but also accounts for uncertainty regarding the timing or likelihood of specific alternative exit events.

Following the closing of this offering, the fair value of our common stock will be determined based on the closing price of our common stock on the Nasdaq Global Market.

## Recent Accounting Pronouncements

See Note 2 to our consolidated financial statements beginning on page F-1 of this prospectus for a description of recent accounting pronouncements applicable to our consolidated financial statements.

## Qualitative and Quantitative Disclosures about Market Risk

### *Interest Rate Risk*

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. As of December 31, 2020, we had cash and cash equivalents of $53.6 million. We generally hold our cash in interest-bearing bank accounts, money market accounts, and repurchase agreements. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. An immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash.

### *Financial Institution Risk*

Substantially all of our cash is held with a single financial institution. Due to its size, this financial institution represents a minimal credit risk. Cash amounts held at financial institutions are insured by the Federal Deposit Insurance Corporation up to $250,000. At December 31, 2020, we had $53.4 million in excess of this insured limit.

### *Foreign Currency Risk*

Our expenses are generally denominated in U.S. dollars. To date, foreign currency transaction gains and losses have not been material to our consolidated financial statements, and we have not had a formal hedging program with respect to foreign currency. A 10.0% increase or decrease in current exchange rates would not have a material effect on our financial results.

***Effects of Inflation***

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the periods presented.

## Emerging Growth Company Status

We are an "emerging growth company," as defined in the JOBS Act, and we may take advantage of reduced reporting requirements that are otherwise applicable to public companies. Section 107 of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies are required to comply with those standards. We have elected to take advantage of the extended transition period for complying with new or revised accounting standards, and as a result of this election, our financial statements may not be comparable to companies that comply with public company effective dates. The JOBS Act also exempts us from having to provide an auditor attestation of internal control over financial reporting under Sarbanes-Oxley Act Section 404(b).

We will remain an "emerging growth company" until the earliest of (1) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more, (2) the last day of the fiscal year in which the fifth anniversary of the completion of this initial public offering occurs, (3) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years or (4) the last day of the fiscal year in which we are deemed to be a large accelerated filer under the rules of the SEC, which generally is when we have more than $700.0 million in market value of our stock held by non-affiliates as of the prior June 30th and we have been a public company for at least 12 months and have filed one annual report.

# BUSINESS

## Overview

Reneo is a clinical stage pharmaceutical company focused on the development of therapies for patients with rare genetic mitochondrial diseases, which are often associated with the inability of mitochondria to produce adenosine triphosphate (ATP). We are developing REN001 to modulate genes critical to metabolism and generation of ATP, which is the primary source of energy for cellular processes. REN001 is a selective peroxisome proliferator-activated receptor delta (PPARd) agonist that has been shown to increase transcription of genes involved in mitochondrial function and increase fatty acid oxidation (FAO), and may increase production of new mitochondria.

We believe REN001 could benefit patients with genetic mitochondrial myopathies who experience weakness, fatigue, cramping, and wasting of muscle due to the mitochondria's inability to produce adequate levels of ATP. These patients often struggle to perform everyday activities, and over time, are at risk of experiencing cardiac and multisystem morbidities and have reduced life expectancy.

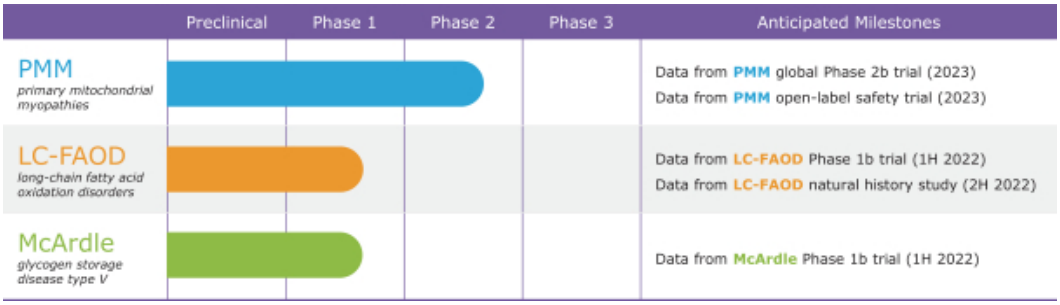
We are initially developing REN001 in three rare genetic diseases that typically present with myopathy and have high unmet medical needs: primary mitochondrial myopathies (PMM), long-chain fatty acid oxidation disorders (LC-FAOD), and glycogen storage disease type V (McArdle disease).

We completed an open-label Phase 1b clinical trial 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 in this trial. Compared to baseline, patients receiving REN001 once-daily for 12 weeks experienced an average increase in distance of 104 meters in the 12-minute walk test distance (12MWT) and an average increase of 1.7mL/kg/min in peak oxygen consumption (peak $VO_2$) as well as a reduction in patient-reported fatigue and pain.

Based on these results, we initiated a global, randomized, double-blind, placebo-controlled Phase 2b clinical trial in patients with PMM and plan to begin enrollment in the first half of 2021. We also plan to conduct an open-label, long-term safety trial outside the United States in a subset of patients from the Phase 2b clinical trial. We anticipate results from these clinical trials in 2023. Following our interactions with the U.S. Food and Drug Administration (FDA) 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 are also conducting two open-label Phase 1b clinical trials of REN001 in patients with LC-FAOD and with McArdle disease. Both Phase 1b clinical trials are currently enrolling and we anticipate results in the first half of 2022. We also plan to explore the potential of REN001 in other rare diseases, such as Duchenne muscular dystrophy and Alport syndrome, where we have supportive preclinical data.

The following table summarizes our pipeline for REN001.



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

- PMM: This rare 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 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.
- McArdle disease: This rare disease has an estimated prevalence of 2:100,000, representing at least 6,000 patients in the United States and 8,000 in Europe. Patients with McArdle disease have a specific inability to break down glycogen to glucose as a source of energy for mitochondria. Patients with McArdle disease experience muscle damage with severe acute fatigue and muscle pain. Breakdown of muscle tissue can also cause kidney damage. We are initially targeting adult patients with McArdle disease.

Muscle cells mainly rely on three sources to generate energy: phosphocreatine, carbohydrates (glycogen), and fatty acids. At the onset of exertion, muscle cells use readily available sources of energy such as phosphocreatine and carbohydrates (glycogen). As these sources of energy become depleted with continued exertion, muscle cells turn to fatty acids as the primary source to generate 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, and 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.

McArdle disease patients are unable to break down glycogen in the muscle. Patients with McArdle disease present with severe acute pain and difficulty moving their muscles after the first few minutes of muscle activity. An increase in fatty acid metabolism may allow patients to overcome the deficiency in glycogen, thereby minimizing the lack of energy associated with their disease.

REN001 is designed to selectively activate PPARd receptors found in the nuclear membrane of muscle and other cells. PPARd 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). PPARd is highly expressed in muscle cells and activation of PPARd 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 in study animals. We believe these are the mechanisms by which REN001 will act to help patients with mitochondrial diseases.

We completed an open-label Phase 1b clinical trial 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 in this trial. Compared to baseline, patients receiving REN001 once-daily for 12 weeks experienced an average increase in distance of 104 meters in the 12-minute walk test distance (12MWT) and an average increase of 1.7mL/kg/min in peak oxygen consumption (peak $VO_2$) as well as a reduction in patient-reported fatigue and pain.

Based on these results, we initiated a global, randomized, double-blind, placebo-controlled Phase 2b clinical trial in patients with PMM and plan to begin enrollment in the first half of 2021. We also plan to conduct an open-label, long-term safety trial outside the United States in a subset of patients from the Phase 2b clinical trial. We anticipate results from these clinical trials 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 are also conducting two open-label Phase 1b clinical trials of REN001 in patients with LC-FAOD and with McArdle disease. Both Phase 1b clinical trials are currently enrolling and we anticipate results in the first half of 2022. We also plan to explore the potential of REN001 in other rare diseases, such as Duchenne muscular dystrophy and Alport syndrome, where we have supportive preclinical data.

As of January 31, 2021, REN001 has been dosed in 112 individuals across multiple clinical trials and was well tolerated, with no drug-related serious adverse events (SAE) reported.

Our experienced management team is led by our President and Chief Executive Officer, Gregory J. Flesher, who has more than 25 years of biopharmaceutical industry experience and has been closely involved with the successful development and commercialization of multiple novel drugs. Mr. Flesher previously served as Chief Executive Officer of Novus Therapeutics, Inc., and has held additional leadership roles at Avanir Pharmaceuticals, Inc. (acquired by Otsuka Pharmaceutical Co., Ltd.), InterMune, Inc. (acquired by Roche Holding AG), Amgen Inc. and Eli Lilly and Company. Our Chief Medical Officer, Alejandro Dorenbaum, M.D., has extensive experience in the development of drugs for rare diseases such as Kuvan, Naglazyme, and Palynziq. Dr. Dorenbaum previously served as Chief Medical Officer at Allakos Inc. and Lumena Pharmaceuticals, Inc. and held other leadership roles at Genentech and BioMarin Pharmaceuticals Inc. Our Chief Financial Officer, Vineet R. Jindal, has extensive experience in the biotechnology public markets, including senior positions at ThinkEquity Partners LLC and Wedbush Morgan Securities Inc. Mr. Jindal oversaw Strategy, Business Development, Corporate Communications and Investor Relations at Reata Pharmaceuticals, Inc. Our Chief Development Officer, Wendy Johnson, has over 30 years of pharmaceutical industry experience, including development of the rare disease drug, Treanda. Ms. Johnson held previous leadership positions at AmpliPhi Biosciences Corporation, Aires Pharmaceuticals, Inc. (acquired by Mast Therapeutics, Inc.), and Salmedix, Inc. (acquired by Cephalon, Inc.).

We are supported by leading life sciences investors, including Novo Holdings A/S, Abingworth, New Enterprise Associates, RiverVest Venture Partners, Pappas Capital, Lundbeckfond Ventures, Rock Springs Capital, Aisling Capital, and Amzak Health.

We licensed exclusive, worldwide rights to develop and commercialize REN001 and other related compounds from vTv Therapeutics in December 2017.

### 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, LC-FAOD, and McArdle disease, 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 PPARd 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 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 recently established proof-of-concept in a Phase 1b clinical trial 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 initiated a global Phase 2b clinical trial in PMM in the first half of 2021, and we plan to conduct a long-term safety trial outside the United States in a subset of patients from the Phase 2b clinical trial. 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.

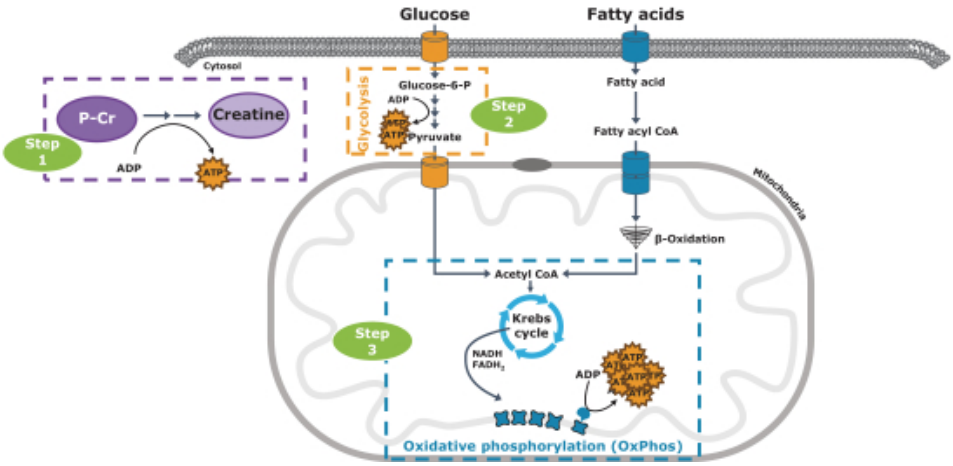
- **Advance REN001 clinical development in LC-FAOD and McArdle disease.** We are conducting two open-label Phase 1b clinical trials of REN001 in patients with LC-FAOD and with McArdle disease, rare genetic diseases with high unmet medical need. LC-FAOD has an estimated prevalence of at least 1.5:100,000 and McArdle disease has an estimated prevalence of at least 2:100,000. Preliminary results from our LC-FAOD Phase 1b clinical trial have demonstrated an improvement in a subset of patients in both exercise tests and symptoms, and the tolerability of REN001 has been consistent with that observed in other REN001 studies. We expect data from both Phase 1b clinical trials in the first half of 2022.
- **Maximize the commercial potential of REN001 in additional rare disease indications.** We also plan to explore the potential of REN001 in other rare diseases, where we have supportive preclinical data. For example, we have shown that REN001 treatment led to improvement in function in a mouse model of DMD, one of the most severe forms of inherited muscular dystrophies. REN001 has also been shown to prevent inflammatory cell death in animal models of ischemic kidney diseases and Alport syndrome.
- **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 other markets, we plan to explore strategic partnerships to bring REN001 to market with the goal of establishing REN001 as standard of care for rare genetic mitochondrial diseases around the world.
- **Expand our rare disease pipeline through acquisitions and/or licensing of complementary programs.** We plan to license or acquire additional programs targeting rare 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 carbohydrates are depleted, mitochondria turn to fatty acids as the source of fuel to create ATP (Figure 1, step 3). FAO becomes the primary pathway to generate energy for muscle and other cells during long periods of exercise.



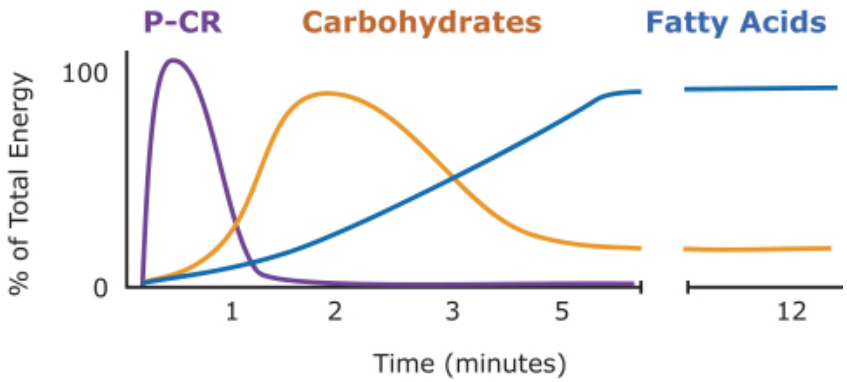



**Figure 1. The energy source used by muscles shifts from phosphocreatine (P-Cr) and carbohydrates to fatty acids as short-term supplies of phosphocreatine and carbohydrates are depleted**

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 either within the mitochondrial or nuclear DNA 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, referred to as mtDNA. mtDNA 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. The 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 though a process known as OxPhos. Mitochondria have specific enzymes that break down each of the fatty acids to produce ATP. Mutations in the genes encoding the enzymes that break down long-chain fatty acids may lead to severe energy deficits. Specific deficiencies include defects in very long-chain acyl-CoA dehydrogenase (VLCAD), LCHAD, mitochondrial trifunctional protein (TFP) 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 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. Energy deficits during exercise can lead to rhabdomyolysis or breakdown of muscle cells, which, in turn, can lead to kidney damage.

*McArdle disease background*

McArdle disease is a rare genetic disorder belonging to a class of diseases known as glycogen storage diseases (GSD). Patients with McArdle disease have a mutation in the gene that encodes a muscle enzyme called myophosphorylase. In healthy individuals, this enzyme converts glycogen stored in the muscles into glucose, which is then metabolized in the mitochondria to produce ATP. McArdle patients are deficient in this enzyme and therefore, cannot convert glycogen to glucose for energy production. Given that the vast majority of carbohydrates available to the muscle cells for consumption is in the form of muscle glycogen, these patients have a lapse in energy production after a short period of physical activity. During this lapse in energy, they experience muscle pain, severe acute fatigue, and elevated heart rate. Following this debilitating lapse in energy, patients get a “second wind” when their muscle cells switch over to metabolism of fatty acids, but this only occurs after several minutes of continuous muscle activity. This lapse in energy sources can severely impact activities of daily living and occasionally result in severe rhabdomyolysis, which could lead to hospitalization and possible acute kidney failure requiring dialysis.

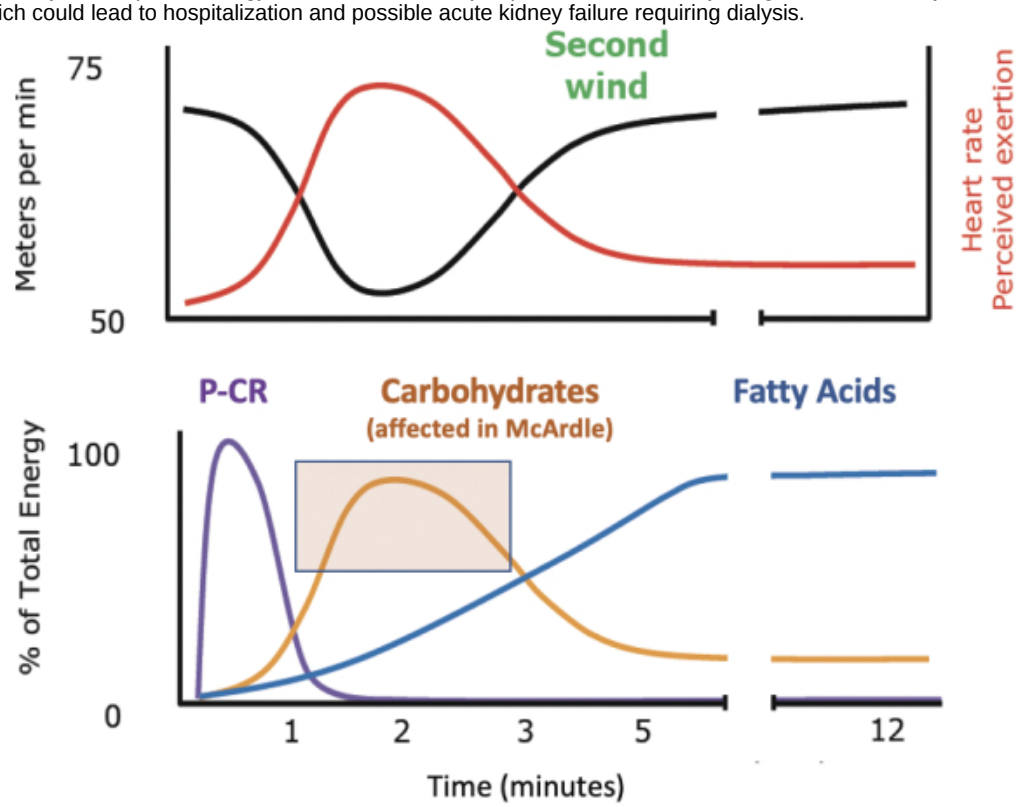



**Figure 2. McArdle patients lack the ability to use glycogen as an energy source resulting in an energy deficit until metabolism switch to FAO giving them a “second wind”**

There are no approved drug therapies for McArdle disease nor, to our knowledge, any drug candidates in clinical development other than REN001. Anecdotal reports from individual patients suggest that a ketogenic diet, that is, a high fat, low carbohydrate diet, may improve exercise capacity and reduces symptoms of the disease. In a pilot open-label clinical trial, three modified ketogenic diet regimens were evaluated in McArdle patients. All regimens improved FAO rates and exercise capacity as indicated by small decrease in heart rate and perceived exertion. Similar to the mechanism of action of ketogenic diets, we believe that REN001 has the potential to augment in the muscle the time to access fatty acids as an energy source and relieve some of the energy deficits experienced by not being able to use glycogen as an energy source.

***PPARd , 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 (a), gamma (g) and delta (d). PPAR a and g agonists drugs have been approved in cardiovascular and endocrine disorders, respectively.

PPARd is highly expressed in muscle cells and activation of PPARd 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 PPARd were shown to be able to run on a treadmill twice the distance compared to normal mice. Conversely, PPARd knockout mice were shown to run approximately 30% less distance compared to normal mice. We believe that a selective agonist of PPARd such as REN001, has potential therapeutic benefits while avoiding some of the adverse events associated with approved PPAR agonists of the PPARa and PPARg class.

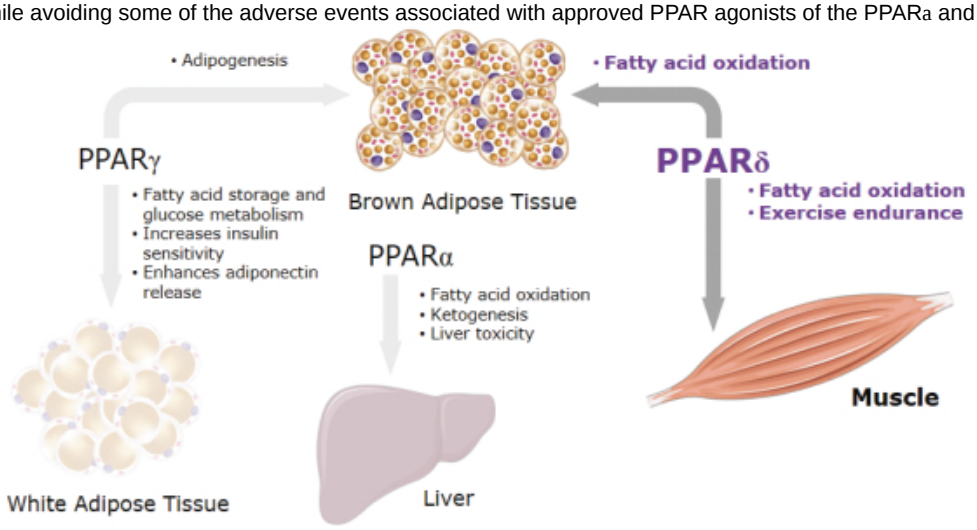



**Figure 3. Members of the PPAR family of nuclear receptors have distinct roles in regulating fatty acid metabolism**

**Our solution, REN001**

REN001 is an oral, small molecule selective PPARd agonist designed to modulate genes critical to metabolism and generation of energy. By selectively targeting PPARd, REN001 may address the cellular energy deficit in patients with genetic mitochondrial myopathies such as PMM, LC-FAOD and McArdle disease by:

- Increasing OxPhos activity of mitochondria resulting in enhanced production of ATP;
- Increasing the formation of new 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 PPARd 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 100mg REN001 orally twice daily (n=12) or placebo (n=12) showed increased expression of PPARd 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 in the United States for PMM and LC-FAOD. Additionally, we have received orphan drug designations for 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.

We have also received Fast Track designation for REN001 in the United States for PMM.

### REN001 for the Treatment of Primary Mitochondrial Myopathies

#### *Phase 1b clinical results in PMM*

We completed an open-label Phase1b clinical trial of REN001 in patients with PMM and myopathy with mitochondrial DNA (mtDNA) mutations, which was conducted under a Clinical Trial Authorisation (CTA) submitted to the MHRA in the 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 nuclear DNA defects to reduce heterogeneity in the study. Also, in contrast to PMM patients with nuclear DNA defects who have all their mitochondria affected, patients with mtDNA mutations harbor both normal and mutated mitochondria in their cells. 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 Part A was 12 weeks and the planned maximum treatment duration for each patient included in both Part A and Part B was 48 weeks. The Phase 1b clinical trial was closed early as a result of the COVID-19 pandemic. At the point of trial closure, a total of 17 patients had completed Part A, 13 patients had entered Part B, and the maximum duration of treatment was approximately 40 weeks. This Phase 1b trial was an open-label study, and therefore, was not designed to show statistical significance as compared to a placebo control arm.

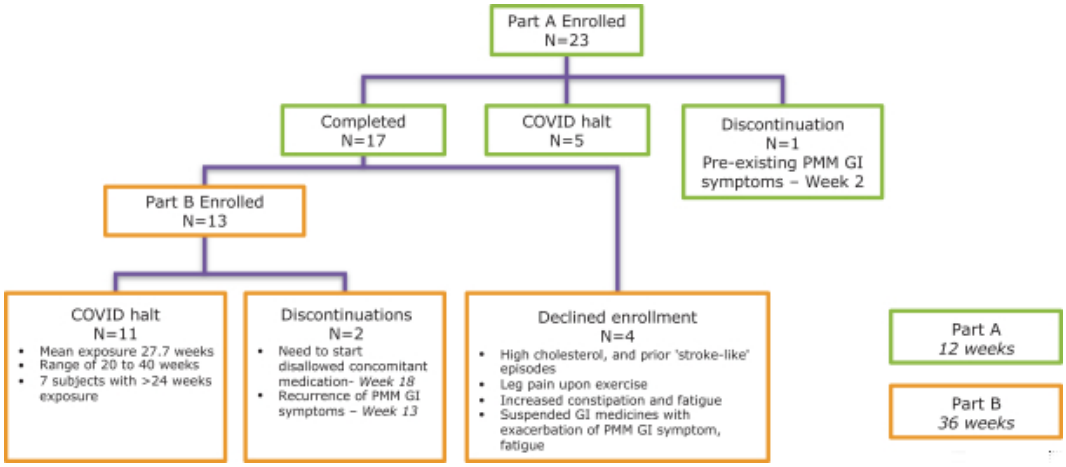



**Figure 4. REN001 PMM Phase 1b clinical trial enrollment**

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. 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.

As of January 31, 2021, we have the following preliminary results from the trial.

REN001 was generally well tolerated with no drug related SAEs observed. There were 91 treatment emergent adverse events (TEAE) experienced by 18 out of 23 (78.4%) patients, with 58 (63.7%) of all TEAEs experienced by 12 patients considered related to study drug. The majority of these TEAEs were mild to moderate in severity. The most commonly reported TEAEs were gastrointestinal (constipation) followed by headache. Two patients had elevations of creatine phosphokinase of moderate severity that were possibly or probably related to study drug.

*Physical Performance Measures*

Following 12 weeks of 100 mg once-daily dosing with REN001, patients achieved an average increase of 104 meters 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.

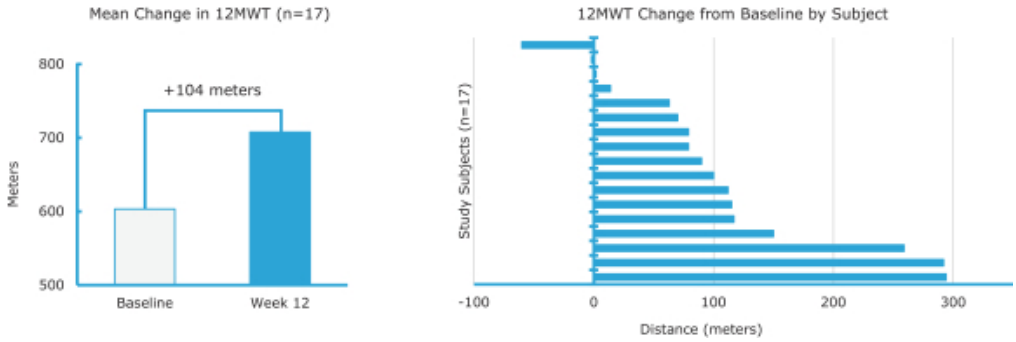



**Figure 5a. REN001-treated PMM patients had improved 12MWT distances after 12 weeks of treatment**

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).

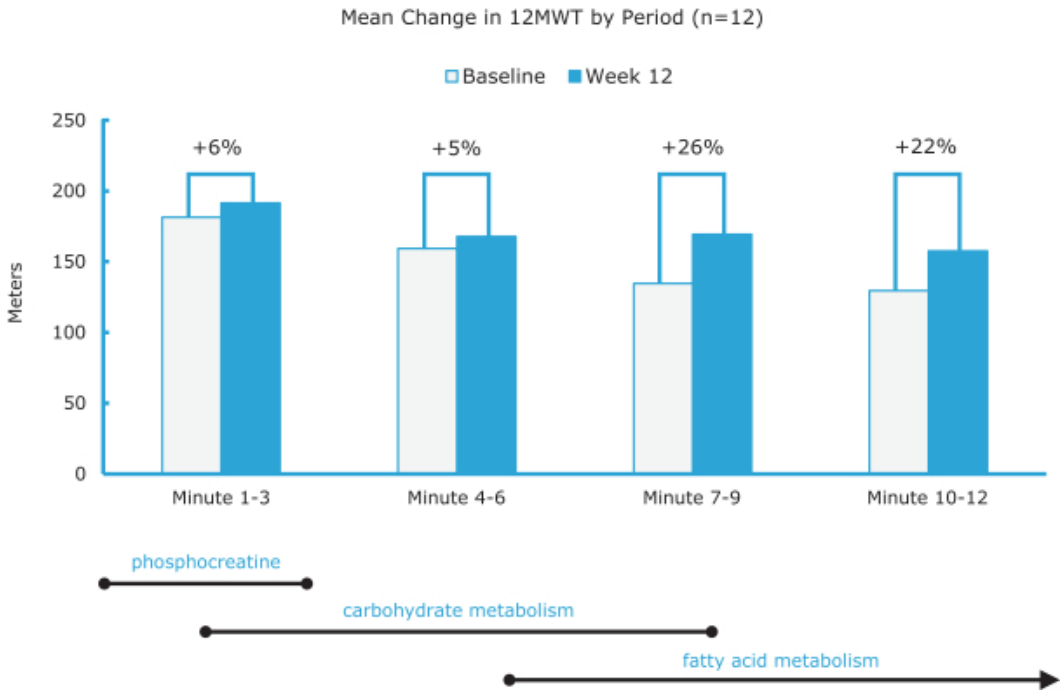



**Figure 5b. REN001-treated PMM patients had greatest improvement in walking distances in the latter half of the 12MWT, consistent with the proposed mechanism of REN001 to stimulate fatty acid metabolism**

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

A mean improvement in peak oxygen consumption, as measured by weight adjusted peak oxygen consumption, of 1.7 mL/kg/min was observed at week 12 compared to baseline (Figure 5c).

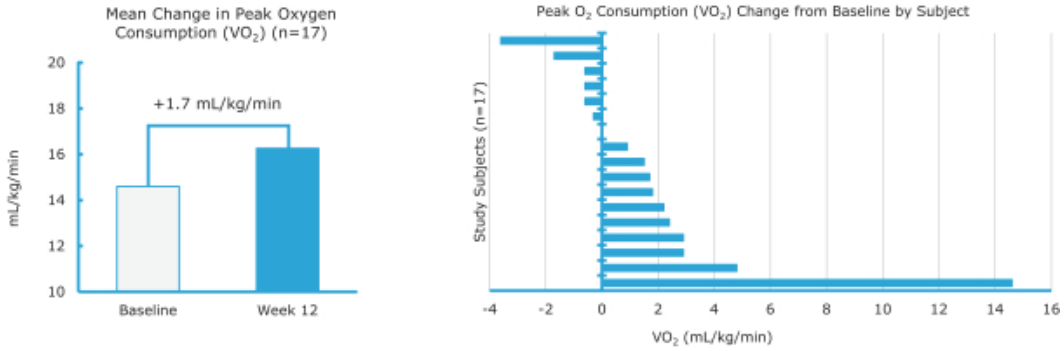



**Figure 5c. Peak exercise oxygen consumption increased in PMM patients after 12 weeks of REN001 treatment.**

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. Only 7 of the 17 patients (41%) were able to complete the 30-minute test at baseline 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 clinical trial were able to perform this task 6.9 times, which is worse than the typical performance of an elderly person in his or her late 80s. After 12 weeks of treatment with 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.

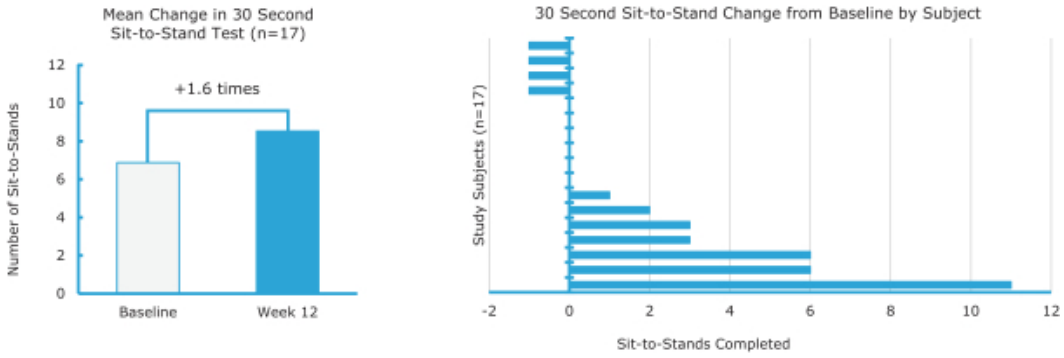



**Figure 5d. PMM patients showed improvements in lower extremity muscle strength and stamina after 12 weeks of REN001 treatment as evaluated with the 30-second sit to stand test**

*Patient Reported Outcome (Evaluation of Symptoms)*

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 score 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 score from 4.5 at baseline to 3.5 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 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.

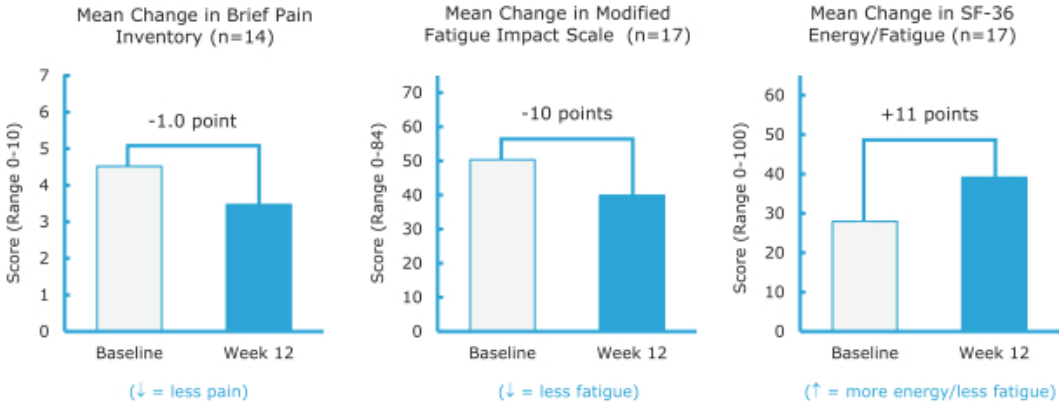



**Figure 5e. Mean Change from Baseline to Week 12 in Patient Reported Outcome Questionnaires in patients with PMM participating in the Phase 1b clinical trial.**

***Clinical development plans in PMM***

We have initiated a global Phase 2b clinical trial of REN001 in patients with PMM and expect to start enrolling patients in the first half of 2021 (STRIDE study). 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 patients with PMM. We anticipate enrolling approximately 200 adult patients with alterations in mtDNA and 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 patient-reported outcomes from baseline including the MFIS, and the Patient Global Impression of Change scale (PGIC).

Other exploratory endpoints include the 30-second sit-to-stand, step counts, and additional patient-reported outcome measures. Data from this trial is expected to be available in 2023. We also plan to evaluate the long-term safety and tolerability of REN001 in an open label extension trial, which will enroll a subset of the patients from the Phase 2b clinical trial, subject first to our completion of carcinogenicity studies discussed below under – “Preclinical results and plans.” Based on interactions with the FDA and several European regulatory agencies, we believe that positive results from the STRIDE study and long-term safety trial could support registration of REN001 for PMM in both the United States and in Europe.

### REN001 for the Treatment of LC-FAOD

***Ongoing Phase1b in LC-FAOD***

We submitted an IND in November 2018 and are currently enrolling an open-label Phase 1b clinical trial 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 plan to enroll approximately 24 patients in this trial and anticipate results in the first half 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.

| 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 |

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

***LC-FAOD prospective survey study***

We are also conducting a non-interventional, international study in approximately 90 adult patients with LC-FAOD to better understand disease characteristics of patients (FORWARD study). We plan to evaluate patients prospectively with exercise tests and symptom questionnaires. This 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 anticipate results of this study in the second half of 2022.

### REN001 for the Treatment of McArdle Disease

***Ongoing Phase1b in McArdle disease***

We are currently enrolling an open-label Phase 1b clinical trial in adult patients with McArdle disease. The primary objective of the trial is to evaluate the safety and tolerability of REN001 in the McArdle patient population, and we will also explore multiple clinical outcomes such as muscle symptoms, physical function, and work productivity. In this clinical trial, patients are dosed with 100 mg REN001 once daily for 12 weeks. Patients will be evaluated using a combination of exercise tests such as the 12-minute *shuttle* walk test, which assesses aerobic capacity and the 'second-wind' by measuring the distance a patient walks per minute and the associated heart rate and patient reported symptom of perceived pain. We plan to enroll approximately 19 patients in this trial, with data anticipated in the first half of 2022.

**Prior Clinical Trial Supporting REN001 Development in Mitochondrial Myopathies**

| 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*<br>• *Decrease in low density lipoprotein (LDL), total cholesterol and triglycerides* |
| Phase 1 RDBPC in healthy subjects (leg immobilization) | 200 mg | 28 days | • *Well tolerated*<br>• *Increase in muscle strength*<br>• *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 in order 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.

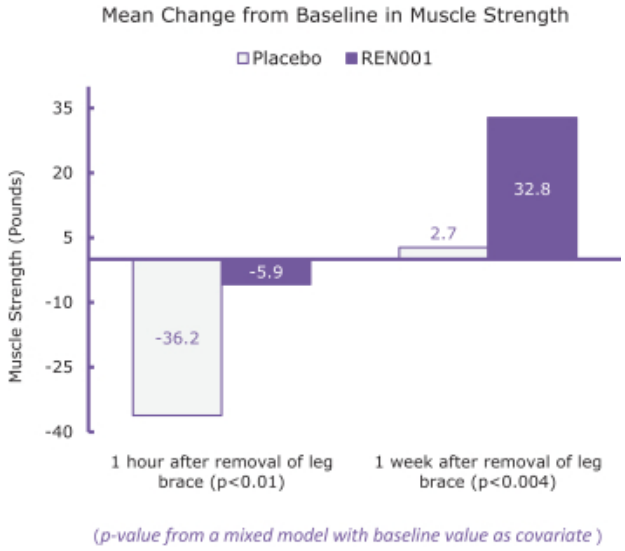



**Figure 7. Results from the muscle strength test from a Phase 1 clinical trial in healthy volunteers**

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 changes in messenger RNA (mRNA) expression of PPARd-regulated genes involved in mitochondrial biogenesis and function. Muscle biopsies obtained from REN001 treated individuals showed substantial increases in the mRNA expression 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 below depicts the changes over time in mRNA expression of PPARd-regulated genes from muscle biopsies obtained from healthy volunteers following treatment with REN001.

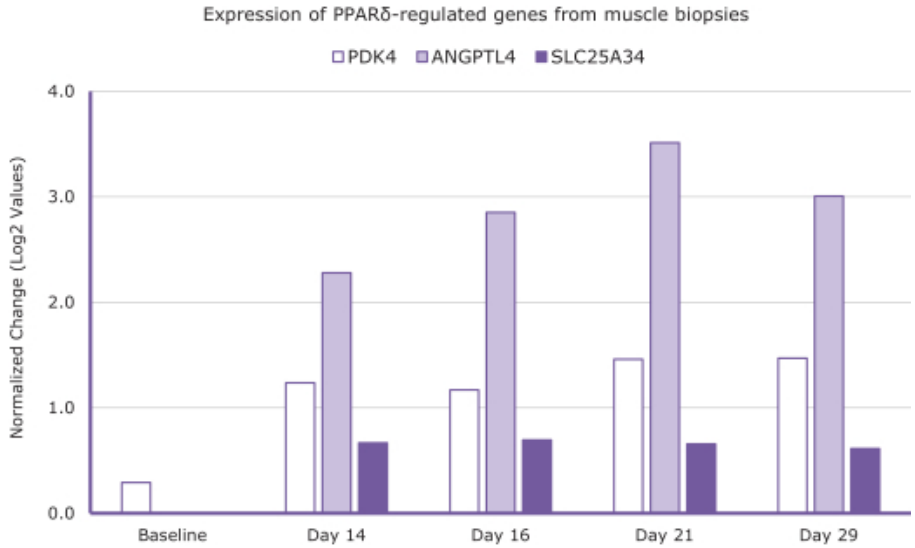



**Figure 8. Change in PPARd-regulated Gene Expression from Human Muscle Following REN001 Treatment from a Phase 1 clinical trial in healthy volunteers.**

***Safety***

Overall, REN001 has been well tolerated in all clinical trials conducted as of January 31, 2021. There have been no deaths or drug related SAEs reported. 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 PPARd with an $EC_{50}$ value of 31 nM for PPARd and over 300-fold increased selectivity over PPARa and PPARg. REN001 has shown minimal or no activity against other ligand-activated nuclear receptors. These other receptors, including the liver X (LXRs) and farnesoid X (FXRs) 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).

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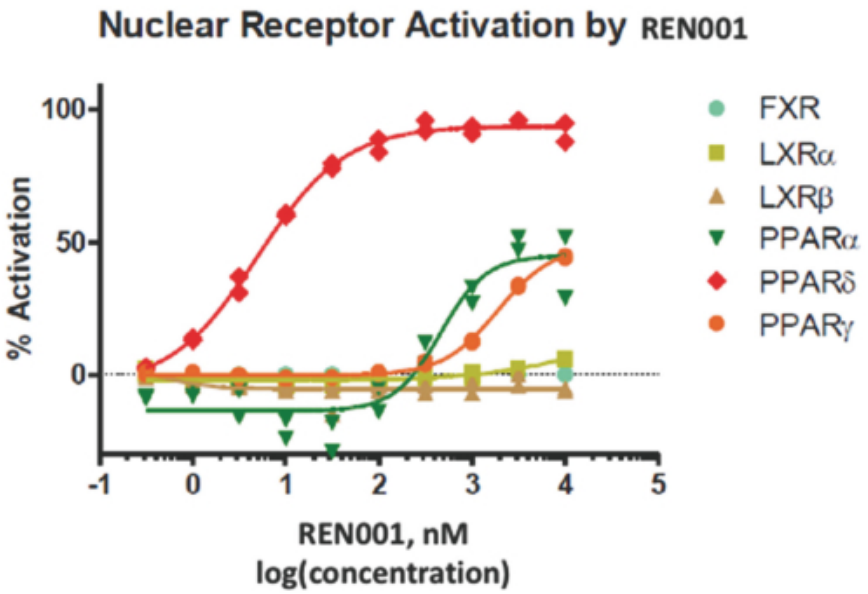


**Figure 9. REN001 is a selective agonist of PPARd**

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.

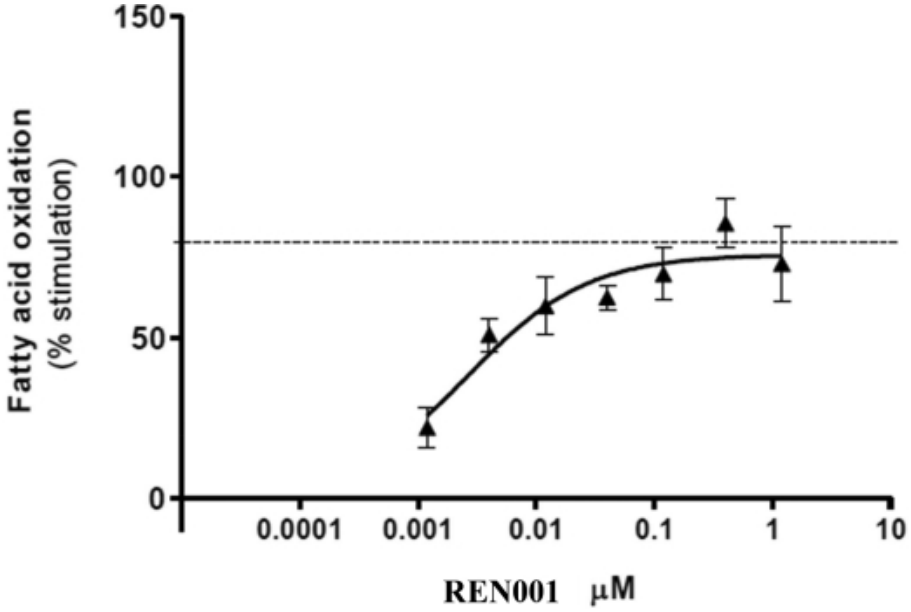


**Figure 10. REN001 led to a concentration-dependent increase in FAO in XM5 human muscle cell line**

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 PGC1a, 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).

| Gene | Name | Description | Fold-change over vehicle (SEM) |
|---|---|---|---|
| PGC1α | PPARγ co-activating factor 1α | Mitochondrial Biogenesis | 1.65 (0.19) |
| CPT1B | Carnitine palmitoyltransferase 1B | Fatty acid metabolism | 1.35 (0.15) |
| PDK4 | Pyruvate dehydrogenase kinase | Fatty acid metabolism | 1.88 (0.17) |
| UCP3 | Mitochondrial uncoupling protein 3 | Fatty acid metabolism | 2.29 (0.27) |

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

PPARa and PPARg 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 studies 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 PPARd agonists. CymaBay Therapeutics clinical development programs includes dosing the selective PPARd 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 PPARd 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 PPARd 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 PPARa or PPARg agonists were observed with administration of REN001 at any dose level.

### Potential applications of REN001 in other indications

We intend to investigate the potential of REN001 in other rare disease indications in which energy deficits have been implicated in disease pathology. For example, patients with a number of muscular dystrophies, including DMD, also suffer from muscle weakness. Studies in mdx mouse models of DMD have shown that muscle cells are deficient in their ability to metabolize fatty acids and activating PPARd resulted in improvement in mitochondrial function. Consistent with literature reports, we have observed in a mouse mdx model that REN001 improved the time-to-exhaustion, decreased serum levels of creatine kinase, a biomarker of muscle damage, and increased the expression of genes associated with FAO.

In addition to muscle cells, PPARd is also expressed in the kidney where it has been shown to be involved in protecting the kidney from inflammatory damage associated with acute kidney disease. During periods of ischemia, kidney cells undergo programmed cell death, or apoptosis, through a process that is dependent on mitochondrial proteins. PPARd agonists have been shown to inhibit this process. We have shown that treatment with REN001 also

protects against renal damage in both a rat surgical model of ischemic kidney disease and in a mouse model of the genetic kidney disease known as Alport syndrome.

### 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 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 LLC

On December 21, 2017, we entered into a License Agreement with vTv Therapeutics, under which we obtained an exclusive, worldwide, sublicensable license under vTv Therapeutics intellectual property relating to vTv Therapeutics' PPARd agonist program, to develop, manufacture and commercialize PPARd agonists and products containing such PPARd 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.

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. If the vTv License Agreement terminates before the initiation of the first Phase 2 clinical trial of any licensed product, we are required to, upon vTv Therapeutics' request, (i) grant to vTv Therapeutics an 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 and (ii) assign and transfer to vTv Therapeutics all regulatory materials and approvals related to the licensed product. If the vTv License Agreement terminates after the initiation of the first Phase 2 clinical trial of any licensed product, 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 regards 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. As of January 31, 2021, we have licensed from vTv Therapeutics six 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 three issued patents in the United States, five issued patents in foreign countries, including Germany, Spain, France, Great Britain, and Italy, one pending application in the United States, and two pending applications in foreign countries, including Canada and 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, as of January 31, 2021, we have filed our own patent applications, of which one is an issued patent in Lebanon, four are pending applications in the United States, three are pending international patent applications, and two are pending in Taiwan. These issued patents and pending applications are directed to various methods of use, methods of manufacturing, and crystalline forms (polymorphs) of REN001. These patent applications, if issued, would be expected to expire between 2040 and 2042, 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 PPARd 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 purchase order basis and do not have long-term supply arrangements in place. We believe there are multiple sources for all of 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 PPARd agonist for PMM and has announced that it is initiating a Phase 2/3 trial in the first quarter of 2021. Other companies are developing therapies for mitochondrial diseases, including 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. There are no approved therapies indicated for the treatment of McArdle disease in any country. We are not aware of any drug interventional studies underway or currently announced for LC-FAOD or for McArdle disease.

Furthermore, it is possible that other companies are also engaged in discovery or nonclinical development of product candidates for PMM, LC-FAOD and McArdle Disease. 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 U.S. Food and Drug Administration (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 Good Laboratory Practices (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 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 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.

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

***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.

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) and teaching hospitals, certain ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, such obligations will include payments and other transfers of value provided in the previous year to certain other healthcare professionals, including physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants, and certified nurse midwives.

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 significant penalties, including without limitation, significant 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 (AMP);

- 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 December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the Affordable Care Act are invalid as well. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. The U.S. Supreme Court is currently reviewing this case, but it is unclear when or how the Supreme Court will rule. Although the U.S. Supreme Court has yet ruled on the constitutionality of the Affordable Care Act, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructs 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 also unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the Affordable Care Act or our business.

Other legislative changes have also been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and due to subsequent legislative amendments to the statute will remain in effect through 2030, except for a temporary suspension from May 1, 2020 through March 31, 2021, unless additional congressional action is taken. Legislation is currently pending in Congress that would further extend the suspension through December 31, 2021. 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.

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 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 released a final rule on September 24, 2020, effective November 30, 2020, providing guidance 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. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. It is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. Some of these and other proposals may require additional authorization to become effective, and it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. Although some of these and other proposals may require additional authorization to become effective, and the likelihood of success of any of these and other Trump administration reform initiatives is uncertain, particularly in light of the new Biden administration. 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***

We may also be subject to federal, state and foreign data privacy and security laws and regulations. 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 (e.g., Section 5 of the FTC Act), govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. HIPAA, as amended by HITECH, and regulations promulgated thereunder, impose requirements relating to the privacy, security and transmission of individually identifiable health information on certain health care providers, health plans and health care clearinghouses, known as covered entities and their business associates that perform certain services that involve creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities as well as their covered subcontractors. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Further, entities that knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA may be subject to criminal penalties.

Even when HIPAA does not apply, according to the FTC, violating consumers' privacy rights or failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5 of the FTC Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and

complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. By way of example, California recently enacted the California Consumer Protection Act (CCPA) which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling certain personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA became effective on January 1, 2020, and became enforceable by the California Attorney General on July 1, 2020. Further, the California Privacy Rights Act (CPRA) was recently voted into law by California residents. The CPRA significantly amends the CCPA, and imposes additional data protection obligations on covered companies doing business in California, including additional consumer rights processes and opt outs for certain uses of sensitive data. It also creates a new California data protection agency specifically tasked to enforce the law, which would likely result in increased regulatory scrutiny of California businesses in the areas of data protection and security. The substantive requirements for businesses subject to the CPRA will go into effect on January 1, 2023, and become enforceable on July 1, 2023. A similar law, the Consumer Data Protection Act (CDPA), was recently passed in Virginia and goes into effect on January 1, 2023.

We also are or will become subject to privacy laws in the jurisdictions in which we are established or in which we sell or market our products or run clinical trials. In particular, the GDPR will apply where we process personal data in relation to participants in our clinical trials in the European Economic Area (EEA) including the health and medical information of these participants. As noted above, the GDPR, which is directly applicable in EEA Member State applies to any processing operations carried out in the context of an establishment in the EEA, as well as certain other processing relating to the offering of goods or services to individuals in the EEA and/or the monitoring of their behavior in the EEA. Also, notwithstanding the UK's withdrawal from the EU, by operation of the UK GDPR, the GDPR continues to apply in substantially equivalent form to processing operations carried out in the context of an establishment in the UK and any processing relating to the offering of goods or services to individuals in the UK and/or monitoring of their behavior in the UK—so, when we refer to the GDPR in this section, we are also making reference to the UK GDPR in the context of the UK, unless the context requires otherwise.

The GDPR created significant and complex compliance burdens for companies such as (i) limiting permitted processing of personal data to only that which is necessary for specified, explicit and legitimate purposes; (ii) requiring the establishment a legal basis for processing personal data; (iii) expressly confirming that 'pseudonymized' or key-coded data constitutes personal data to which the GDPR applies; (iv) creating obligations for controllers and processors to appoint data protection officers in certain circumstances; (v) increasing transparency obligations to data subjects for controllers (including presentation of certain information in a concise, intelligible and easily accessible form about how their personal data is used and their rights vis-à-vis that data and its use); (vi) introducing the obligation to carry out so-called data protection impact assessments in certain circumstances; (vii) establishing limitations on collection and retention of personal data through 'data minimization' and 'storage limitation' principles; (viii) establishing obligations to implement 'privacy by design'; (ix) introducing obligations to honor increased rights for data subjects (such as rights for individuals to be 'forgotten,' rights to data portability, rights to object etc. in certain circumstances); (x) formalizing a heightened and codified standard of data subject consent; (xi) establishing obligations to implement certain technical and organizational safeguards to protect the security and confidentiality of personal data; (xii) introducing obligations to agree to certain specific contractual terms and to take certain measures when engaging third-party processors and joint controllers; (xiii) introducing the obligation to provide notice of certain significant personal data breaches to the relevant supervisory authority(ies) and affected individuals; and (xiv) mandating the appointment of representatives in the UK and/or EU in certain circumstances. The processing of "special category personal data" has also imposed heightened compliance burdens under the GDPR and is a topic of active interest among relevant regulators.

The GDPR provides that EEA Member States may make their own further laws and regulations to introduce specific requirements related to the processing of "special categories of personal data", including personal data related to

health, biometric data used for unique identification purposes and genetic information; as well as personal data related to criminal offences or convictions—in the UK, the Data Protection Act 2018 complements the UK GDPR in this regard. This fact may lead to greater divergence on the law that applies to the processing of such data types across the EEA and/or UK, compliance with which, as and where applicable, may increase our costs and could increase our overall compliance risk. Such country-specific regulations could also limit our ability to collect, use and share data in the context of our EEA and/or UK operations, and/or could cause our compliance costs to increase, ultimately having an adverse impact on our business and harming our business and financial condition.

A particular issue presented by certain data protection laws, including the GDPR, is that they generally restrict transfers of personal data from Europe, including the EEA, the UK and Switzerland, to the United States, and most other countries unless the parties to the transfer have implemented specific safeguards to protect the transferred personal data. One of the primary safeguards allowing U.S. companies to import personal data from Europe had been certification to the EU-U.S. Privacy Shield and Swiss-U.S. Privacy Shield frameworks administered by the U.S. Department of Commerce. However, the EU-U.S. Privacy Shield was invalidated in July 2020 by the Court of Justice of the European Union (the CJEU) in a case known colloquially as “Schrems II.” As it was handed down during the Brexit transitional period, the Schrems II decision by the CJEU is binding on UK courts, which means that it also applies to transfers of personal data from the UK during the transitional period. Also, the Swiss Federal Data Protection and Information Commissioner (the FDPIC) announced that the Swiss-U.S. Privacy Shield does not provide adequate safeguards for the purposes of personal data transfers from Switzerland to the United States. While the FDPIC does not have authority to invalidate the Swiss-U.S. Privacy Shield regime, the FDPIC’s announcement casts doubt on the viability of the Swiss-U.S. Privacy Shield as a future compliance mechanism for Swiss-U.S. data transfers. The CJEU’s decision in Schrems II also raised questions about whether one of the primary alternatives to the EU-U.S. Privacy Shield, namely, the European Commission’s Standard Contractual Clauses, can lawfully be used for personal data transfers from Europe to the United States or other third countries that are not the subject of an adequacy decision of the European Commission. While the CJEU upheld the adequacy of the Standard Contractual Clauses in principle in Schrems II, it made clear that reliance on those Clauses may not necessarily be sufficient in all circumstances. Use of the Standard Contractual Clauses must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular regarding applicable surveillance laws and relevant rights of individuals, with respect to the transferred data. In the context of any given transfer, where the legal regime applicable in the destination country may or does conflict with the intended operation of the Standard Contractual Clauses and/or applicable European law, the decision in Schrems II and subsequent draft guidance from the European Data Protection Board (EDPB) would require the parties to that transfer to implement certain supplementary technical, organizational and/or contractual measures to rely on the Standard Contractual Clauses as a compliant ‘transfer mechanism.’ However, the aforementioned draft guidance from the EDPB on such supplementary technical, organizational and/or contractual measures appears to conclude that no combination of such measures could be sufficient to allow effective reliance on the Standard Contractual Clauses in the context of transfers of personal data ‘in the clear’ to recipients in countries where the power granted to public authorities to access the transferred data goes beyond that which is ‘necessary and proportionate in a democratic society’—which may, following the CJEU’s conclusions in Schrems II on relevant powers of United States public authorities and commentary in that draft EDPB guidance, include the United States in certain circumstances (e.g., where Section 702 of the US Foreign Intelligence Surveillance Act applies). At present, there are few, if any, viable alternatives to the EU-U.S. Privacy Shield and the Standard Contractual Clauses. If we are unable to implement a valid solution for personal data transfers from Europe, including, for example, obtaining individuals’ explicit consent to transfer their personal data from Europe and the United Kingdom to the United States or other countries, we will face increased exposure to regulatory actions, substantial fines and injunctions against processing personal data from Europe and the United Kingdom. Inability to import personal data from Europe, including the EEA, United Kingdom or Switzerland, may also (i) restrict our activities in Europe and the United Kingdom; (ii) limit our ability to collaborate with partners as well as other service providers, contractors and other companies subject to data protection laws; and (iii) require us to increase our data processing capabilities in Europe and/or the United Kingdom at significant expense or otherwise cause us to change the geographical location or segregation of our relevant systems and operations—any or all of which could adversely affect our financial results. Additionally, other countries outside of Europe and the United Kingdom have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of

delivering our services and operating our business. The type of challenges we face in Europe and the United Kingdom will likely also arise in other jurisdictions that adopt laws similar in construction to the GDPR or regulatory frameworks of equivalent complexity.

Further, the United Kingdom's decision to leave the EU, often referred to as Brexit, created uncertainty with regard to data protection regulation in the United Kingdom. Following December 31, 2020, the GDPR's data protection obligations continue to apply to the United Kingdom in substantially unvaried form under the UK GDPR or more explicitly, the GDPR continues to form part of the laws in the United Kingdom by virtue of section 3 of the European Union (Withdrawal) Act 2018, as amended (including by the various Data Protection, Privacy and Electronic Communications (EU Exit) Regulations), which exposes us to two parallel data protection regimes. In addition, it is still unclear whether the transfer of personal data from the EU to the United Kingdom will in the future continue to remain lawful under the GDPR. Pursuant to a post-Brexit agreement between the United Kingdom and the EU, the European Commission will continue to treat the United Kingdom as if it remained a member state of the EU in relation to transfers of personal data from the EEA to the United Kingdom, meaning such transfers may be made without a need for additional safeguards, for four months from January 1, 2021, with a potential additional two month extension. This "transition" period, however, will end if and when the European Commission adopts an adequacy decision in respect of the United Kingdom or the United Kingdom amends certain UK data protection laws, or relevant aspects thereof, without the EU's consent (unless those amendments are made simply to align those UK data protection laws with the EU's data protection regime). The European Commission published a draft adequacy decision on February 19, 2021. If adopted, the decision will enable data transfers from EU member states to the United Kingdom for a four-year period, subject to subsequent extensions. If the European Commission does not adopt an adequacy decision with regard to personal data transfers to the United Kingdom before the expiration of the transition period, or if an adequacy decision is allowed to lapse in the future, from that point onwards, the United Kingdom will be a 'third country' under the GDPR and such transfers will need to be made subject to GDPR-compliant safeguards (for example, the Standard Contractual Clauses).

The GDPR also provides for more robust regulatory enforcement and greater penalties for noncompliance than previously applicable and data protection laws, including fines of up to €20 million or 4% of an undertaking's total worldwide annual turnover for the preceding financial year, whichever is higher. In addition to administrative fines, a wide variety of other potential enforcement powers are available to competent supervisory authorities in respect of potential and suspected violations of the GDPR, including extensive audit and inspection rights, and powers to order temporary or permanent bans on all or some processing of personal data carried out by noncompliant actors. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Additionally, as noted above, the UK has transposed the GDPR into the laws of the United Kingdom by way of the UK GDPR, which could expose us to two parallel regimes, each of which potentially authorizes similar fines, with the UK GDPR permitting fines of up to the higher of £17.5 million or 4% of global annual revenue of any noncompliant organizations for the preceding financial year as well as other potentially divergent enforcement actions for certain violations. Implementing mechanisms to endeavor to ensure compliance with the GDPR and relevant local legislation in EEA Member States and the UK may be onerous and may interrupt or delay our development activities, and adversely affect our business, financial condition, results of operations, and prospects. In addition to the foregoing, a breach of the GDPR or other applicable privacy and data protection laws and regulations could result in regulatory investigations, reputational damage, orders to cease / change our use of data, enforcement notices, or potential civil claims including class action-type litigation. While we have taken steps to comply with the GDPR where applicable, including by reviewing our security procedures, engaging data protection personnel and entering into data processing agreements with relevant contractors, our efforts to achieve and remain in compliance may not be fully successful.

***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. In the EU, for example, a Clinical Trial Application (CTA) must be submitted to the national health authority and an independent ethics committee in each country in which we intend to conduct clinical trials, much like the FDA and IRB, respectively. Once the CTA is approved by the national health authority and the ethics committee has granted a positive opinion in relation to the conduct of the trial in the relevant member state(s) in accordance with a country's requirements, clinical trial development may proceed in that country. Under the new Regulation on Clinical Trials, which is expected to take effect in 2022, there will be a centralized application procedure in respect of clinical trials to be conducted in the EU where one national authority takes the lead in reviewing the application and the other national authorities have more limited involvement. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be notified to or approved by the relevant competent authorities and ethics committees. The Clinical Trials Regulation will not apply to clinical trials in the UK.

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. Currently, CTAs must be submitted to the competent authority in each EU member state in which the trial will be conducted. Under the new Regulation on Clinical Trials, which is currently expected to take effect by early 2022, there will be a centralized application procedure where one national authority takes the lead in reviewing the application and the other national authorities have only limited involvement. 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 European Union (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 marketing authorization application (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 (the 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 European Economic Area (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 separate GB 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 marketing authorization 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, future EU laws on clinical trials (including the impending EU Clinical Trials Regulation, EU CTR) will no be longer applicable in GB. The United Kindgom 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 it is unclear whether the United Kingdom will have access to new EU clinical trial databases such as the Clinical Trial Information System going forward, (the centralized EU Portal for clinical trial information storage). 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 after Brexit, 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, 2020, we employed 23 employees, 12 of whom are full-time, consisting of clinical, research, operations, regulatory, and finance personnel. Three of our employees hold Ph.D. or M.D. degrees. None of our employees is subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

### Facilities

We have entered into a lease agreement for approximately 3,748 square feet of space for our headquarters in San Diego, California, which will expire in late 2023. We also have entered into a lease agreement for approximately 1,455 square feet of space in Sandwich, United Kingdom, which will expire in late 2021. 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.

### Legal Proceedings

We are currently not a party to any material legal proceedings. We may, however, in the ordinary course of business face various claims brought by third parties, and we may, from time to time, make claims or take legal actions to assert our rights, including intellectual property rights as well as claims relating to employment matters and the safety or efficacy of our products. Any of these claims could subject us to costly litigation, and, while we generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny coverage, may be inadequately capitalized to pay on valid claims, or our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our operations, cash flows and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business.

# MANAGEMENT

## Executive Officers and Directors

The following table sets forth information regarding our executive officers and directors as of March 31, 2021.

| NAME | AGE | POSITION |
|---|---|---|
| *Executive Officers:* | | |
| Gregory J. Flesher | 50 | President, Chief Executive Officer and Director |
| Wendy Johnson | 69 | Chief Development Officer |
| Alejandro Dorenbaum, M.D. | 60 | Chief Medical Officer |
| Vineet R. Jindal | 44 | Chief Financial Officer |
| Michael Cruse | 49 | Senior Vice President, Corporate Operations |
| Michael Grey | 68 | Executive Chairman |
| *Non-Employee Directors:* | | |
| Lon Cardon, Ph.D. (1) (2) | 55 | Director |
| Eric M. Dube, Ph.D.(2) (3) | 48 | Director |
| Kenneth Harrison, Ph.D. (3) | 41 | Director |
| Johan Kördel, Ph.D. (4) | 58 | Director |
| Edward T. Mathers (1) | 60 | Director |
| Bali Muralidhar, M.D., Ph.D. (1) (2) | 41 | Director |
| Niall O'Donnell, Ph.D. | 48 | Director |
| Stacey D. Seltzer (3) | 44 | Director |

(1) Member of the compensation committee.
(2) Member of the nominating and corporate governance committee.
(3) Member of the audit committee.
(4) Dr. Kördel resigned as a member of our board of directors effective as of immediately prior to the time that the registration statement of which this prospectus forms a part was declared effective.

## Executive Officers

***Gregory J. Flesher*** has served as our President and Chief Executive Officer and a member of our board of directors since November 2020. Prior to joining us, Mr. Flesher served as the Chief Executive Officer and a member of the board of directors of Novus Therapeutics, Inc., a public specialty pharmaceutical company, from May 2017 to November 2020. Mr. Flesher previously served as Chief Executive Officer and a member of the board of directors for Otic Pharma, Ltd., a private pharmaceutical company, from July 2015 to May 2017. Mr. Flesher also served as Senior Vice President of Corporate Development and Chief Business Officer, and other executive management roles at Avanir Pharmaceuticals, Inc., a public pharmaceutical company, from 2006 to 2015. Mr. Flesher has served as a member of the board of directors for Adynxx, Inc., a pharmaceutical company, since 2019. Mr. Flesher received his B.S. in Biology from Purdue University and studied Biochemistry and Molecular Biology at Indiana University School of Medicine. We believe Mr. Flesher's extensive senior leadership experience at numerous biopharmaceutical companies qualify him to serve on our board of directors.

***Wendy Johnson*** has served as our Chief Development Officer since January 2021 and previously served as our Chief Operating Officer from January 2017 to January 2021. Prior to joining us, Ms. Johnson served as the interim Chief Operating Officer of AmpliPhi Biosciences Corporation (AmpliPhi) (now Armata Pharmaceuticals, Inc.), a public biotechnology company, from September 2014 to January 2017. Ms. Johnson previously served as the President and Chief Executive Officer of Aires Pharmaceuticals, Inc., a private pharmaceutical company, from November 2006 to March 2014 and as a Venture Partner at ProQuest Investments, a private venture capital firm, from 2005 to 2014. Ms. Johnson also served as Senior Vice President of Corporate Development at Salmedix Inc., a private oncology drug development company, until its acquisition by Cephalon, Inc., and held executive roles at Women First HealthCare, Inc., Selective Genetics, Inc. and Cytel Inc. Earlier in her career, Ms. Johnson was assistant director of the Center for Devices and Radiological Health at the U.S. Food and Drug Administration. Ms. Johnson has served as a member of the board of directors of MorphoSys AG, a public biotechnology company, since May 2015 and has been a member

of the board of directors of Exagen, Inc., a public life sciences company, since October 2020. Previously, Ms. Johnson served as a member of the board of directors of AmpliPhi from May 2014 to May 2019. Ms. Johnson received an M.B.A. from Loyola University, an M.S. in clinical microbiology from the Hahnemann Medical School and a B.S. in microbiology from the University of Maryland.

***Alejandro Dorenbaum, M.D.*** has served as our Chief Medical Officer since January 2018. Prior to joining us, Dr. Dorenbaum served as the Chief Medical Officer of Allakos Inc., a public clinical-stage biopharmaceutical company, from August 2014 to June 2017, and the Chief Medical Officer at Lumena Pharmaceuticals, Inc., a private biopharmaceutical company, from 2013 to 2014, until its acquisition by Shire Pharmaceuticals Ltd. Dr. Dorenbaum also worked at Genentech, Inc., a private biotechnology company, where he was responsible for the respiratory programs for asthma and cystic fibrosis, and at BioMarin Pharmaceutical Inc., a biopharmaceutical company, where he worked on the clinical development of Kuvan. Dr. Dorenbaum began his career at Chiron Corporation, a private biotechnology company. Dr. Dorenbaum maintains an active academic position as Clinical Professor in Pediatrics at Stanford University School of Medicine, where he specializes in allergy and immunology. Dr. Dorenbaum received an M.D. from the National Autonomous University in Mexico City, completed his residency in pediatrics at University of Texas Health Science Center and held a fellowship in allergy and immunology at Baylor College of Medicine.

***Vineet R. Jindal*** has served as our Chief Financial Officer since March 2021. Prior to joining us, Mr. Jindal served as Vice President, Strategy and Investor Relations for Reata Pharmaceuticals, Inc., a public biopharmaceutical company, from November 2016 to March 2021. Mr. Jindal previously served as Chief Executive Officer, Co-Founder and a member of the board of directors of Stockr, Inc., a social media platform focused on connecting investors with public companies, from 2009 to 2014. Mr. Jindal also founded Bay Street Advisors, a strategic consulting firm focusing on therapeutic and capital markets, where he served from 2008 to 2010. Mr. Jindal has also served as the Managing Director and Head of Healthcare Equity Research at ThinkEquity Partners, a boutique investment bank, as the Vice President of Biotechnology Equity Research at Wedbush Morgan Securities, a financial services firm, as a Biotechnology and Specialty Pharmaceuticals Research Analyst at Origin Capital Management, an investment management firm, and as a Biotechnology Equity Research Associate at Lehman Brothers, a financial services firm. Mr. Jindal received a B.A. in Integrative Biology from the University of California, Berkeley, a M.A. in Endocrinology from the University of California, Berkeley and a M.S. in Pharmacology from Cornell University.

***Michael Cruse*** has served as our Senior Vice President, Corporate Operations since December 2020. Prior to joining us, Mr. Cruse served as Vice President Corporate Operations at Novus Therapeutics, Inc., a public specialty pharmaceutical company, from May 2017 to June 2020, and as Vice President Corporate Operations at Otic Pharma, Ltd., a private pharmaceutical company, from September 2015 to May 2017. Mr. Cruse previously held various positions at Avanir Pharmaceuticals, a public pharmaceutical company, including Executive Director, Sales Operations, Executive Director Technology and Facilities Management, Senior Director, Information Technology and Director, Information Technology. Mr. Cruse previously served as Manager of Information Technology and Senior Client Consultant at Noesis Consulting Group, Inc., a consulting services company, Manager, Information Technology at Spy Optic, Inc., a retail company, Senior Information Technology Consultant and Founding Partner at Senatron, LLP, an information technology consulting firm, and Promotional Product Manager at Vision Technologies, LLC, an information technology consulting firm. Mr. Cruse received a B.S. in Business Administration and Management from Franklin University.

***Michael Grey*** has served as Executive Chairman of our board of directors since December 2017. Mr. Grey previously served as our Chairman and Chief Executive Officer from September 2014 to December 2017. In addition, Mr. Grey has served as Chairman of Mirum Pharmaceuticals, Inc. (Mirum) a public biopharmaceutical company, since January 2020, and has been a director of Mirum since May 2018. Mr. Grey previously served as Executive Chairman of Mirum from March 2019 to December 2019 and Chief Executive Officer of Mirum from May 2018 to March 2019. Mr. Grey has served as Executive Chairman of Amplyx Pharmaceuticals, Inc. or Amplyx, a private pharmaceutical company, since January 2017, and Spruce Biosciences, Inc., a public biotechnology company, since April 2017. Mr. Grey has also served as a venture partner at Pappas Ventures, a venture capital firm, since January 2010, and as a director of Curzion Pharmaceuticals, Inc. (Curzion) a private pharmaceutical company, which was acquired in

April 2020 by Horizon Therapeutics Public Limited Company (Horizon) a pharmaceutical company, from January 2019 to April 2020. Mr. Grey served as President and Chief Executive Officer of Curzion from January 2019 to September 2019 and as President and Chief Executive Officer of Amplyx from October 2015 to January 2017. From February 2011 to June 2014, Mr. Grey served as President and Chief Executive Officer of Lumena Pharmaceuticals, Inc., a private biopharmaceutical company, which was acquired by Shire plc, in June 2014. Mr. Grey has more than 45 years of experience in the pharmaceutical and biotechnology industries and has held senior positions at a number of companies, including President and Chief Executive Officer of SGX Pharmaceuticals, Inc. (sold to Lilly in 2008), President and Chief Executive Officer of Trega Biosciences, Inc. (sold to LION Bioscience, Inc. in 2001) and President of BioChem Therapeutic Inc. Prior to these, Mr. Grey served in various roles with Glaxo, Inc., and Glaxo Holdings PLC, culminating in his position as Vice President, Corporate Development and director of international licensing. Mr. Grey also serves on the boards of directors of BioMarin Pharmaceutical Inc., Horizon, and Mirati Therapeutics Inc., each a public biotechnology company and Plexium, Inc., a private biotechnology company. Mr. Grey received a B.S. in chemistry from the University of Nottingham in the United Kingdom. We believe Mr. Grey's extensive experience managing and leading both early stage and established companies within the pharmaceutical and biotechnology industries qualify him to serve on our board of directors.

### Non-Employee Directors

***Lon Cardon, Ph.D.*** has served as a member of our board of directors since January 2019. Dr. Cardon has served as Chief Scientific Officer at BioMarin Pharmaceutical Inc. (BioMarin) a biopharmaceutical company, since September 2017. Prior to joining BioMarin, Dr. Cardon served as a Senior Vice President of Genetics, Alternative Drug Discovery and Target Sciences at GlaxoSmithKline plc, a global healthcare company, from 2008 to September 2017. Dr. Cardon previously served as a professor at the University of Oxford and as a professor of biostatistics and human biology at the University of Washington and the Fred Hutchinson Cancer Research Center. Dr. Cardon is a past council member of the NIH/National Human Genome Research Institute and a present advisor to the All of Us Precision Medicine Initiative. Dr. Cardon served as a member of the board of directors and institutional founder of the Altius Institute for Biomedical Sciences, Centre for Therapeutic Target Validation (now Open Targets) and the GSK/Avalon Center of Excellence. Dr. Cardon is an elected fellow of the UK's Academy of Medical Sciences and the American Association for the Advancement of Science. Dr. Cardon received a B.S. in Psychology/Biology from the University of Puget Sound, a Ph.D. from the University of Colorado, Boulder and did his postdoctoral training at Stanford University. We believe Dr. Cardon's expertise and experience in the biopharmaceutical industry qualify him to serve on our board of directors.

***Eric M. Dube, Ph.D.*** has served as a member of our board of directors since March 2021. Since January 2019, Dr. Dube has served as the President and Chief Executive Officer and as a member of the board of directors of Travere Therapeutics, Inc., a public biopharmaceutical company. Prior to that, Dr. Dube served as the Head, North America of Viiv Healthcare Limited, a pharmaceuticals company, since January 2018. From June 2015 to December 2017, Dr. Dube served as Sr. Vice President and Head, Global Respiratory Franchise of GlaxoSmithKline Pharmaceuticals plc (GSK), a pharmaceutical company. From February 2013 to May 2015, Dr. Dube served as Senior Vice President and Business Unit Head, Respiratory Japan of GSK. Prior to that, Dr. Dube held senior leadership roles at GSK in Strategy, Planning & Operations, Oncology, Managed Markets and Marketing, and earlier in his career held other positions of increasing responsibility at GSK. Dr. Dube holds a B.S. from Santa Clara University and a M.A. and Ph.D. from Cornell University. We believe Dr. Dube's expertise and experience in the biopharmaceutical industry and senior leadership experience qualify him to serve on our board of directors.

***Kenneth Harrison*** has served as a member of our board of directors since December 2020. Dr. Harrison has been employed as a Partner at Novo Ventures (U.S.) Inc. (Novo), which provides consulting services to Novo Holdings A/S, an investment firm focused on life sciences and finances, since November 2015. Prior to joining Novo, Dr. Harrison served as Senior Market Planning Manager at Genentech, USA Inc., a private biotechnology company, from 2013 to 2015, where he helped guide strategic decision making for the Ophthalmology and HER2 franchises. Dr. Harrison previously worked as a management consultant at L.E.K. Consulting LLC, a consulting firm, and as the Entrepreneurship Program Manager at QB3, a nonprofit research and technology commercialization institute, and Mission Bay Capital LLC, an early stage life science venture capital firm, where he helped create new programs to launch and support life sciences companies in the Bay Area. Dr. Harrison studied cellular lipid storage and metabolism as an A.P. Giannini Foundation Fellow at the J. David Gladstone Institutes, received a Ph.D. in

pharmacology from Yale University, and received a B.S. in molecular biology from Texas Tech University, where he was a Howard Hughes Medical Institute undergraduate research fellow. We believe Dr. Harrison's investment experience in the life science industry qualifies him to serve on our board of directors.

***Johan Kördel, Ph.D.*** has served as a member of our board of directors January 2018. From April 2010 to December 2019, Dr. Kördel has served as a Senior Partner at Lundbeckfond Ventures, an evergreen life science venture fund. Since January 1, 2020, Dr. Kördel has served as a Senior Advisor to Lundbeckfond Ventures. Since October 2019, Dr. Kördel has served as a Senior Advisor to Industrifonden, a venture capital firm. From May 2008 to February 2010, Dr. Kördel served as Chief Executive Officer of Sound Biotech ApS, a biotechnology development company which Dr. Kördel co-founded. From October 2000 to August 2003, Dr. Kördel served as Senior Vice President of Research of Biovitrum AB (Biovitrum) a pharmaceutical company which Dr. Kördel co-founded, and from September 2003 to January 2006, Dr. Kördel served as Senior Vice President of Business Development for Biovitrum. Previously, Dr. Kördel held a number of positions in research and development including that of Deputy Head of Metabolic Diseases and Endocrinology Discovery Research at Pharmacia Corporation before its acquisition by Pfizer Inc. in April 2003. Dr. Kördel has been an Associate Professor of Physical Chemistry at Lund University, Sweden since 1994. Earlier in his career, Dr. Kördel worked at Scripps Research Institute in La Jolla, California, and Harvard Medical School in Boston, Massachusetts. Dr. Kördel presently serves on the board of directors of the private companies, Amplyx Pharmaceuticals, Inc., Athera Biotechnologies AB, Enterome S. A., SARomics Biostructures AB and VHsquared Ltd. Dr. Kördel previously served as a member of the board of directors of the public companies, Acacia Pharma Ltd. from March 2011 to April 2020, BoneSupport AB from August 2011 to December 2016, Celladon Corporation from January 2012 to March 2014, EQL Pharma AB from April 2007 to June 2015 and Karo Bio AB from April 2009 to May 2011. Dr. Kördel received a Ph.D. in physical chemistry and an M.Sc. from Lund University, Sweden. We believe Dr. Kördel's expertise and experience in the biotechnology industry qualifies him to serve on our board of directors. Dr. Kördel resigned as a member of our board of directors effective as of immediately prior to the time that the registration statement of which this prospectus forms a part was declared effective.

***Edward Mathers*** has served as a member of our board of directors since December 2017. Mr. Mathers has served as a General Partner at New Enterprise Associates, Inc. (NEA), a private venture capital firm focusing on technology and healthcare investments, since November 2019. Mr. Mathers served as partner at NEA from August 2008 to October 2019. Prior to joining NEA, Mr. Mathers served as Executive Vice President, Corporate Development and Venture at MedImmune, Inc., a biopharmaceutical company, and led its venture capital subsidiary, MedImmune Ventures, Inc. Mr. Mathers currently serves on the board of directors of Akouos, Inc., Inozyme Pharma, Inc., Mirum Pharmaceuticals, Inc., ObsEva SA, Rhythm Pharmaceuticals, Inc., Synlogic, Inc. (formerly known as Mirna Therapeutics, Inc.) and Trevi Therapeutics, Inc., all public pharmaceutical companies, and he previously served on the board of directors of Liquidia Technologies, Inc., a public life sciences company, from April 2009 to May 2019 and Ra Pharma, a public pharmaceutical company, from February 2010 to April 2020. Mr. Mathers received a B.S. in chemistry from North Carolina State University. We believe Mr. Mathers' experience as a venture capitalist, as an executive and in business development and his experience in serving on the board of directors for several public and private pharmaceutical and life sciences companies qualify him to serve on our board of directors.

***Bali Muralidhar, M.D., Ph.D.*** has served as a member of our board of directors since December 2020. Dr. Muralidhar has served as Managing Partner at Abingworth LLP (Abingworth) an international investment group dedicated to life sciences, since December 2020. Dr. Muralidhar previously served as a Partner at Abingworth from March 2019 to December 2020. Prior to joining Abingworth, Dr. Muralidhar was a Senior Partner at MVM Partners LLP (MVM) a life science investment fund, from November 2012 to March 2019. Prior to MVM, Dr. Muralidhar was a member of Bain Capital LP's, a private multi-asset alternative investment firm, leveraged buyout team, focusing on healthcare from April 2011 to November 2012. Dr. Muralidhar has served as a director of Nucana plc since October 2020, Spruce Biosciences, Inc. since February 2020 and Exicure, Inc. since August 2019, each a public biotechnology company. Dr. Muralidhar previously served on the board of directors of Wilson Therapeutics, a public biopharmaceutical company in Sweden, from March 2014 to April 2018, and Valneva SE, a French biotechnology company traded on the Vienna Stock Exchange from May 2017 to December 2019. Dr. Muralidhar received a degree in clinical medicine from the University of Oxford and received a Ph.D. in translational cancer research from the MRC Cancer Cell Unit, University of Cambridge. We believe Dr. Muralidhar's investment experience in the healthcare industry qualifies him to serve on our board of directors.

***Niall O'Donnell, Ph.D.*** has served as a member of our board of directors since December 2017. Dr. O'Donnell is our co-founder and previously served as our President and Chief and Executive Officer from December 2017 to November 2020. Dr. O'Donnell is currently a managing director at RiverVest Venture Partners (RiverVest) a venture capital firm, a position he has held since April 2014. Dr. O'Donnell joined RiverVest in 2006 where he has focused on biopharmaceutical, diagnostic and medical device opportunities and contributes to the formation, development, and business strategies of RiverVest affiliated portfolio companies. From 2011 to 2013, Dr. O'Donnell served as acting Chief Interim Medical Officer at Lumena Pharmaceuticals, Inc., a private biopharmaceutical company, where he led the development and execution of the company's clinical strategy leading up to its acquisition by Shire plc. From February 2019 to April 2020, Dr. O'Donnell co-founded and served as a member of the board of directors of Curzion Pharmaceuticals, Inc., a private pharmaceutical company. Dr. O'Donnell has been a member of the board of directors of Spruce Biosciences, Inc., a public biotechnology company, since May 2016, and Mirum Pharmaceuticals, Inc., a public biopharmaceutical company, since December 2018, and is also a member of the board of directors of the private biopharmaceutical companies, Amplyx Pharmaceuticals, Inc. and Avalyn Pharma, Inc. Dr. O'Donnell received a Ph.D. in biochemistry from the University of Dundee, Scotland, an M.A. in biochemistry from Pembroke College, Oxford, and an M.B.A. from the Rady School of Management of the University of California, San Diego. We believe Dr. O'Donnell's substantial experience in developing and managing biopharmaceutical companies qualifies him to serve on our board of directors.

***Stacey D. Seltzer*** has served as a member of our board of directors since December 2020. Since 2014, Ms. Seltzer has served as a partner at Aisling Capital LLC, a venture capital and private equity firm, where she previously served as principal from 2008 to 2014. From 2004 to 2008, Ms. Seltzer held various positions at Schering-Plough Corporation, a pharmaceutical company, including U.S. Schering-Plough Brand Lead for Zetia, Associate Director, U.S. Marketing, Senior Manager, Global Licensing and Management Associate. From 2001 to 2002, Ms. Seltzer served as Director of Business Development for Akceli, Inc., a biotechnology company. Ms. Seltzer has served on the board of directors of Prommentis Pharmaceuticals, Inc., a private biopharmaceutical company, since November 2016 and is currently a board observer for Prolacta Bioscience Inc., a private biopharmaceutical company. Ms. Seltzer previously served on the board of directors of Miramar Labs, Inc., a public global medical device company, from May 2013 to July 2017, Aimmune Therapeutics, Inc., a public biopharmaceutical company, from January 2015 to October 2020, and as a board observer for public companies, Agile Therapeutics, Inc., a women's healthcare company and Durata Therapeutics, Inc., a pharmaceutical company. Ms. Seltzer received a B.S. and M.S. in Molecular Biophysics and Biochemistry from Yale University and an M.B.A. from the Wharton School at the University of Pennsylvania. We believe that Ms. Seltzer is qualified to serve on our Board due to her investment and management experience in the life science industry.

### Composition of Our Board of Directors

Our business and affairs are organized under the direction of our board of directors. After the resignation of Dr. Kördel, our board of directors consists of nine members. The primary responsibilities of our board of directors are to provide oversight, strategic guidance, counseling and direction to our management. Our board of directors meets on a regular basis and additionally as required.

Certain members of our board of directors were elected under the provisions of our Voting Agreement, which is defined below. Under the terms of our Voting Agreement, the stockholders who are party to the Voting Agreement have agreed to vote their respective shares to elect: (i) one director designated by Novo Holdings A/S, currently Dr. Harrison, (ii) one director designated by Abingworth Ventures 8 LP, currently Dr. Muralidhar, (iii) one director designated by Aisling Capital V, L.P., currently Ms. Seltzer, (iv) one director designated by New Enterprise Associates 15, L.P., currently Mr. Mathers, (v) one director designated by RiverVest Venture Fund IV, L.P., currently Dr. O'Donnell, (vi) one director designated by Lundbeckfond Invest A/S, currently Dr. Kördel, (vii) one director designated by the holders of our common stock and who shall be our then-current Chief Executive Officer, currently Mr. Flesher, (viii) one director designated by the holders of a majority of our common stock, currently Mr. Grey, and (ix) two directors designated by a majority of the other members of our board of directors and who shall be outside industry experts, currently Dr. Cardon and Dr. Dube. The Voting Agreement will terminate upon the closing of this offering, and thereafter no stockholder will have any special rights regarding the election or designation of the members of our board of directors. Our current directors elected to our board of directors pursuant to the Voting

Agreement will continue to serve as directors until their successors are duly elected and qualified by holders of our common stock.

Our board of directors may establish the authorized number of directors from time to time by resolution. In accordance with our amended and restated certificate of incorporation to be filed in connection with this offering, immediately after this offering, our board of directors will be divided into three classes with staggered three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Our directors will be divided among the three classes as follows:

- the Class I directors will be Dr. Cardon, Dr. Dube and Dr. Harrison, and their terms will expire at the annual meeting of stockholders to be held in 2022;
- the Class II directors will be Mr. Mathers, Dr. Muralidhar and Ms. Seltzer, and their terms will expire at the annual meeting of stockholders to be held in 2023; and
- the Class III directors will be Mr. Flesher, Mr. Grey and Dr. O'Donnell, and their terms will expire at the annual meeting of stockholders to be held in 2024.

We expect that any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control.

### Board Leadership Structure

Our board of directors is currently chaired by Mr. Grey who has authority, among other things, to call and preside over board of directors meetings, to set meeting agendas and to determine materials to be distributed to the board of directors. Accordingly, the Executive Chairman has substantial ability to shape the work of the board of directors. We believe that separation of the positions of Executive Chairman and Chief Executive Officer reinforces the independence of the board of directors in its oversight of our business and affairs. In addition, we have a separate chair for each committee of our board of directors. The chair of each committee is expected to report annually to our board of directors on the activities of their committee in fulfilling their responsibilities as detailed in their respective charters or specify any shortcomings should that be the case.

### Role of the Board in Risk Oversight

The audit committee of our board of directors is primarily responsible for overseeing our risk management processes on behalf of our board of directors. Going forward, we expect that the audit committee will receive reports from management at least quarterly regarding our assessment of risks. In addition, the audit committee reports regularly to our board of directors, which also considers our risk profile. The audit committee and our board of directors focus on the most significant risks we face and our general risk management strategies. While our board of directors oversees our risk management, management is responsible for day-to-day risk management processes. Our board of directors expects management to consider risk and risk management in each business decision, to proactively develop and monitor risk management strategies and processes for day-to-day activities and to effectively implement risk management strategies adopted by the audit committee and our board of directors. We believe this division of responsibilities is the most effective approach for addressing the risks we face and that our board of directors' leadership structure, which also emphasizes the independence of our board of directors in its oversight of its business and affairs, supports this approach.

### Director Independence

Under the listing requirements and rules of Nasdaq, independent directors must comprise a majority of our board of directors as a listed company within one year of the listing date.

Our board of directors has undertaken a review of the independence of each director. Based on information provided by each director concerning her or his background, employment, and affiliations, our board of directors has determined that Dr. Cardon, Dr. Dube, Dr. Harrison, Dr. Kördel, Mr. Mathers, Dr. Muralidhar and Ms. Seltzer do not have relationships that would interfere with the exercise of independent judgment in carrying out the responsibilities

of a director and that each of these directors is "independent" as that term is defined under the listing standards. In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our shares by each non-employee director and the transactions described in "Certain Relationships and Related Person Transactions."

### Family Relationships

There are no family relationships among any of our executive officers or directors.

### Committees of Our Board of Directors

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee. The composition and responsibilities of each of the committees of our board of directors are described below. Members serve on these committees until their resignation or until otherwise determined by our board of directors. Our board of directors may establish other committees as it deems necessary or appropriate from time to time. Each committee has a written charter that satisfies the applicable rules and regulations of the SEC and Nasdaq Listing Rules, which we will post on our website at www.reneopharma.com. Information contained in, or that can be accessed through, our website is not incorporated by reference into this prospectus.

#### *Audit Committee*

Our audit committee currently consists of Dr. Dube, Dr. Harrison and Ms. Seltzer, each of whom our board of directors has determined satisfies the independence requirements under listing standards and Rule 10A-3(b)(1) of the Exchange Act. The chair of our audit committee is Dr. Dube. Our board of directors has determined that Dr. Dube is an "audit committee financial expert" within the meaning of SEC regulations and that each member of our audit committee can read and understand fundamental financial statements in accordance with applicable requirements. In arriving at these determinations, the board of directors has examined each audit committee member's scope of experience and the nature of their employment in the corporate finance sector.

The primary purpose of the audit committee is to discharge the responsibilities of our board of directors with respect to our corporate accounting and financial reporting processes, systems of internal control and financial-statement audits, and to oversee our independent registered accounting firm. Specific responsibilities of our audit committee include:

- helping our board of directors oversee our corporate accounting and financial reporting processes;
- managing the selection, engagement, qualifications, independence, and performance of a qualified firm to serve as the independent registered public accounting firm to audit our consolidated financial statements;
- discussing the scope and results of the audit with the independent registered public accounting firm, and reviewing, with management and the independent accountants, our interim and year-end operating results;
- developing procedures for employees to submit concerns anonymously about questionable accounting or audit matters;
- reviewing related person transactions;
- obtaining and reviewing a report by the independent registered public accounting firm, that describes our internal quality control procedures, any material issues with such procedures, and any steps taken to deal with such issues when required by applicable law; and
- approving, or, as permitted, pre-approving, audit and permissible non-audit services to be performed by the independent registered public accounting firm.

#### *Compensation Committee*

Our compensation committee currently consists of Dr. Cardon, Mr. Mathers and Dr. Muralidhar. The chair of our compensation committee is Mr. Mathers. Our board of directors has determined that each member of the compensation committee is independent under Nasdaq listing standards and a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act.

The primary purpose of our compensation committee is to discharge the responsibilities of our board of directors in overseeing our compensation policies, plans, and programs and to review and determine the compensation to be paid to our executive officers, directors, and other senior management, as appropriate. Specific responsibilities of our compensation committee include:

- reviewing and approving the compensation of our chief executive officer, other executive officers and senior management;
- reviewing and approving to our board of directors the compensation paid to our directors;
- reviewing and approving the compensation arrangements with our executive officers and other senior management;
- administering our equity incentive plans and other benefit programs;
- reviewing, adopting, amending and terminating the terms of any employment agreements, stock option plans, stock appreciation rights plans, severance arrangements, pension and, profit sharing plans, incentive plans, stock bonus plans, stock purchase plans, bonus plans, deferred compensation plans, change-of-control protections and any other compensatory arrangements for our executive officers and other senior management;
- reviewing, evaluating and recommending to our board of directors succession plans for our executive officers; and
- reviewing and establishing general policies relating to compensation and benefits of our employees, including our overall compensation philosophy.

***Nominating and Corporate Governance Committee***

Our nominating and corporate governance committee consists of Dr. Cardon, Dr. Dube and Dr. Muralidhar. The chair of our nominating and corporate governance committee is Dr. Cardon. Our board of directors has determined that each member of the nominating and corporate governance committee is independent under Nasdaq listing standards. Specific responsibilities of our nominating and corporate governance committee include:

- identifying and evaluating candidates, including the nomination of incumbent directors for reelection and nominees recommended by stockholders, to serve on our board of directors;
- considering and making recommendations to our board of directors regarding the composition and chairmanship of the committees of our board of directors;
- instituting plans or programs for the continuing education of our board of directors and orientation of new directors;
- developing and making recommendations to our board of directors regarding corporate governance guidelines and matters; and
- overseeing periodic evaluations of the board of directors' performance, including committees of the board of directors and management.

## Code of Conduct

We have adopted 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 will be posted on our website at www.reneopharma.com. We intend to disclose on our website any future amendments of our Code of Conduct or waivers that exempt any principal executive officer, principal financial officer, principal accounting officer or controller, persons performing similar functions or our directors from provisions in the Code of Conduct. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus, and you should not consider information on our website to be part of this prospectus.

## Compensation Committee Interlocks and Insider Participation

None of the members of the compensation committee is currently, or has been at any time, one of our officers or employees. None of our executive officers currently serves, or has served during the last calendar year, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

### Director Compensation

We have historically not paid cash, equity or other compensation to any of our directors who are also our employees for service on our board of directors, nor have we paid cash or equity compensation to our non-employee directors, except as set forth below. No such compensation was paid to any of our directors in the year ended December 31, 2020.

We have reimbursed and will continue to reimburse all of our non-employee directors for their reasonable out-of-pocket expenses incurred in attending board of directors and committee meetings. Michael Grey, our Executive Chairman, is a director and an executive officer who did not receive any additional compensation for his services provided as a director during the year ended December 31, 2020. Gregory J. Flesher, our President and Chief Executive Officer, Niall O'Donnell, Ph.D., our former President and Chief Executive Officer, are also directors but did not receive any additional compensation for their service as directors during the year ended December 31, 2020. See the section titled "Executive Compensation" for more information regarding the compensation earned by Mr. Flesher and Dr. O'Donnell.

We entered into a letter agreement with Lon Cardon, Ph.D., one of our non-employee directors, in January 2019 confirming his appointment as a member of our board of directors. Pursuant to his agreement, Dr. Cardon was entitled to a stock option to purchase an aggregate of 29,051 shares of our common stock, which was granted in January 2019 under our 2014 Equity Incentive Plan (2014 Plan), the terms of which are described in more detail below under the section titled "Executive Compensation—Employee Benefit Plans—2014 Equity Incentive Plan." The option was granted with an exercise price of $2.28 per share and vests in a series of 48 successive equal monthly installments measured from January 30, 2019, subject to Dr. Cardon's continued service to us. The option provides for "early exercise" prior to vesting in exchange for shares of restricted shares that vest on the option's vesting schedule and the vesting of this option will accelerate in full immediately prior to a Change in Control (as defined in the 2014 Plan) that occurs during Dr. Cardon's continued service to us.

In January 2021, we granted Dr. Cardon an option to purchase 17,877 shares of our common stock under our 2014 Plan. The option was granted with an exercise price of $4.88 per share and vests in a series of 48 successive equal monthly installments measured from December 9, 2020, subject to Dr. Cardon's continued service to us. The option provides for "early exercise" prior to vesting in exchange for shares of restricted shares that vest on the option's vesting schedule.

We entered into a letter agreement with Eric M. Dube, Ph.D., one of our non-employee directors, in March 2021 confirming his appointment as a member of our board of directors. Pursuant to his agreement, Dr. Dube was entitled to a stock option to purchase an aggregate of 44,694 shares of our common stock, which was granted in March 2021 under our 2014 Plan. The option was granted with an exercise price of $6.35 per share and vests in a series of 36 successive equal monthly installments measured from March 12, 2021, subject to Dr. Dube's continued service to us. The option provides for "early exercise" prior to vesting in exchange for shares of restricted shares that vest on the option's vesting schedule and the vesting of this option will accelerate in full immediately prior to a Change in Control (as defined in the 2014 Plan) that occurs during Dr. Dube's continued service to us.

As of December 31, 2020, the aggregate number of shares underlying outstanding options to purchase our common stock held by our directors was: Dr. Cardon, 29,051 shares; Dr. O'Donnell, 116,971 shares; and Mr. Grey, 149,809 shares. As of December 31, 2020, none of our directors held other unvested stock awards.

We have granted, effective immediately prior to the execution and delivery of the underwriting agreement related to this offering, at an exercise price equal to $15.00 per share, the public offering price set forth on the cover page of this prospectus, an option to purchase 14,000 shares of our common stock to each of Ms. Seltzer, Messrs. Grey and Mathers and Drs. Cardon, Harrison, Muralidhar and O'Donnell. Such options will vest in full on the one year anniversary of the grant date and will fully vest on an accelerated basis in the event we are subject to a change in control.

#### *Non-Employee Director Compensation Policy*

We adopted a non-employee director compensation policy in March 2021 that became effective immediately prior to the execution and delivery of the underwriting agreement related to this offering and is applicable to all of our non-

employee directors. This compensation policy provides that each such non-employee director will receive the following compensation for service on our board of directors:

- an annual cash retainer of $40,000;
- an additional cash retainer of $30,000 for service as the non-executive chair of our board of directors;
- an additional annual cash retainer of $7,500, $5,000 and $4,000 for services as a non-chair member of the audit committee, compensation committee and the nominating and corporate governance committee, respectively;
- an additional annual cash retainer of $15,000, $10,000 and $8,000 for service as chair of the audit committee, compensation committee and the nominating and corporate governance committee, respectively;
- an initial option grant to purchase 25,000 shares of our common stock on the date of each such non-employee director's election or appointment to our board of directors; and
- an annual option grant to purchase 12,500 shares of our common stock on the date of each of our annual stockholder meetings.

Each of the option grants described above will be granted under our 2021 Plan, the terms of which are described in more detail below under the section titled "Executive Compensation—Employee Benefit Plans—2021 Equity Incentive Plan." The initial option grant described above will vest and become exercisable in equal monthly installments over a three-year period of continuous service following the date of grant. Each annual option grant will vest and become exercisable in full on the earlier of the first anniversary of the date of grant or the day immediately prior to the next annual stockholder meeting following the date of grant. All options granted to our non-employee directors will vest in full if we are subject to a change in control prior to termination of the non-employee director's continuous service. The term of each option will be ten years, subject to earlier termination as provided in the 2021 Plan and the applicable stock option agreement.

## EXECUTIVE COMPENSATION

Our named executive officers for the year ended December 31, 2020, consisting of our current and former principal executive officers and the next two most highly compensated executive officers who were serving in such capacity as of December 31, 2020, were:

- Gregory J. Flesher, our President and Chief Executive Officer;
- Niall O'Donnell, Ph.D., our former President and Chief Executive Officer;
- Alejandro Dorenbaum, M.D., our Chief Medical Officer; and
- Wendy Johnson, our Chief Development Officer.

### Summary Compensation Table

The following table presents all of the compensation awarded to or earned by or paid to our named executive officers during the fiscal year ended December 31, 2020.

| NAME AND PRINCIPAL POSITION | FISCAL YEAR | SALARY ($) | NON-EQUITY INCENTIVE PLAN COMPENSATION ($) (1) | ALL OTHER COMPENSATION ($) | TOTAL ($) |
|---|---|---|---|---|---|
| Gregory J. Flesher<br>*President and Chief Executive Officer (2)* | 2020 | 79,167 | 39,600 | 14,180 (3) | 132,947 |
| Niall O'Donnell, Ph.D.<br>*Former President and Chief Executive Officer (4)* | 2020 | — | — | — | — |
| Alejandro Dorenbaum, M.D.<br>*Chief Medical Officer* | 2020 | 353,750 | 123,900 | — | 477,650 |
| Wendy Johnson<br>*Chief Development Officer* | 2020 | 339,500 | 118,900 | — | 458,400 |

(1) The amounts disclosed represent performance bonuses earned in 2020 and paid in January 2021. Mr. Flesher's bonus was pro-rated to reflect his partial year of service.
(2) Mr. Flesher has served as our President and Chief Executive Officer since November 2020.
(3) Represents the cost of the apartment that Mr. Flesher maintains in San Diego, California ($9,612) plus a tax gross up on such benefits ($4,567).
(4) Dr. O'Donnell served as our President and Chief Executive Officer until November 2020.

### Annual Base Salary

The 2020 annual base salaries for our named executive officers (other than Dr. O'Donnell, who did not receive a base salary for 2020) are set forth in the table below.

| NAME | 2020 BASE SALARY |
|---|---|
| Gregory J. Flesher | $ 475,000 |
| Alejandro Dorenbaum, M.D. (1) | $ 425,000 |
| Wendy Johnson (2) | $ 339,500 |

(1) Dr. Dorenbaum's base salary increased from $339,500 to $425,000, effective November 1, 2020.
(2) Ms. Johnson's base salary increased from $339,500 to $365,000, effective January 1, 2021.

### Non-Equity Incentive Plan Compensation

We seek to motivate and reward our executives for achievements relative to our corporate goals as approved by our board of directors or the compensation committee thereof on an annual basis. Each of our named executive officers (other than Dr. O'Donnell) is eligible to receive an annual performance bonus based on the achievement of performance goals as determined by our board of directors or the compensation committee thereof. For 2020, these goals included financing, clinical, nonclinical, CMC and regulatory objectives. Each executive officer is assigned a

target bonus expressed as a percentage of his or her base salary. The target bonus amounts for Mr. Flesher, Dr. Dorenbaum and Ms. Johnson for 2020 were set at 50%, 35%, and 35%, respectively. In December 2020, our board of directors determined that the 2020 corporate goals were achieved at 100% and, as a result, approved annual performance bonuses for Mr. Flesher, Dr. Dorenbaum and Ms. Johnson in the amounts of $39,600 (determined based on his pro-rated base salary for 2020), $123,900, and $118,900, respectively, as reflected in the "Non-Equity Incentive Plan Compensation" column of the Summary Compensation Table above.

### Equity-Based Incentive Awards

We have granted stock options to each of our named executive officers prior to this offering pursuant to our 2014 Plan, the terms of which are described below under "—Employee Benefit and Stock Plans—2014 Equity Incentive Plan." We did not grant any stock options or other equity awards to our named executive officers during 2020.

In January 2021, we granted stock options to each of Mr. Flesher, Dr. Dorenbaum and Ms. Johnson to purchase 1,052,647, 100,563 and 75,981 shares of our common stock, respectively, each at an exercise price equal to $4.88 per share. The stock options granted to Mr. Flesher and Dr. Dorenbaum vest over a four year period (measured from November 2, 2020 in the case of Mr. Flesher and December 9, 2020 in the case of Dr. Dorenbaum) and the stock option granted to Ms. Johnson vests over a two year period (measured from December 9, 2020), each subject to the executive's continued service with us. Each of the option grants includes an early exercise feature.

Following the closing of this offering, we may grant additional equity awards to our executive officers pursuant to our 2021 Plan, the terms of which are described below under "—Employee Benefit and Stock Plans—2021 Equity Incentive Plan."

### Outstanding Equity Awards as of December 31, 2020

The following table presents the outstanding equity incentive plan awards held by each named executive officer as of December 31, 2020.

| | | OPTION AWARDS (1) | | | |
|---|---|---|---|---|---|
| NAME | GRANT DATE | NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) EXERCISABLE | NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) UNEXERCISABLE | OPTION EXERCISE PRICE PER SHARE ($) (2) | OPTION EXPIRATION DATE |
| Gregory J. Flesher | — | — | — | — | — |
| Niall O'Donnell, Ph.D.(3) | 04/05/2018 | 84,568 | — | $ 1.97 | 04/04/2028 |
| | 06/26/2019 (4) | 32,403 | — | $ 3.76 | 06/25/2029 |
| Alejandro Dorenbaum, M.D. | 04/05/2018 (5) | 90,590 | — | $ 1.97 | 04/04/2028 |
| | 06/26/2019 (6) | 41,119 | — | $ 3.76 | 06/25/2029 |
| Wendy Johnson | 04/05/2018 | 111,736 | — | $ 1.97 | 04/04/2028 |
| | 06/26/2019 (6) | 69,723 | — | $ 3.76 | 06/25/2029 |

(1) All of the option awards were granted under the 2014 Plan, the terms of which plan is described below under "—Employee Benefit and Stock Plans—2014 Equity Incentive Plan."

(2) All of the option awards were granted with a per share exercise price equal to the fair market value of one share of our common stock on the date of grant, as determined in good faith by our board of directors.

(3) Dr. O'Donnell ceased serving as our President and Chief Executive Officer and as an employee of our company in November 2020 but continues to serve as a non-employee director on our board of directors.

(4) One-fourth of the shares subject to the option award vested on May 1, 2020, and thereafter one-forty-eighth of the shares subject to the option award vested on each monthly anniversary until November 2020. In November 2020, the option was accelerated in full in connection with Mr. Flesher replacing Dr. O'Donnell as our President and Chief Executive Officer.

(5) One-fourth of the shares subject to the option award vested on January 1, 2019, and thereafter one-forty-eighth of the shares subject to the option award vest on each monthly anniversary, subject to continuous service with us. The option includes an early exercise feature.

(6) One-fourth of the shares subject to the option award vested on May 1, 2020, and thereafter one-forty-eighth of the shares subject to the option award vest on each monthly anniversary, subject to continuous service with us. The option includes an early exercise feature.

Options held by certain of our named executive officers are eligible for accelerated vesting under specified circumstances as further described under the section titled "—Potential Payments Upon Termination or Change of Control" below.

## Employment, Letter, Severance and Change in Control Agreements

### *Employment and Letter Agreements*

Below are descriptions of our employment and letter agreements with our named executive officers. For a discussion of the severance pay and other benefits to be provided in connection with a termination of employment and/or a change in control under the arrangements with our named executive officers, please see "—Potential Payments Upon Termination or Change of Control" below. Each of our named executive officers is employed "at will."

*Mr. Flesher*. We entered into an employment agreement with Mr. Flesher in November 2020, which governs the current terms of Mr. Flesher's employment with us. Pursuant to the employment agreement, Mr. Flesher is entitled to an initial annual base salary of $475,000, is eligible to receive an annual performance bonus with a target achievement of 50% of his base salary, as determined by our board of directors or the compensation committee, and an initial stock option, which was granted in January 2021 covering 1,052,647 shares and is described above under "—Equity-Based Incentive Awards". Mr. Flesher is also entitled to receive a special performance bonus in the amount of $7.5 million, payable at our discretion in cash, common stock or a combination of cash and common stock, in the event that during Mr. Flesher's continued service to us (i) our market value exceeds $750 million utilizing the volume-weighted average of the closing sale price of our 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 our stockholders in connection with a change in control (as defined in our severance benefit plan described below under "—Potential Payments Upon Termination or Change of Control"), as determined in good faith by our board of directors, exceeds $750 million. Mr. Flesher is also entitled to certain severance benefits, the terms of which are described below under "—Potential Payments Upon Termination or Change of Control." Mr. Flesher is also eligible for standard company benefits, for reimbursement of business expenses, and to participate in employee benefit plans and programs.

*Dr. O'Donnell*. We entered into a letter agreement with Dr. O'Donnell in February 2018, which governed the terms of Dr. O'Donnell's employment with us. Pursuant to the agreement, Dr. O'Donnell was granted an option to purchase 84,568 shares of our common stock, which was granted in April 2018. Dr. O'Donnell was not entitled to any base salary, annual performance bonus or other compensation or benefits under the agreement. Dr. O'Donnell ceased to serve as our President and Chief Executive Officer and as an employee of our company in November 2020, but continues to serve as a non-employee director on our board of directors.

*Dr. Dorenbaum*. We entered into an employment agreement with Dr. Dorenbaum, effective January 2018, which governs the current terms of Dr. Dorenbaum's employment with us. Pursuant to the employment agreement, Dr. Dorenbaum is entitled to an initial annual base salary of $320,000 (most recently increased to $425,000), is eligible to receive an annual performance bonus with a target achievement of 35% of his base salary, as determined by our board of directors or the compensation committee, and a stock option to purchase an aggregate of 117,406 shares of our common stock, which was granted in April 2018. Dr. Dorenbaum exercised 13,408 shares of his initial option grant in February 2019, an additional 13,408 shares in September 2020 and an additional 75,556 shares in March 2021. Dr. Dorenbaum is also entitled to certain severance benefits, the terms of which are described below under "—Potential Payments Upon Termination or Change of Control." Dr. Dorenbaum is also eligible for standard company benefits, for reimbursement of business expenses, and to participate in employee benefit plans and programs.

*Ms. Johnson*. We entered into an employment agreement with Ms. Johnson in February 2018, which governs the current terms of Ms. Johnson's employment with us. Pursuant to the employment agreement, Ms. Johnson is entitled to an initial annual base salary of $320,000 (most recently increased to $365,000), is eligible to receive an annual performance bonus with a target achievement of 35% of her base salary, as determined by our board of directors or the compensation committee, and a stock option to purchase an aggregate of 111,736 shares of our common stock, which was granted in April 2018. Ms. Johnson is also entitled to certain severance benefits, the terms of which are described below under "—Potential Payments Upon Termination or Change of Control." Ms. Johnson is also eligible

for standard company benefits, for reimbursement of business expenses, and to participate in employee benefit plans and programs.

***Potential Payments Upon Termination or Change of Control***

Regardless of the manner in which a named executive officer's service terminates, the named executive officer (other than Dr. O'Donnell) is entitled to receive amounts earned during his or her term of service, including salary and unused vacation pay.

We maintain a severance benefit plan and have entered into a severance benefit plan participation agreement, as amended from time to time, with each of our named executive officers (other than Dr. O'Donnell). Upon a termination without "cause" or resignation for "good reason" (each as defined below), each of our named executive officers (other than Dr. O'Donnell) will be entitled to continued payment of base salary and premiums under COBRA, to the extent so elected (12 months for Mr. Flesher and nine months for Dr. Dorenbaum and Ms. Johnson), and accelerated vesting of outstanding equity awards (full acceleration of equity awards for Dr. Dorenbaum and Ms. Johnson and 12 months' acceleration of equity awards that are subject to time-based vesting for Mr. Flesher measured from the date of termination. In addition, upon a termination without cause or resignation for good reason during the period commencing three months prior to, and ending 12 months following, a "change in control" (as defined below), each of our named executive officers (other than Dr. O'Donnell) will be entitled to continued payment of base salary, payment of premiums under COBRA, to the extent so elected (18 months for Mr. Flesher and 12 months for Dr. Dorenbaum and Ms. Johnson), and payment of a prorated incentive bonus (assuming achievement at 100% of target) reflecting the length of the severance period. Additionally, each of our named executive officers (other than Dr. O'Donnell) will be entitled to accelerated vesting in full of all outstanding equity awards.

All such benefits are subject to execution of an effective release of claims against us and certain related parties.

For purposes of the severance benefit plan, the following definitions apply:

- "cause" generally means the occurrence of any of the following events, conditions or actions with respect to the executive: (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) attempted commission of, or participation in, a fraud or act of dishonesty against us; (iii) intentional, material violation of any contract or agreement between the executive and us or of any statutory duty owed to us; (iv) unauthorized use or disclosure of our confidential information or trade secrets; or (v) gross misconduct
- "good reason" generally means the following events, conditions or actions taken by us with respect to the executive without cause and without the executive's consent: (i) a material reduction of the executive's annual base salary, which is a reduction of at least 10% of such executive's base salary (unless pursuant to a salary reduction program applicable generally to our similarly situated employees); (ii) a material reduction in the executive's authority, duties or responsibilities; (iii) a material reduction in the authority, duties, or responsibilities of the supervisor to whom the executive is required to report; (iv) a relocation of the executive's principal place of employment to a place that increases such executive's one-way commute by more than 50 miles as compared to such executive's then-current principal place of employment immediately prior to such relocation
- "change in control" generally means the following events: (i) a change in ownership of representing more than 50% of the combined voting power of our outstanding securities, other than by virtue of a merger, consolidation or similar transaction; (ii) a merger, consolidation or similar transaction in which our stockholders do not own more than 50% of the combined voting power of the surviving entity or its parent; (iii) a dissolution or liquidation, except for a liquidation into a parent corporation; and (iv) a sale, lease, exclusive license or other disposition of all or substantially all of our assets

Dr. O'Donnell's stock option granted in June 2019 accelerated vesting in full as a result of his cessation of employment with us in November 2020. Dr. O'Donnell did not receive any other severance benefits in connection with his separation.

### Other Compensation and Benefits

All of our current named executive officers (except for Dr. O'Donnell) are eligible to participate in our employee benefit plans, including our medical, dental, vision, and life plans, in each case on the same basis as all of our other employees. We pay the premiums for the life, disability, accidental death, and dismemberment insurance for all of our employees, including our named executive officers. We generally do not provide perquisites or personal benefits to our named executive officers, except in limited circumstances. During 2020, we paid rental expenses for Mr. Flesher to maintain an apartment in San Diego and related tax gross-up.

### Employee Benefit Plans

We believe that our ability to grant equity-based awards is a valuable and necessary compensation tool that aligns the long-term financial interests of our employees, consultants and directors with the financial interests of our stockholders. In addition, we believe that our ability to grant options and other equity-based awards helps us to attract, retain and motivate employees, consultants, and directors, and encourages them to devote their best efforts to our business and financial success. The principal features of our equity incentive plans and our 401(k) plan are summarized below. These summaries are qualified in their entirety by reference to the actual text of the plans, which, other than the 401(k) plan, are filed as exhibits to the registration statement of which this prospectus is a part.

#### *2021 Equity Incentive Plan*

Our board of directors adopted our 2021 Plan in March 2021 and our stockholders approved our 2021 Plan in April 2021. Our 2021 Plan provides for the grant of incentive stock options (ISOs) to employees, including employees of any parent or subsidiary, and for the grant of nonstatutory stock options (NSOs) stock appreciation rights, restricted stock awards, restricted stock unit awards, performance awards and other forms of stock awards to employees, directors, and consultants, including employees and consultants of our affiliates. Our 2021 Plan is a successor to and continuation of our 2014 Plan, which is described below. The 2021 Plan became effective immediately prior to the execution of the underwriting agreement related to this offering.

*Authorized Shares*. Initially, the maximum number of shares of our common stock that may be issued under our 2021 Plan after it becomes effective will not exceed 5,418,766 shares, which is the sum of (1) 2,187,524 new shares, plus (2) the number of shares that remained available for issuance under our 2014 Plan at the time our 2021 Plan became effective, plus (3) any shares subject to outstanding stock options or other stock awards that were granted under our 2014 Plan that, on or after the date the 2021 Plan became effective, terminate or expire prior to exercise or settlement; are settled in cash; are forfeited or repurchased because of the failure to vest; or are reacquired or withheld to satisfy a tax withholding obligation or the purchase or exercise price in accordance with the terms of the 2014 Plan. In addition, the number of shares of our common stock reserved for issuance under our 2021 Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2022 through January 1, 2031, in an amount equal to 5% of the total number of shares of our common stock outstanding on December 31 of the fiscal year before the date of each automatic increase, or a lesser number of shares determined by our board of directors prior to the applicable January 1. The maximum number of shares of our common stock that may be issued upon the exercise of incentive stock options under our 2021 Plan is 16,250,000.

Shares subject to stock awards granted under our 2021 Plan that expire or terminate without being exercised in full, or that are paid out in cash rather than in shares, do not reduce the number of shares available for issuance under our 2021 Plan. Additionally, shares become available for future grant under our 2021 Plan if they were issued under stock awards under our 2021 Plan if we repurchase them or they are forfeited. This includes shares used to pay the exercise price of a stock award or to satisfy the tax withholding obligations related to a stock award.

*Plan Administration*. Our board of directors, or a duly authorized committee of our board of directors, will administer our 2021 Plan. Our board of directors has delegated concurrent authority to administer our 2021 Plan to the compensation committee. We refer to the board of directors, or the applicable committee with the power to administer our 2021 Plan, as the plan administrator. Our plan administrator may also delegate to one or more of our officers the authority to (1) designate employees (other than officers) to receive specified stock awards and (2) determine the number of shares subject to such stock awards. Under our 2021 Plan, our board of directors has

the authority to determine award recipients, grant dates, the numbers and types of stock awards to be granted, the applicable fair market value, and the provisions of each stock award, including the period of exercisability and the vesting schedule applicable to a stock award. The plan administrator has the power to modify outstanding awards under our 2021 Plan. Subject to the terms of our 2021 Plan, the plan administrator has the authority to reprice any outstanding stock award, cancel and re-grant any outstanding stock award in exchange for new stock awards, cash or other consideration, or take any other action that is treated as a repricing under generally accepted accounting principles, with the consent of any adversely affected participant.

*Stock Options.* ISOs and NSOs are granted under stock option agreements adopted by the plan administrator. The plan administrator determines the exercise price for stock options, within the terms and conditions of the 2021 Plan, provided that the exercise price of a stock option generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Options granted under the 2021 Plan vest at the rate specified in the stock option agreement as determined by the plan administrator.

*Tax Limitations on ISOs*. The aggregate fair market value, determined at the time of grant, of our common stock with respect to ISOs that are exercisable for the first time by an optionholder during any calendar year under all of our stock plans may not exceed $100,000. Options or portions thereof that exceed such limit will generally be treated as NSOs. No ISO may be granted to any person who, at the time of the grant, owns or is deemed to own stock possessing more than 10% of our total combined voting power or that of any of our affiliates unless (1) the option exercise price is at least 110% of the fair market value of the stock subject to the option on the date of grant, and (2) the term of the ISO does not exceed five years from the date of grant.

*Restricted Stock Unit Awards.* Restricted stock units are granted under restricted stock unit award agreements adopted by the plan administrator. Restricted stock units may be granted in consideration for any form of legal consideration that may be acceptable to our board of directors and permissible under applicable law. A restricted stock unit may be settled by cash, delivery of stock, a combination of cash and stock as deemed appropriate by the plan administrator, or in any other form of consideration set forth in the restricted stock unit agreement. Additionally, dividend equivalents may be credited in respect of shares covered by a restricted stock unit. Except as otherwise provided in the applicable award agreement or other written agreement between us and the participant, restricted stock units that have not vested will be forfeited once the participant's continuous service ends for any reason.

*Restricted Stock Awards.* Restricted stock awards are granted under restricted stock award agreements adopted by the plan administrator. A restricted stock award may be awarded in consideration for cash, check, bank draft or money order, services to us, or any other form of legal consideration that may be acceptable to our board of directors and permissible under applicable law. The plan administrator determines the terms and conditions of restricted stock awards, including vesting and forfeiture terms. If a participant's service relationship with us ends for any reason, we may receive any or all of the shares of common stock held by the participant that have not vested as of the date the participant terminates service with us through a forfeiture condition or a repurchase right.

*Stock Appreciation Rights.* Stock appreciation rights are granted under stock appreciation grant agreements adopted by the plan administrator. The plan administrator determines the purchase price or strike price for a stock appreciation right, which generally cannot be less than 100% of the fair market value of our common stock on the date of grant. A stock appreciation right granted under the 2021 Plan vests at the rate specified in the stock appreciation right agreement as determined by the plan administrator.

*Performance Awards*. The 2021 Plan permits the grant of performance-based stock and cash awards. The plan administrator may structure awards so that the shares of our stock, cash, or other property will be issued or paid only following the achievement of certain pre-established performance goals during a designated performance period. The performance criteria that will be used to establish such performance goals may be based on any measure of performance selected by the plan administrator.

The performance goals may be based on a company-wide basis, with respect to one or more business units, divisions, affiliates, or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Unless specified otherwise (i) in the award agreement at the time the award is granted or (ii) in such other document setting forth the performance goals at the time the goals are established, we will appropriately make adjustments in the method of calculating the

attainment of performance goals as follows: (1) to exclude restructuring and/or other nonrecurring charges; (2) to exclude exchange rate effects; (3) to exclude the effects of changes to generally accepted accounting principles; (4) to exclude the effects of any statutory adjustments to corporate tax rates; (5) to exclude the effects of items that are "unusual" in nature or occur "infrequently" as determined under generally accepted accounting principles; (6) to exclude the dilutive effects of acquisitions or joint ventures; (7) to assume that any portion of our business which is divested achieved performance objectives at targeted levels during the balance of a performance period following such divestiture; (8) to exclude the effect of any change in the outstanding shares of our common stock by reason of any stock dividend or split, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common stockholders other than regular cash dividends; (9) to exclude the effects of stock based compensation and the award of bonuses under our bonus plans; (10) to exclude costs incurred in connection with potential acquisitions or divestitures that are required to be expensed under generally accepted accounting principles; and (11) to exclude the goodwill and intangible asset impairment charges that are required to be recorded under generally accepted accounting principles. In addition, we retain the discretion to reduce or eliminate the compensation or economic benefit due upon attainment of the goals. The performance goals may differ from participant to participant and from award to award.

*Other Stock Awards.* The plan administrator may grant other awards based in whole or in part by reference to our common stock. The plan administrator will set the number of shares under the stock award (or cash equivalent) and all other terms and conditions of such awards.

*Non-Employee Director Compensation Limit*. The aggregate value of all compensation granted or paid to any non-employee director with respect to any calendar year, including stock awards granted and cash fees paid by us to such non-employee director, will not exceed $750,000 in total value, or in the event such non-employee director is first appointed or elected to the board during such annual period, $1,000,000 in total value (in each case, calculating the value of any such stock awards based on the grant date fair value of such stock awards for financial reporting purposes).

*Changes to Capital Structure.* In the event there is a specified type of change in our capital structure, such as a stock split, reverse stock split, or recapitalization, appropriate adjustments will be made to (1) the class and maximum number of shares reserved for issuance under the 2021 Plan, (2) the class and maximum number of shares by which the share reserve may increase automatically each year, (3) the class and maximum number of shares that may be issued upon the exercise of incentive stock options, and (4) the class and number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding stock awards.

*Corporate Transactions.* The following applies to stock awards under the 2021 Plan in the event of a corporate transaction, unless otherwise provided in a participant's stock award agreement or other written agreement with us or one of our affiliates or unless otherwise expressly provided by the plan administrator at the time of grant.

In the event of a corporate transaction, any stock awards outstanding under the 2021 Plan may be assumed, continued or substituted for by any surviving or acquiring corporation (or its parent company), and any reacquisition or repurchase rights held by us with respect to the stock award may be assigned to the successor (or its parent company). If the surviving or acquiring corporation (or its parent company) does not assume, continue or substitute for such stock awards, then with respect to any such stock awards that are held by participants whose continuous service has not terminated prior to the effective time of the transaction, or current participants, the vesting (and exercisability, if applicable) of such stock awards will be accelerated in full to a date prior to the effective time of the transaction (contingent upon the effectiveness of the transaction), and such stock awards will terminate if not exercised (if applicable) at or prior to the effective time of the transaction, and any reacquisition or repurchase rights held by us with respect to such stock awards will lapse (contingent upon the effectiveness of the transaction). With respect to performance awards with multiple vesting levels depending on performance level, unless otherwise provided by an award agreement or by the administrator, the award will accelerate at 100% of target. If the surviving or acquiring corporation (or its parent company) does not assume, continue or substitute for such stock awards, then with respect to any such stock awards that are held by persons other than current participants, such awards will terminate if not exercised (if applicable) prior to the effective time of the transaction, except that any reacquisition or repurchase rights held by us with respect to such stock awards will not terminate and may continue to be exercised

notwithstanding the transaction. The plan administrator is not obligated to treat all stock awards or portions of stock awards in the same manner and is not obligated to take the same actions with respect to all participants.

In the event a stock award will terminate if not exercised prior to the effective time of a corporate transaction, the plan administrator may provide, in its sole discretion, that the holder of such stock award may not exercise such stock award but instead will receive a payment equal in value to the excess (if any) of (1) the value of the property the participant would have received upon the exercise of the stock award over (2) any exercise price payable by such holder in connection with such exercise.

Under our 2021 Plan, a corporate transaction is defined to include the consummation of: (1) a sale of all or substantially all of our assets, (2) the sale or disposition of at least 50% of our outstanding securities, (3) a merger or consolidation where we do not survive the transaction, and (4) a merger or consolidation where we do survive the transaction but the shares of our common stock outstanding before such transaction are converted or exchanged into other property by virtue of the transaction, unless otherwise provided in an award agreement or other written agreement between us and the award holder.

*Change in Control*. Awards granted under the 2021 Plan may be subject to acceleration of vesting and exercisability upon or after a change in control (as defined in the 2021 Plan) as may be provided in the applicable stock award agreement or in any other written agreement between us or any affiliate and the participant, but in the absence of such provision, no such acceleration will automatically occur.

Under the 2021 Plan, a change in control is defined to include (1) the acquisition by any person or company of more than 50% of the combined voting power of our then outstanding stock; (2) a consummated merger, consolidation or similar transaction in which our stockholders immediately before the transaction do not own, directly or indirectly, more than 50% of the combined voting power of the surviving entity (or the parent of the surviving entity); (3) the approval by the stockholders or the board of directors of a plan of complete dissolution or liquidation of the company, or the occurrence of a complete dissolution or liquidation of the company, except for a liquidation into a parent corporation; (4) a consummated sale, lease, exclusive license or other disposition of all or substantially all of our assets other than to an entity more than 50% of the combined voting power of which is owned by our stockholders; and (5) an unapproved change in the majority of the board of directors.

*Transferability.* A participant may not transfer stock awards under our 2021 Plan other than by will, the laws of descent and distribution, or as otherwise provided under our 2021 Plan.

*Plan Amendment or Termination.* Our board of directors has the authority to amend, suspend, or terminate our 2021 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our stockholders. No incentive stock options may be granted after the tenth anniversary of the date our board of directors adopted our 2021 Plan. No stock awards may be granted under our 2021 Plan while it is suspended or after it is terminated.

***2014 Equity Incentive Plan***

The 2014 Plan was first adopted in 2014 and subsequently amended by our board of directors and stockholders, most recently in March 2021, respectively. All references in this prospectus to the 2014 Plan shall be deemed to refer to our 2014 Equity Incentive Plan, as amended, unless the context otherwise requires. As of December 31, 2020, there were 2,156,744 shares remaining available for the future grant of stock awards under our 2014 Plan. As of December 31, 2020, there were outstanding stock options covering a total of 935,478 shares of our common stock that were granted under our 2014 Plan.

*Stock Awards.* Our 2014 Plan provides for the grant of ISOs within the meaning of Section 422 of the Code to employees, including employees of any parent or subsidiary, and for the grant of NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards and other stock awards to employees, directors and consultants, including employees and consultants of our affiliates. We have granted stock options under the 2014 Plan.

*Authorized Shares.* Subject to certain capitalization adjustments, the aggregate number of shares of common stock that may be issued pursuant to stock awards under the 2014 Plan will not exceed 3,383,974 shares. The maximum number of shares of our common stock that may be issued pursuant to the exercise of ISOs under our 2014 Plan is 6,767,498 shares.

Shares subject to stock awards granted under our 2014 Plan that expire or terminate without being exercised in full or that are settled in cash rather than in shares do not reduce the number of shares available for issuance under our 2014 Plan. Additionally, if any shares issued pursuant to a stock award are forfeited back to or repurchased because of the failure to meet a contingency or condition required to vest, then the shares that are forfeited or repurchased will revert to and again become available for issuance under the 2014 Plan. This includes shares used to pay the exercise price of a stock award or to satisfy the tax withholding obligations related to a stock award.

*Plan Administration.* Our board of directors, or a duly authorized committee of our board of directors, will administer our 2014 Plan and is referred to as the "plan administrator" herein. The plan administrator may also delegate to one or more of our officers the authority to (1) designate employees (other than officers) to receive specified stock awards and (2) determine the number of shares subject to such stock awards. Under our 2014 Plan, the plan administrator has the authority to determine award recipients, dates of grant, the numbers and types of stock awards to be granted, the applicable fair market value and the provisions of each stock award, including the period of their exercisability and the vesting schedule applicable to a stock award.

Under the 2014 Plan, the plan administrator also generally has the authority to effect, with the consent of any adversely affected participant, (A) the reduction of the exercise, purchase, or strike price of any outstanding award; (B) the cancellation of any outstanding award and the grant in substitution therefore of other awards, cash, or other consideration; or (C) any other action that is treated as a repricing under generally accepted accounting principles.

*Stock Options.* ISOs and NSOs are granted under stock option agreements adopted by the plan administrator. The plan administrator determines the exercise price for stock options, within the terms and conditions of the 2014 Plan, provided that the exercise price of a stock option generally cannot be less than 100% of the fair market value of our common stock on the date of grant (or 110% of the fair market value for ISOs granted to 10% stockholders as required by the Code). Options granted under the 2014 Plan vest at the rate specified in the stock option agreement as determined by the plan administrator.

The plan administrator determines the term of stock options granted under the 2014 Plan, up to a maximum of 10 years. If an optionholder's service relationship with us or any of our affiliates ceases for any reason other than disability, death or cause, the optionholder may generally exercise any vested options for a period of three months following the cessation of service. This period may be extended in the event that exercise of the option is prohibited by applicable securities laws or our insider trading policy. If an optionholder's service relationship with us or any of our affiliates ceases due to death, or an optionholder dies within a certain period following cessation of service, the optionholder or a beneficiary may generally exercise any vested options for a period of 18 months following the date of death. If an optionholder's service relationship with us or any of our affiliates ceases due to disability, the optionholder may generally exercise any vested options for a period of 12 months following the cessation of service.

In the event of a termination for cause, options generally terminate upon the termination date. In no event may an option be exercised beyond the expiration of its term.

*Changes to Capital Structure*. In the event there is a specified type of change in our capital structure, such as a stock split, reverse stock split, or recapitalization, appropriate adjustments will be made to (1) the class and maximum number of shares reserved for issuance under the 2014 Plan, (2) the class and maximum number of shares that may be issued upon the exercise of ISOs and (3) the class and number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding stock awards.

*Corporate Transactions*. Our 2014 Plan provides that in the event of certain specified significant corporate transactions, unless otherwise provided in an award agreement or other written agreement between us and the award holder, the plan administrator may take one or more of the following actions with respect to such stock awards:

- arrange for the assumption, continuation, or substitution of a stock award by a surviving or acquiring corporation;
- arrange for the assignment of any reacquisition or repurchase rights held by us to the surviving or acquiring corporation;
- accelerate the vesting, in whole or in part, of the stock award and provide for its termination if not exercised (if applicable) at or before the effective time of the transaction;

- arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us;
- cancel or arrange for the cancellation of the stock award, to the extent not vested or not exercised before the effective time of the transaction, in exchange for such cash payment, if any as the plan administrator deems appropriate; and
- make a payment equal to the excess, if any, of (A) the value of the property the participant would have received on exercise of the award immediately before the effective time of the transaction, over (B) any exercise price payable by the participant in connection with the exercise.

The plan administrator is not obligated to treat all stock awards or portions of stock awards in the same manner and is not obligated to treat all participants in the same manner.

Under the 2014 Plan, a corporate transaction is generally the consummation of: (1) a sale of all or substantially all of our assets, (2) the sale or disposition of at least 90% of our outstanding securities, (3) a merger or consolidation where we do not survive the transaction, or (4) a merger or consolidation where we do survive the transaction but the shares of our common stock outstanding immediately before such transaction are converted or exchanged into other property by virtue of the transaction.

*Change in Control.* A stock award under the 2014 Plan may be subject to additional acceleration of vesting and exercisability upon or after a change in control as may be provided in the award agreement or other written agreement between us and the participant, but in the absence of such provision, no such acceleration will occur, except as described above. Under the 2014 Plan, a change in control is generally (1) the acquisition by any person or company of more than 50% of the combined voting power of our then outstanding stock, (2) a merger, consolidation or similar transaction in which our stockholders immediately before the transaction do not own, directly or indirectly, more than 50% of the combined voting power of the surviving entity (or the parent of the surviving entity) in substantially the same proportions as their ownership immediately prior to such transaction, or (3) a sale, lease, exclusive license or other disposition of all or substantially all of our assets other than to an entity more than 50% of the combined voting power of which is owned by our stockholders in substantially the same proportions as their ownership of our outstanding voting securities immediately prior to such transaction.

*Plan Amendment or Termination*. Our board of directors has the authority to amend, suspend, or terminate our 2014 Plan, provided that such action does not impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our stockholders. Unless terminated sooner, the 2014 Plan will automatically terminate on November 18, 2024. No stock awards may be granted under our 2014 Plan while it is suspended or after it is terminated.

*UK Sub-Plan*. Our board of directors has also adopted the UK Sub-Plan to the 2014 Plan (2014 UK Sub-Plan) to apply to grants made to our UK Service Providers. The 2014 UK Sub-Plan allows us to grant options to the UK Service Providers under the 2014 Plan under similar terms to those in the 2014 Plan, however, the 2014 UK Sub-Plan provides for the grant of EMI options compliant with the requirements of the EMI code set out in the ITEPA.

***2021 Employee Stock Purchase Plan***

Our board of directors adopted our 2021 Employee Stock Purchase Plan (ESPP) in March 2021 and our stockholders approved our ESPP in April 2021. The ESPP became effective immediately prior to the execution of the underwriting agreement related to this offering. The purpose of the ESPP is to secure the services of new employees, to retain the services of existing employees, and to provide incentives for such individuals to exert maximum efforts toward our success and that of our affiliates. The ESPP includes two components. One component is designed to allow eligible U.S. employees to purchase our common stock in a manner that may qualify for favorable tax treatment under Section 423 of the Code. In addition, purchase rights may be granted under a component that does not qualify for such favorable tax treatment because of deviations necessary to permit participation by eligible employees who are foreign nationals or employed outside of the U.S. while complying with applicable foreign laws.

*Share Reserve.* Following this offering, the ESPP authorizes the issuance of 243,058 shares of our common stock under purchase rights granted to our employees or to employees of any of our designated affiliates. The number of

shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year, beginning on January 1, 2022 through January 1, 2031, by the lesser of (1) 1% of the total number of shares of our common stock outstanding on the last day of the fiscal year before the date of the automatic increase, and (2) 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 (1) and (2). As of the date hereof, no shares of our common stock have been purchased under the ESPP.

*Administration.* Our board of directors administers the ESPP and may delegate its authority to administer the ESPP to our compensation committee. The ESPP is implemented through a series of offerings under which eligible employees are granted purchase rights to purchase shares of our common stock on specified dates during such offerings. Under the ESPP, we may specify offerings with durations of not more than 27 months, and may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which shares of our common stock will be purchased for employees participating in the offering. An offering under the ESPP may be terminated under certain circumstances.

*Payroll Deductions.* Generally, all regular employees, including executive officers, employed by us or by any of our designated affiliates, may participate in the ESPP and may contribute, normally through payroll deductions, up to 20% of their earnings (as defined in the ESPP) for the purchase of our common stock under the ESPP. Unless otherwise determined by our board of directors, common stock will be purchased for the accounts of employees participating in the ESPP at a price per share that is at least the lesser of (1) 85% of the fair market value of a share of our common stock on the first date of an offering, or (2) 85% of the fair market value of a share of our common stock on the date of purchase.

*Limitations*. Employees may have to satisfy one or more of the following service requirements before participating in the ESPP, as determined by our board of directors, including: (1) being customarily employed for more than 20 hours per week, (2) being customarily employed for more than five months per calendar year, or (3) continuous employment with us or one of our affiliates for a period of time (not to exceed two years). No employee may purchase shares under the ESPP at a rate in excess of $25,000 worth of our common stock based on the fair market value per share of our common stock at the beginning of an offering for each calendar year such a purchase right is outstanding. Finally, no employee will be eligible for the grant of any purchase rights under the ESPP if immediately after such rights are granted, such employee has voting power over 5% or more of our outstanding capital stock measured by vote or value under Section 424(d) of the Code.

*Changes to Capital Structure.* In the event that there occurs a change in our capital structure through such actions as a stock split, merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, large nonrecurring cash dividend, liquidating dividend, combination of shares, exchange of shares, change in corporate structure, or similar transaction, the board of directors will make appropriate adjustments to: (1) the class(es) and maximum number of shares reserved under the ESPP, (2) the class(es) and maximum number of shares by which the share reserve may increase automatically each year, (3) the class(es) and number of shares subject to and purchase price applicable to outstanding offerings and purchase rights, and (4) the number of shares that are subject to purchase limits under ongoing offerings.

*Corporate Transactions.* In the event of certain significant corporate transactions, including the consummation of (1) a sale of all or substantially all of our assets, (2) the sale or disposition of more than 50% of our outstanding securities, (3) a merger or consolidation where we do not survive the transaction, or (4) a merger or consolidation where we do survive the transaction but the shares of our common stock outstanding immediately before such transaction are converted or exchanged into other property by virtue of the transaction, any then-outstanding rights to purchase our stock under the ESPP may be assumed, continued or substituted for by any surviving or acquiring entity (or its parent company). If the surviving or acquiring entity (or its parent company) elects not to assume, continue, or substitute for such purchase rights, then the participants' accumulated payroll contributions will be used to purchase shares of our common stock within ten business days before such corporate transaction, and such purchase rights will terminate immediately.

*ESPP Amendment or Termination*. Our board of directors has the authority to amend or terminate our ESPP, provided that except in certain circumstances such amendment or termination may not materially impair any outstanding purchase rights without the holder's consent. We will obtain stockholder approval of any amendment to our ESPP as required by applicable law or listing requirements.

***401(k) Plan***

We maintain a 401(k) plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees are able to defer eligible compensation up to certain Code limits, which are updated annually. The 401(k) plan provides for automatic enrollment for eligible employees who do not make a deferral election. As the 401(k) plan is a safe harbor 401(k) plan, we are required to make a certain level of matching contributions. We may make discretionary contributions to the 401(k) plan but currently, do not. The 401(k) plan is intended to be qualified under Section 401(a) of the Code, with the related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan are deductible by us when made, and contributions and earnings on those amounts are not generally taxable to the employees until withdrawn or distributed from the 401(k) plan.

## Limitations on Liability and Indemnification

Upon the closing of this offering, our amended and restated certificate of incorporation will contain provisions that limit the liability of our current and former directors for monetary damages to the fullest extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to the corporation or its stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions; or
- any transaction from which the director derived an improper personal benefit.

Such limitation of liability does not apply to liabilities arising under federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our amended and restated certificate of incorporation will authorize us to indemnify our directors, officers, employees and other agents to the fullest extent permitted by Delaware law. Our amended and restated bylaws will provide that we are required to indemnify our directors and officers to the fullest extent permitted by Delaware law and may indemnify our other employees and agents. Our amended and restated bylaws will also provide that, on satisfaction of certain conditions, we will advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee, or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under the provisions of Delaware law. We have entered and expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by the board of directors. With certain exceptions, these agreements provide for indemnification for related expenses including attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding.

We believe that these amended and restated certificate of incorporation and amended and restated bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain customary directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted for directors, executive officers, or persons controlling us, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

### Rule 10b5-1 Plans

Our directors and officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades under parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers may also buy or sell additional shares outside of a Rule 10b5-1 plan when they do not possess of material nonpublic information, subject to compliance with the terms of our insider trading policy. During the first 180 days from this offering, the sale of any shares under such plan would be subject to the lock-up agreement that the director or officer has entered into with the underwriters.

## CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

The following includes a summary of transactions since January 1, 2018 to which we have been a party in which the amount involved exceeded or will exceed the lesser of $120,000 or 1% of the average of our total assets as of December 31, 2019 and 2020, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under “Management—Director Compensation” and “Executive Compensation.” We also describe below certain other transactions with our directors, executive officers and stockholders.

### Series A Convertible Preferred Stock Financing

In December 2017, we completed the first initial closing of an aggregate of 3,006,175 shares of our Series A convertible preferred stock at a purchase price of $2.16 per share. In January 2018, we completed the second initial closing of an aggregate of an additional 9,722,222 shares of our Series A convertible preferred stock, at the same purchase price per share. In May 2019, we completed the milestone closing of an aggregate of an additional 11,574,075 shares of our Series A convertible preferred stock, at the same purchase price per share.

The following table summarizes purchases of shares of our Series A convertible preferred stock by holders of more than 5% of our capital stock (at the time of the applicable transaction) and entities affiliated with members of our board of directors.

| PARTICIPANTS (1) | SHARES OF SERIES A CONVERTIBLE PREFERRED STOCK PURCHASED AT FIRST INITIAL CLOSING | AGGREGATE PURCHASE PRICE AT FIRST INITIAL CLOSING | SHARES OF SERIES A CONVERTIBLE PREFERRED STOCK PURCHASED AT SECOND INITIAL CLOSING | AGGREGATE PURCHASE PRICE AT SECOND INITIAL CLOSING | SHARES OF SERIES A CONVERTIBLE PREFERRED STOCK PURCHASED AT MILESTONE CLOSING | AGGREGATE PURCHASE PRICE AT MILESTONE CLOSING |
|---|---|---|---|---|---|---|
| Entities affiliated with New Enterprise Associates (2) | 1,508,349 (3) | $3,137,761.97 (4) | 3,395,062 (5) | $7,333,333.92 | 4,629,630 (5) | $10,000,000.80 |
| The Grey Family Trust dated November 12, 1999 (6) | 90,222 | $ 155,904.11 (4) | — | — | — | — |
| Susan E. Dubé Trust, dated May 6, 2002 (7) | 18,044 | $ 31,180.82 (4) | — | — | — | — |
| Entities affiliated with Pappas Capital, LLC (8) | 403,979 (9) | $ 533,334.24 (4) | 679,012 (10) | $1,466,665.92 | 925,926 (11) | $ 2,000,000.16 |
| Entities affiliated with RiverVest Venture Fund III, L.P. (12) | 296,081 (13) | $ 511,630.14 (4) | 2,314,815 (14) | $5,000,000.40 | 2,314,815 (14) | $ 5,000,000.40 |
| Lundbeckfond Invest A/S (15) | — | — | 2,314,815 | $5,000,000.40 | 2,314,815 | $ 5,000,000.40 |

(1) Additional details regarding these stockholders and their equity holdings are included in this prospectus under the caption “Principal Stockholders.”
(2) Mr. Mathers, a member of our board of directors, is employed as a Partner at New Enterprise Associates, Inc., which is affiliated with New Enterprise Associates 15, L.P. (NEA 15) and NEA Ventures 2017, Limited Partnership (NEA Ventures).
(3) Consists of (i) 1,501,960 shares of Series A convertible preferred stock purchased by NEA 15 and (ii) 6,389 shares of Series A convertible preferred stock purchased by NEA Ventures.
(4) All or a portion of the consideration paid for such shares of Series A convertible preferred stock was funded through the conversion of the aggregate principal amount and accrued interest of a convertible promissory note.
(5) Consists of shares of Series A convertible preferred stock purchased by NEA 15.
(6) Mr. Grey, our Executive Chairman, is trustee of The Grey Family Trust dated November 12, 1999.
(7) Susan E. Dubé, a former member of our board of directors and our former Secretary, is the trustee of the Susan E. Dubé Trust, dated May 6, 2002.
(8) Mr. Grey, our Executive Chairman, is a venture partner at Pappas Capital, LLC. Arthur Pappas and Scott Weiner, each a former member of our board of directors, is or was affiliated with Pappas Capital, LLC.

(9) Consists of (i) 157,065 shares of Series A convertible preferred stock purchased by Pappas Capital, LLC, (ii) 228,173 shares of Series A convertible preferred stock purchased by A. M. Pappas Life Science Ventures V, LP and (iii) 18,741 shares of Series A convertible preferred stock purchased by PV V CEO Fund, LP.
(10) Consists of (i) 627,475 shares of Series A convertible preferred stock purchased by A. M. Pappas Life Science Ventures V, LP and (ii) 51,537 shares of Series A convertible preferred stock purchased by PV V CEO Fund, LP.
(11) Consists of (i) 855,648 shares of Series A convertible preferred stock purchased by A. M. Pappas Life Science Ventures V, LP and (ii) 70,278 shares of Series A convertible preferred stock purchased by PV V CEO Fund, LP.
(12) Dr. O'Donnell, our former President and Chief Executive Officer and a member of our board of directors, is a manager at RiverVest Venture Partners and is an affiliate of RiverVest Venture Fund III, L.P., RiverVest Venture Fund III (Ohio), L.P. and RiverVest Venture Fund IV, L.P.
(13) Consists of (i) 281,159 shares of Series A convertible preferred stock purchased by RiverVest Venture Fund III, L.P. and (ii) 14,922 shares of Series A convertible preferred stock purchased by RiverVest Venture Fund III (Ohio), L.P.
(14) Consists of shares of Series A convertible preferred stock purchased by RiverVest Venture Fund IV, L.P.
(15) Dr. Kördel, a member of our board of directors, is employed as a senior advisor at Lundbeckfond Ventures, an entity affiliated with Lundbeckfond Invest A/S.

### Series B Convertible Preferred Stock Financing

In December 2020, we completed the initial closing of an aggregate of 23,440,514 shares of our Series B convertible preferred stock at a purchase price of $2.0215 per share. In March 2021, we completed the milestone closing of an aggregate of an additional 23,440,514 shares of our Series B convertible preferred stock, at the same purchase price per share.

The following table summarizes purchases of shares of our Series B convertible preferred stock by holders of more than 5% of our capital stock (at the time of the applicable transaction) and entities affiliated with members of our board of directors.

| PARTICIPANTS (1) | SHARES OF SERIES B CONVERTIBLE PREFERRED STOCK PURCHASED AT INITIAL CLOSING | AGGREGATE PURCHASE PRICE AT INITIAL CLOSING | SHARES OF SERIES B CONVERTIBLE PREFERRED STOCK PURCHASED AT MILESTONE CLOSING | AGGREGATE PURCHASE PRICE AT MILESTONE CLOSING |
|---|---|---|---|---|
| Novo Holdings A/S (2) | 6,183,527 | $12,499,999.84 | 6,183,527 | $ 12,499,999.84 |
| New Enterprise Associates 15, L.P. (3) | 4,452,140 | $ 9,000,001.01 | 4,452,140 | $ 9,000,001.01 |
| Abingworth Bioventures 8 LP (4) | 3,710,116 | $ 7,499,999.50 | 3,710,116 | $ 7,499,999.50 |
| Entities affiliated with RiverVest Venture Fund III, L.P. (5) | 1,855,058 (6) | $ 3,749,999.75 | 1,855,058 (6) | $ 3,749,999.75 |
| Lundbeckfond Invest A/S (7) | 1,484,047 | $ 3,000,001.02 | 1,484,047 | $ 3,000,001.02 |
| Aisling Capital V, L.P. (8) | 1,236,705 | $ 2,499,999.16 | 1,236,705 | $ 2,499,999.16 |
| Entities affiliated with Pappas Capital, LLC (9) | 593,619 (10) | $ 1,200,000.81 | 593,619 (10) | $ 1,200,000.81 |

(1) Additional details regarding these stockholders and their equity holdings are included in this prospectus under the caption "Principal Stockholders."
(2) Dr. Harrison, a member of our board of directors, is employed as a partner at Novo Ventures (US) Inc., which provides certain consultancy services to Novo Holdings A/S. Dr. Harrison is not deemed to hold any beneficiary ownership or reportable pecuniary interest in the shares held by Novo Holdings A/S.
(3) Mr. Mathers, a member of our board of directors, is employed as a Partner at New Enterprise Associates, Inc., which is affiliated with NEA 15.
(4) Dr. Muralidhar, a member of our board of directors, is employed as a partner at Abingworth LLP, an entity affiliated with Abingworth Bioventures 8 LP.
(5) Dr. O'Donnell, our former President and Chief Executive Officer and a member of our board of directors, is a manager at RiverVest Venture Partners and is an affiliate of RiverVest Venture Fund IV, L.P.
(6) Consists of shares of Series B convertible preferred stock purchased by RiverVest Venture Fund IV, L.P.
(7) Dr. Kördel, a member of our board of directors, is employed as a senior advisor at Lundbeckfond Ventures, an entity affiliated with Lundbeckfond Invest A/S.
(8) Ms. Seltzer, a member of our board of directors, is employed as a partner at Aisling Capital LLC, an entity affiliated with Aisling Capital V, L.P.

(9) Mr. Grey, our Executive Chairman, is a venture partner at Pappas Capital, LLC.
(10) Consists of (i) 549,106 shares of Series B convertible preferred stock purchased by A. M. Pappas Life Science Ventures V, LP and (ii) 44,513 shares of Series B convertible preferred stock purchased by PV V CEO Fund, LP.

### Agreements with vTv Therapeutics

Below is a description of the agreements we have entered into with vTv Therapeutics, a 5% holder of our capital stock.

#### *Common Stock Issuance Agreements*

In January 2018, we entered into a Common Stock Issuance Agreement with vTv Therapeutics pursuant to which we issued vTv Therapeutics an aggregate of 87,717 shares of our common stock as partial consideration of the rights granted to us pursuant to the vTv License Agreement. See "Business—License Agreement with vTv Therapeutics LLC" for a description of the vTv License Agreement

In May 2019, we entered into a Common Stock Issuance Agreement with vTv Therapeutics pursuant to which we issued vTv Therapeutics an aggregate of 179,150 shares of our common stock as partial consideration of the rights granted to us pursuant to the vTv License Agreement.

The above listed issuances and a prior issuance of common stock to vTv Therapeutics in December 2017 satisfied in full our obligations under the vTv License Agreement to issue shares of our common stock to vTv Therapeutics as partial consideration of the rights granted to us pursuant to the vTv License Agreement.

### Employment Agreements, Letter Agreement and Stock Option Grants to Directors and Executive Officers

We have entered into employment agreements and a letter agreement with certain of our named executive officers, and granted stock options to our named executive officers and certain of our directors, as more fully described in the sections titled "Executive Compensation" and "Management—Director Compensation."

### Investors' Rights Agreement

In December 2020, we entered into an Amended and Restated Investors' Rights Agreement (the Rights Agreement) with certain affiliates of our directors and certain holders of more than 5% of our outstanding capital stock, including entities affiliated with New Enterprise Associates, Novo Holdings A/S, entities affiliated with RiverVest Venture Fund III, L.P., Lundbeckfond Invest A/S, Abingworth Bioventures 8 LP, and entities affiliated with Pappas Capital, LLC.

The Rights Agreement grants certain rights to the holders of our outstanding preferred stock and to certain holders of our outstanding common stock, including certain registration rights with respect to the registrable securities held by them. See "Description of Capital Stock—Registration Rights" for additional information.

In addition, the Rights Agreement imposes certain affirmative obligations on us, including our obligation to, among other things, grant (i) each holder who holds at least 223,473 shares of our common stock issuable or issued upon conversion of shares of our convertible preferred stock and (ii) certain holders who hold at least 223,473 shares of our common stock and our common stock issuable or issued upon conversion of shares of our convertible preferred stock in the aggregate (collectively the Major Investors) and vTv Therapeutics, a right of first offer with respect to future sales of our equity, excluding the shares to be offered and sold in this offering, and grant certain information and inspection rights to such Major Investors. Other than the registration rights, each of these obligations will terminate in connection with the closing of this offering.

### Voting Agreement

In December 2020, we entered into an Amended and Restated Voting Agreement, which was amended in March 2021 (the Voting Agreement), with certain affiliates of our directors, trusts for the benefit of immediate family members of an executive officer and certain holders of more than 5% of our outstanding capital stock, including entities affiliated with New Enterprise Associates, Novo Holdings A/S, entities affiliated with RiverVest Venture Fund III, L.P., Lundbeckfond Invest A/S, Abingworth Bioventures 8 LP, and entities affiliated with Pappas Capital, LLC.

Pursuant to the Voting Agreement, each of Novo Holdings A/S, Abingworth Bioventures 8 LP, Aisling Capital V, L.P., New Enterprise Associates 15, L.P, RiverVest Venture Fund IV, L.P. and Lundbeckfond Invest A/S have the right to designate one member to be elected to our board of directors. See “Management—Composition of our Board of Directors.” The Voting Agreement will terminate in connection with the closing of this offering and none of our stockholders will have any continuing rights regarding the election or designation of members of our board of directors following this offering.

### Right of First Refusal and Co-Sale Agreement

In December 2020, we entered into an Amended and Restated Right of First Refusal and Co-Sale Agreement (the Co-Sale Agreement) with certain affiliates of our directors, trusts for the benefit of immediate family members of an executive officer and certain holders of more than 5% of our outstanding capital stock, including entities affiliated with New Enterprise Associates, Novo Holdings A/S, entities affiliated with RiverVest Venture Fund III, L.P., Lundbeckfond Invest A/S, Abingworth Bioventures 8 LP, and entities affiliated with Pappas Capital, LLC.

Pursuant to the Co-Sale Agreement, we have a right of first refusal in respect of certain sales of securities by certain holders of our common stock and preferred stock, including certain affiliates of our directors, trusts for the benefit of immediate family members of an executive officer and certain holders of more than 5% of our outstanding capital stock. To the extent we do not exercise such right in full, the Major Investors are granted certain rights of first refusal and co-sale in respect of such sale. The Co-Sale Agreement will terminate in connection with the closing of this offering.

### Indemnification Agreements

Our amended and restated certificate of incorporation will contain provisions limiting the liability of directors, and our amended and restated bylaws will provide that we will indemnify each of our directors and officers to the fullest extent permitted under Delaware law. Our amended and restated certificate of incorporation and amended and restated bylaws will also provide our board of directors with discretion to indemnify our employees and other agents when determined appropriate by the board. In addition, we have entered into or intend to enter into an indemnification agreement with each of our directors and executive officers, which will require us to indemnify them. For more information regarding these agreements, see “Executive Compensation—Limitations on Liability and Indemnification Matters.”

### Policies and Procedures for Transactions with Related Persons

We have adopted a written policy that our executive officers, directors, nominees for election as a director, beneficial owners of more than 5% of any class of our common stock and any members of the immediate family of any of the foregoing persons are not permitted to enter into a related person transaction with us without the approval or ratification of our board of directors or our audit committee. Any request for us to enter into a transaction with an executive officer, director, nominee for election as a director, beneficial owner of more than 5% of any class of our common stock, or any member of the immediate family of any of the foregoing persons, in which the amount involved exceeds $120,000 (or, if less, 1% of the average of our total assets in a fiscal year) and such person would have a direct or indirect interest, must be presented to our board of directors or our audit committee for review, consideration and approval. In approving or rejecting any such proposal, our board of directors or our audit committee is to consider the material facts of the transaction, including whether the transaction is on terms comparable to the terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person’s interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

## PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding beneficial ownership of our capital stock as of March 31, 2021 by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our common stock;
- each of our directors;
- each of our named executive officers; and
- all of our current executive officers and directors as a group.

We have determined beneficial ownership in accordance with the rules and regulations of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Except as indicated by the footnotes below, we believe, based on information furnished to us, that the persons and entities named in the table below have sole voting and sole investment power with respect to all shares that they beneficially own, subject to applicable community property laws.

Applicable percentage ownership before the offering is based on 18,055,822 shares of our common stock outstanding as of March 31, 2021, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into 15,907,629 shares of our common stock in connection with the closing of this offering.

Applicable percentage ownership after the offering is based on 24,305,822 shares of common stock outstanding immediately after the closing of this offering, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into 15,907,629 shares of our common stock in connection with the closing of this offering. The percentage ownership information assumes no exercise of the underwriters' option to purchase additional shares and no purchases of any shares of common stock in this offering by the beneficial owners identified in the table below. In computing the number of shares beneficially owned by a person and the percentage ownership of such person, we deemed to be outstanding all shares subject to options held by the person that are currently exercisable, or exercisable within 60 days of March 31, 2021. However, except as described above, we did not deem such shares outstanding for the purpose of computing the percentage ownership of any other person.

Unless otherwise indicated, the address for each beneficial owner listed in the table below is c/o Reneo Pharmaceuticals, Inc., 12230 El Camino Real, Suite 230, San Diego, California 92130.

| NAME OF BENEFICIAL OWNER | NUMBER OF SHARES BENEFICIALLY OWNED | PERCENTAGE OF SHARES BENEFICIALLY OWNED | |
|---|---|---|---|
| | | BEFORE OFFERING | AFTER OFFERING |
| **Greater than 5% Holders:** | | | |
| Entities affiliated with New Enterprise Associates (1) | 4,120,255 | 22.8% | 17.0% |
| Novo Holdings A/S (2) | 2,763,711 | 15.3% | 11.4% |
| Entities affiliated with RiverVest Venture Fund III, L.P. (3) | 2,209,220 | 12.2% | 9.1% |
| Lundbeckfond Invest A/S (4) | 1,697,891 | 9.4% | 7.0% |
| Abingworth Bioventures 8 LP (5) | 1,658,226 | 9.2% | 6.8% |
| **Named Executive Officers and Directors:** | | | |
| Gregory J. Flesher (6) | 1,052,647 | 5.5% | 4.2% |
| Niall O'Donnell, Ph.D. (7) | 1,980,684 | 10.9% | 8.1% |
| Alejandro Dorenbaum, M.D. (8) | 232,272 | 1.3% | * |
| Wendy Johnson (9) | 257,440 | 1.4% | 1.0% |
| Lon Cardon, Ph.D. (10) | 46,928 | * | * |
| Eric M. Dube, Ph.D. (11) | 44,694 | * | * |
| Michael Grey (12) | 829,218 | 4.5% | 3.4% |
| Kenneth Harrison, Ph.D. | — | * | * |
| Johan Kördel, Ph.D. (4) | 1,697,891 | 9.4% | 7.0% |
| Edward Mathers | — | * | * |
| Bali Muralidhar, M.D., Ph.D. | — | * | * |
| Stacey D. Seltzer | — | * | * |
| All executive officers, directors and director nominee as a group (14 persons) (13) | 6,605,408 | 32.3% | 24.7% |

* Represents beneficial ownership of less than 1%.

(1) Consists of (i) 2,128,956 shares of common stock issuable upon conversion of the Series A convertible preferred stock held by New Enterprise Associates 15, L.P. (NEA 15), (ii) 1,427 shares of common stock issuable upon conversion of the Series A convertible preferred stock held by NEA Ventures 2017, L. P. (NEA Ventures) and (iii) 1,989,872 shares of common stock issuable upon conversion of the Series B convertible preferred stock held by NEA 15. The shares directly held by NEA 15 are indirectly held by NEA Partners 15, L.P. (NEA Partners 15) the sole general partner of NEA 15, NEA 15 GP, LLC (NEA 15 LLC) the sole general partner of NEA Partners 15 and each of the individual managers of NEA 15 LLC. The individual managers, or collectively, the managers, of NEA 15 LLC are Forest Baskett, Anthony A. Florence, Jr., Mohamad Makhzoumi, Joshua Makower, Scott D. Sandell and Peter Sonsini. The managers share voting and dispositive power with regard to the shares held by NEA 15. Karen P. Welsh, the general partner of NEA Ventures, has sole voting and dispositive power with regard to the shares held by NEA Ventures. Edward Mathers, a member of our board of directors, is employed as a General Partner at New Enterprise Associates, Inc., has no voting or investment power over the shares owned of record by NEA 15 or NEA Ventures, and disclaims beneficial ownership of the shares held by NEA 15 and NEA Ventures. All indirect owners of the above referenced shares, disclaim beneficial ownership of all applicable shares except to the extent of their actual pecuniary interest in such shares. The address of New Enterprise Associates 15, L.P. and its affiliated entity is c/o New Enterprise Associates, 1954 Greenspring Drive, Suite 600, Timonium, Maryland 21093.

(2) Consists of 2,763,711 shares of common stock issuable upon conversion of the Series B convertible preferred stock held by Novo Holdings A/S (Novo). The board of directors of Novo has shared voting and investment power with respect to the shares held by Novo and may exercise such control only with the support of a majority of the members of the Novo board of directors. As such, no individual member of the Novo board of directors is deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Novo. Kenneth Harrison, Ph.D., a member of our board of directors, is employed as a partner at Novo Ventures (US) Inc., which provides certain consultancy services to Novo, and Dr. Harrison is not deemed to have beneficial ownership of the shares held by Novo. The address of Novo Holdings A/S is Tuborg Havnevej 19, DK-2900 Hellerup, Denmark.

(3) Consists of (i) 265,263 shares of common stock held by RiverVest Venture Fund III, L.P., (ii) 14,079 shares of common stock held by RiverVest Venture Fund III (Ohio), L.P., (iii) 1,034,600 shares of common stock issuable upon conversion of the Series A convertible preferred stock held by RiverVest Venture Fund IV, L.P., (iv) 62,831 shares of common stock issuable upon conversion of the Series A convertible preferred stock held by RiverVest Venture Fund III, L.P., (v) 3,334 shares of common stock issuable upon conversion of the Series A convertible preferred stock held by RiverVest Venture Fund III (Ohio), L.P. and (vi) 829,113 shares of common stock issuable upon conversion of the Series B convertible preferred stock held by RiverVest Venture Fund IV, L.P. The shares held directly by RiverVest Venture Fund III, L.P. are indirectly held by RiverVest Venture Partners III, L.P., its general partner (RiverVest Partners III). The shares held directly by RiverVest Venture Fund III (Ohio), L.P. are indirectly held by RiverVest Venture Partners III (Ohio), LLC, its general partner (RiverVest Partners (Ohio) III). RiverVest Partners III is the sole member of RiverVest Partners (Ohio) III. RiverVest Venture Partners III, LLC is the general partner of RiverVest Partners III. The individual managers of RiverVest Ventures Partners III, LLC are Thomas C. Melzer, Jay Schmelter and John P. McKearn, Ph.D. RiverVest Partners III, RiverVest Partners (Ohio) III, RiverVest Venture Partners III, LLC and each of the individual managers share voting and dispositive power with regard to our securities directly held by RiverVest Venture Fund III, L.P. and RiverVest Venture Fund III (Ohio), L.P. Niall O'Donnell, Ph.D., a member of our board of directors and an affiliate of RiverVest Venture Fund III, L.P. and RiverVest Venture Fund III (Ohio), L.P., has no voting or investment control over any of the shares held by these entities and disclaims beneficial ownership of all shares owned by RiverVest Venture Fund III, L.P. and RiverVest Venture Fund III (Ohio), L.P., except to the extent of any pecuniary interest therein. All indirect holders of the above referenced securities disclaim beneficial ownership of the above referenced securities except to the extent of their pecuniary interests therein. The shares held directly by RiverVest Venture Fund IV, L.P. are indirectly held by RiverVest Venture Partners IV, L.P., its general partner (RiverVest Partners IV). RiverVest Venture Partners IV, LLC is the general partner of RiverVest Partners IV. The individual managers of RiverVest Ventures Partners IV, LLC are Jay Schmelter, John P. McKearn, Ph.D. and Niall O'Donnell, Ph.D., a member of our board of directors. RiverVest Partners IV, RiverVest Venture Partners IV, LLC and each of the individual managers share voting and dispositive power with regard to our securities directly held by RiverVest Venture Fund IV, L.P. All indirect holders of the above referenced securities disclaim beneficial ownership of the above referenced securities except to the extent of their pecuniary interests therein. The address of RiverVest Venture Fund III and its affiliated entities is 101 South Hanley Road, Suite 1850, St. Louis, Missouri 63105.

(4) Consists of (i) 1,034,600 shares of common stock issuable upon conversion of the Series A convertible preferred stock held by Lundbeckfond Invest A/S and (ii) 663,291 shares of common stock issuable upon conversion of the Series B convertible preferred stock held by Lundbeckfond Invest A/S. Johan Kördel, Ph.D., a member of our board of directors, shares voting and investment power with respect to the shares held by Lundbeckfond Invest A/S. Dr. Kördel disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of Lundbeckfond Invest A/S is Scherfigsvej 7 DK-2100, Copenhagen Ø, Denmark. Dr. Kördel resigned as a member of our board of directors effective as of immediately prior to the time that the registration statement of which this prospectus forms a part was declared effective.

(5) Consists of 1,658,226 shares of common stock issuable upon conversion of the Series B convertible preferred stock held by Abingworth Bioventures 8 LP (ABV 8). Abingworth Bioventures 8 GP LP, a Scottish limited partnership, serves as the general partner of ABV 8. Abingworth General Partner 8 LLP, an English limited liability partnership, serves as the general partner of Abingworth Bioventures 8 GP LP. ABV 8 (acting by its general partner Abingworth Bioventures 8 GP LP, acting by its general partner Abingworth General Partner 8 LLP) has delegated to Abingworth LLP (Abingworth) all investment and dispositive power over the securities held by ABV 8. An investment committee of Abingworth, or the investment committee, comprised of Timothy Haines, Kurt von Emster, Genghis Lloyd-Harris, Brian Gallagher, Andrew Sinclair and Bali Muralidhar, a member of our board of directors, approves investment and voting decisions by a defined majority vote, and no individual member has the sole control or voting power over the securities held by ABV 8. Each of Abingworth, Abingworth Bioventures 8 GP LP, Abingworth General Partner 8 LLP, and each member of the investment committee disclaims beneficial ownership of the shares of our Series B convertible preferred stock held by ABV 8. The address of Abingworth Bioventures 8 LP is 38 Jermyn Street, London SW1Y 6DN, United Kingdom.

(6) Consists of 1,052,647 shares of common stock subject to options held by Mr. Flesher that are exercisable within 60 days of March 31, 2021.
(7) Consists of (i) 1,034,600 shares of common stock issuable upon conversion of the Series A convertible preferred stock held by RiverVest Venture Fund IV, L.P., (ii) 829,113 shares of common stock issuable upon conversion of the Series B convertible preferred stock held by RiverVest Venture Fund IV, L.P. and (iii) 116,971 shares of common stock subject to options held by Dr. O'Donnell that are exercisable within 60 days of March 31, 2021.
(8) Consists of (i) 75,556 shares of common stock and (ii) 156,716 shares of common stock subject to options held by Dr. Dorenbaum that are exercisable within 60 days of March 31, 2021.
(9) Consists of 257,440 shares of common stock subject to options held by Ms. Johnson that are exercisable within 60 days of March 31, 2021.
(10) Consists of 46,928 shares of common stock subject to options held by Dr. Cardon that are exercisable within 60 days of March 31, 2021.
(11) Consists of 44,694 shares of common stock subject to options held by Dr. Dube that are exercisable within 60 days of March 31, 2021.
(12) Consists of (i) 424,600 shares of common stock held by The Grey Family Trust dated November 12, 1999 (the Grey 1999 Trust), (ii) 134,084 shares of common stock held by Michael George Grey and Rondi Rauch Grey, Co-Trustees of The Grey 2014 Irrevocable Children's Trust u/a/d 12/17/14 (the Grey 2014 Trust), (iii) 20,162 shares of common stock issuable upon conversion of the Series A convertible preferred stock held by the Grey 1999 Trust, and (iv) 250,372 shares of common stock subject to options held by Michael Grey that are exercisable within 60 days of March 31, 2021. Mr. Grey, our Executive Chairman, is trustee of each of the Grey 1999 Trust and Grey 2014 Trust, and in such capacity has the power to vote and dispose of such shares held by the Grey 1999 Trust and Grey 2014 Trust.
(13) Consists of the shares described in notes 4 and 6 through 12 above and (i) 229,477 shares of common stock subject to options held by Michael Cruse that are exercisable within 60 days of March 31, 2021 and (ii) 234,158 shares of common stock subject to options held by Vineet R. Jindal that are exercisable within 60 days of March 31, 2021.

# DESCRIPTION OF CAPITAL STOCK

## General

The following description of our capital stock and certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws, each of which will become effective upon the closing of this offering. Copies of these documents have been filed with the SEC as exhibits to our registration statement, of which this prospectus forms a part. The descriptions of the common stock and preferred stock reflect changes to our capital structure that will be in effect on the closing of this offering.

Upon filing of our amended and restated certificate of incorporation and the closing of this offering, our authorized capital stock will consist of 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. All of our authorized shares of preferred stock will be undesignated.

As of December 31, 2020, after giving effect to the issuance and sale of 23,440,514 shares of our Series B convertible preferred stock in March 2021 and the conversion of all outstanding shares of our convertible preferred stock into 15,907,629 shares of our common stock in connection with the closing of this offering, there were 17,960,699 shares of common stock outstanding and held of record by 33 stockholders.

## Common Stock

### *Voting Rights*

The 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 will 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. See the section titled “Dividend Policy” for further information.

*Liquidation Rights*. On our liquidation, dissolution, or winding-up, the holders of 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 our shares of common stock are not entitled to preemptive rights, and are not subject to conversion, redemption or sinking fund provisions.

### *Fully Paid and Non-Assessable*

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering will be, fully paid and nonassessable.

### Preferred Stock

As of December 31, 2020, there were 24,302,472 shares of our Series A convertible preferred stock outstanding, held of record by 16 holders, and 46,881,028 shares of our Series B convertible preferred stock outstanding, after giving effect to the issuance and sale of 23,440,514 shares of our Series B convertible preferred stock in March 2021, held of record by 15 holders. In connection with the closing of this offering, every 4.4748 outstanding shares of our convertible preferred stock will convert into one share of our common stock. In addition, in connection with the closing of this offering, our certificate of incorporation will be amended and restated to delete all references to such shares of convertible preferred stock. Under the amended and restated certificate of incorporation, our board of directors will have 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 the common stock and the voting and other rights of the holders of common stock. We have no current plans to issue any shares of preferred stock.

### Options

As of December 31, 2020, options to purchase an aggregate of 935,478 shares of our common stock, with a weighted-average exercise price of $2.56 per share, were outstanding. In addition, an aggregate of 2,273,285 shares of our common stock are issuable upon the exercise of outstanding stock options granted subsequent to December 31, 2020, with a weighted-average exercise price of $5.06 per share. For additional information regarding terms of our equity incentive plans, see the section titled “Executive Compensation—Employee Benefit Plans.”

### Registration Rights

We are party to the Rights Agreement, which provides, in relevant part, that certain holders of our capital stock, including certain holders of at least 5% of our capital stock and entities affiliated with certain of our directors, shall have certain registration rights, as set forth below. The registration of shares of our common stock by the exercise of registration rights described below would enable the holders to sell these shares without restriction under the Securities Act when the applicable registration statement is declared effective. We are obligated to pay the registration expenses, other than underwriting discounts and commissions, of the shares registered by the demand, piggyback and Form S-3 registrations described below.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares such holders may include. The demand, piggyback and Form S-3 registration rights described below with respect to any holder will expire upon the earliest to occur of: (i) any time following the initial public offering when the holder holds less than 1% of our outstanding securities and all of such holder’s registrable securities may be sold without any restriction on volume or manner of sale in any three-month period under Rule 144 or any successor; and (b) the fifth anniversary of the initial public offering.

#### *Demand Registration Rights*

After this offering, the holders of an aggregate of 16,819,282 shares of our common stock will be entitled to certain demand registration rights. With certain exceptions, at any time beginning 180 days after the effective date of the registration statement, of which this prospectus is a part, the holders of a majority of these shares may request that we register all or a portion of their shares. In connection with a request for demand registration, we are not required to effect more than two registration statements which are declared or ordered effective. Such request for registration must cover shares with an anticipated aggregate offering price, net of underwriter discounts and commissions and certain fees, of at least $10.0 million.

***Piggyback Registration Rights***

In connection with this offering, the holders of an aggregate of 16,819,282 shares of our common stock were entitled to, and the necessary percentage of holders waived, their rights to notice of this offering and to include their shares of registrable securities in this offering. After this offering, in the event that we propose to register any of our securities under the Securities Act, either for our own account or for the account of other security holders, the holders of these shares will be entitled to certain piggyback registration rights allowing the holder to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to a demand registration or a registration (i) relating to the sale of securities to employees of us or our subsidiaries pursuant an equity incentive, stock option, stock purchase, or similar plan, (ii) relating to an SEC Rule 145 transaction, (iii) on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of registrable securities, or (iv) in which the only common stock being registered is common stock issuable upon conversion of debt securities that are also being registered, the holders of these shares are entitled to notice of the registration and have the right to include their shares in the registration, subject to limitations that the underwriters may impose on the number of shares included in the offering.

***Form S-3 Registration Rights***

After this offering, the holders of an aggregate of 16,819,282 shares of our common stock will be entitled to certain Form S-3 registration rights. Any holder of these shares can make a request that we register their shares on Form S-3 if we are qualified to file a registration statement on Form S-3 and if the reasonably anticipated aggregate net proceeds of the shares offered would equal or exceed $1.0 million. We will not be required to effect more than two registrations on Form S-3 within any 12-month period.

***Indemnification***

The Rights Agreement contains customary cross indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in a registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

***Expenses***

Generally, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing and accounting fees, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling securityholders not to exceed $50,000.

## Anti-Takeover Provisions

The provisions of Delaware law, our amended and restated certificate of incorporation and our 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 to be in Effect on the Closing of this Offering***

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 to be effective on the closing of this offering will provide for stockholder actions 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 or president. Our amended and restated certificate of incorporation will also eliminate the right of stockholders to act by written consent without a meeting. Our amended and restated bylaws will 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.

As described above in “Management—Composition of Our Board of Directors,” in accordance with our amended and restated certificate of incorporation to be filed in connection with this offering, immediately after this offering, our board of directors will be 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 will be 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 current amended and restated certificate of incorporation provides, and our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective in connection with the closing of this offering, will provide, that the Court of Chancery of the State of Delaware will 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 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 current amended and restated certificate of incorporation, and our amended and restated certificate of incorporation and our amended and restated bylaws, which will become effective in connection with the closing of this offering, will 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 current amended and restated certificate of incorporation, and our amended and restated certificate of incorporation and our amended and restated bylaws, which will become effective in connection with the closing of this offering.

Further, our current amended and restated certificate of incorporation provides, and our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective in connection with the

closing of this offering, will 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.

### Limitations on Liability and Indemnification

See "Executive Compensation—Limitations on Liability and Indemnification."

### Exchange Listing

Our common stock has been approved for listing on the Nasdaq Global Market under the symbol "RPHM."

### Transfer Agent and Registrar

Upon the closing of this offering, the transfer agent and registrar for our common stock will be American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, New York 11219.

## SHARES ELIGIBLE FOR FUTURE SALE

Before the closing of this offering, there has been no public market for our common stock. Future sales of substantial amounts of our common stock, including shares issued upon the exercise of outstanding options, in the public market after this offering, or the possibility of these sales or issuances occurring, could adversely affect the prevailing market price for our common stock or impair our ability to raise equity capital.

Based on our shares outstanding as of December 31, 2020, upon the closing of this offering, a total of 24,210,699 shares of common stock will be outstanding, after giving effect to the issuance and sale of 23,440,514 shares of our Series B convertible preferred stock in March 2021 and assuming the conversion of all outstanding shares of our convertible preferred stock into 15,907,629 shares of our common stock in connection with the closing of this offering. Of these shares, all of the common stock sold in this offering by us, plus any shares sold by us upon exercise of the underwriters' option to purchase additional common stock, will be freely tradable in the public market without restriction or further registration under the Securities Act, unless these shares are held by "affiliates," as that term is defined in Rule 144 under the Securities Act.

The remaining shares of common stock will be, and shares of common stock subject to stock options will be on issuance, "restricted securities," as that term is defined in Rule 144 under the Securities Act. These restricted securities are eligible for public sale only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below. Restricted securities may also be sold outside of the United States to non-U.S. persons in accordance with Rule 904 of Regulation S.

Subject to the lock-up agreements described below and the provisions of Rule 144 or Regulation S under the Securities Act, as well as our insider trading policy, these restricted securities will be available for sale in the public market after the date of this prospectus.

### Rule 144

In general, under Rule 144 as currently in effect, once we have been subject to public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, an eligible stockholder is entitled to sell such shares without complying with the manner of sale, volume limitation or notice provisions of Rule 144, subject to compliance with the public information requirements of Rule 144. To be an eligible stockholder under Rule 144, such stockholder must not be deemed to have been one of our affiliates for purposes of the Securities Act at any time during the 90 days preceding a sale and must have beneficially owned the shares proposed to be sold for at least six months, including the holding period of any prior owner other than our affiliates. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than our affiliates, then such person is entitled to sell such shares without complying with any of the requirements of Rule 144, subject to the expiration of the lock-up agreements described below.

In general, under Rule 144, as currently in effect, our affiliates or persons selling shares on behalf of our affiliates, who have beneficially owned the shares proposed to be sold for at least six months, are entitled to sell shares on expiration of the lock-up agreements described below. Beginning 90 days after the date of this prospectus, within any three-month period, such stockholders may sell a number of shares that does not exceed the greater of:

- 1% of the number of shares of common stock then outstanding, which will equal approximately 242,106 shares immediately after this offering, assuming no exercise of the underwriters' option to purchase additional shares of common stock from us; or
- the average weekly trading volume of our common stock on the Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Sales under Rule 144 by our affiliates or persons selling shares on behalf of our affiliates are also subject to certain manner of sale provisions and notice requirements and to the availability of current public information about us.

### Rule 701

Rule 701 generally allows a stockholder who was issued shares under a written compensatory plan or contract and who is not deemed to have been an affiliate of our company during the immediately preceding 90 days, to sell these shares in reliance on Rule 144, but without being required to comply with the public information, holding period, volume limitation, or notice provisions of Rule 144. Rule 701 also permits affiliates of our company to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144. All holders of Rule 701 shares, however, are required by that rule to wait until 90 days after the date of this prospectus before selling those shares under Rule 701, subject to the expiration of the lock-up agreements described below.

### Form S-8 Registration Statements

We intend to file one or more registration statements on Form S-8 under the Securities Act with the SEC to register the offer and sale of shares of our common stock that are issuable under our 2014 Plan, 2021 Plan and ESPP. These registration statements will become effective immediately on filing. Shares covered by these registration statements will then be eligible for sale in the public markets, subject to vesting restrictions, any applicable lock-up agreements described below, and Rule 144 limitations applicable to affiliates.

### Lock-Up Arrangements

We, and all of our directors, executive officers and the holders of substantially all of our common stock and securities exercisable for or convertible into our common stock outstanding immediately upon the closing of this offering, have agreed with the underwriters that, until 180 days after the date of the underwriting agreement related to this offering, we and they will not, without the prior written consent of Jefferies LLC, SVB Leerink LLC and Piper Sandler & Co., directly or indirectly, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of any of our shares of common stock, or any securities convertible into or exercisable or exchangeable for shares of our common stock, or enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the securities, whether any such swap or transaction is to be settled by delivery of our common stock or other securities, in cash or otherwise. These agreements are described in “Underwriting—No Sale of Similar Securities.” Jefferies LLC, SVB Leerink LLC, and Piper Sandler & Co. may, in their sole discretion, release any of the securities subject to these lock-up agreements at any time.

### Registration Rights

Upon the closing of this offering, pursuant to our amended and restated investors’ rights agreement, the holders of 16,819,282 shares of our common stock, or their transferees, will be entitled to certain rights with respect to the registration of the offer and sale of their shares under the Securities Act, subject to the terms of the lock-up agreements described under “—Lock-Up Arrangements” above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. Substantial sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock. See “Description of Capital Stock—Registration Rights” for additional information.

## MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following is a summary of the material U.S. federal income tax consequences to non-U.S. holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering. This discussion is not a complete analysis of all potential U.S. federal income tax consequences relating thereto, and does not address any estate or gift tax consequences or any tax consequences arising under any state, local or foreign tax laws, or any other U.S. federal tax laws. This discussion is based on the Internal Revenue Code of 1986, as amended (the Code) Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the Internal Revenue Service (the IRS) all as in effect on the date of this prospectus. These authorities are subject to differing interpretations and may change, possibly retroactively, resulting in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the IRS with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS or a court will agree with such statements and conclusions.

This discussion is limited to non-U.S. holders who purchase our common stock pursuant to this offering and who hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all of the U.S. federal income tax consequences that may be relevant to an individual holder in light of such holder's particular circumstances, including the impact of the Medicare contribution tax on net investment income and the alternative minimum tax . This discussion also does not consider any specific facts or circumstances that may be relevant to holders subject to special rules under the U.S. federal income tax laws, including:

- certain former citizens or long-term residents of the United States;
- partnerships or other pass-through entities (and investors therein);
- "controlled foreign corporations";
- "passive foreign investment companies";
- corporations that accumulate earnings to avoid federal income tax;
- banks, financial institutions, investment funds, insurance companies, brokers, dealers, or traders in securities;
- tax-exempt organizations and governmental organizations;
- tax-qualified retirement plans;
- persons subject to special tax accounting rules under Section 451(b) of the Code;
- persons that own or have owned, actually or constructively, more than 5% of our common stock;
- persons who have elected to mark securities to market; and
- persons holding our common stock as part of a hedging or conversion transaction or straddle, or a constructive sale, or other risk reduction strategy or integrated investment.

If an entity or arrangement that is classified as a partnership for U.S. federal income tax purposes holds our common stock, the U.S. federal income tax treatment of a partner in the partnership will generally depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Partnerships holding our common stock and the partners in such partnerships are urged to consult their tax advisors about the particular U.S. federal income tax consequences to them of holding and disposing of our common stock.

**THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR TAX ADVISORS REGARDING THE PARTICULAR U.S. FEDERAL INCOME TAX CONSEQUENCES TO THEM OF ACQUIRING, OWNING AND DISPOSING OF OUR COMMON STOCK, AS WELL AS ANY TAX CONSEQUENCES ARISING UNDER ANY STATE, LOCAL OR FOREIGN TAX LAWS AND ANY OTHER U.S. FEDERAL TAX LAWS.**

### Definition of Non-U.S. Holder

For purposes of this discussion, a non-U.S. holder is any beneficial owner of our common stock that is not a "U.S. person" or a partnership (including any entity or arrangement treated as a partnership) for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen of the United States;
- a corporation created or organized under the laws of the United States, any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust (1) whose administration is subject to the primary supervision of a U.S. court and which has one or more U.S. persons who have the authority to control all substantial decisions of the trust or (2) that has a valid election in effect under applicable Treasury Regulations to be treated as a U.S. person.

### Distributions on Our Common Stock

As described under "Dividend Policy," we do not anticipate declaring or paying, in the foreseeable future, any cash dividends on our capital stock. However, if we do distribute cash or other property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and will first be applied against and reduce a holder's tax basis in our common stock, but not below zero. Any excess will be treated as gain realized on the sale or other disposition of our common stock and will be treated as described under "—Gain on Disposition of Our Common Stock" below.

Subject to the discussions below regarding effectively connected income, backup withholding and FATCA (as defined below), dividends paid to a non-U.S. holder of our common stock generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends or such lower rate specified by an applicable income tax treaty. To receive the benefit of a reduced treaty rate, a non-U.S. holder must furnish us or our withholding agent with a valid IRS Form W-8BEN or IRS Form W-8BEN-E (or applicable successor form) certifying such holder's qualification for the reduced rate. This certification must be provided to us or our withholding agent before the payment of dividends and must be updated periodically. If the non-U.S. holder holds our common stock through a financial institution or other agent acting on the non-U.S. holder's behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to us or our withholding agent, either directly or through other intermediaries.

If a non-U.S. holder holds our common stock in connection with the conduct of a trade or business in the United States, and dividends paid on our common stock are effectively connected with such holder's U.S. trade or business (and are attributable to such holder's permanent establishment or fixed base in the United States if required by an applicable tax treaty), the non-U.S. holder will be exempt from U.S. federal withholding tax. To claim the exemption, the non-U.S. holder must generally furnish a valid IRS Form W-8ECI (or applicable successor form) to the applicable withholding agent.

However, any such effectively connected dividends paid on our common stock generally will be subject to U.S. federal income tax on a net income basis at the regular U.S. federal income tax rates in the same manner as if such holder were a resident of the United States. A non-U.S. holder that is a foreign corporation also may be subject to an additional branch profits tax equal to 30% (or such lower rate specified by an applicable income tax treaty) of its effectively connected earnings and profits for the taxable year, as adjusted for certain items.

Non-U.S. holders that do not provide the required certification on a timely basis, but that qualify for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

### Gain on Disposition of Our Common Stock

Subject to the discussions below regarding backup withholding and FATCA, a non-U.S. holder generally will not be subject to U.S. federal income tax on any gain realized on the sale or other disposition of our common stock, unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States and, if required by an applicable income tax treaty, is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States;
- the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition, and certain other requirements are met; or
- our common stock constitutes a "United States real property interest" by reason of our status as a United States real property holding corporation (a USRPHC) for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding the disposition or the non-U.S. holder's holding period for our common stock, and our common stock is not considered regularly traded on an established securities market at the time of the sale or other disposition.

Determining whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our other trade or business assets and our foreign real property interests. We believe that we are not currently, and we do not anticipate becoming a USRPHC for U.S. federal income tax purposes, although there can be no assurance we will not in the future become a USRPHC.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular U.S. federal income tax rates in the same manner as if such holder were a resident of the United States. A non-U.S. holder that is a foreign corporation also may be subject to an additional branch profits tax equal to 30% (or such lower rate specified by an applicable income tax treaty) of its effectively connected earnings and profits for the taxable year, as adjusted for certain items. Gain described in the second bullet point above will be subject to U.S. federal income tax at a flat 30% rate (or such lower rate specified by an applicable income tax treaty), but may be offset by certain U.S.-source capital losses (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses. Gain described in the third bullet point above will generally be subject to U.S. federal income tax in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply.

Non-U.S. holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

### Information Reporting and Backup Withholding

Annual reports are required to be filed with the IRS and provided to each non-U.S. holder indicating the amount of distributions on our common stock paid to such holder and the amount of any tax withheld with respect to those distributions. These information reporting requirements apply even if no withholding was required because the distributions were effectively connected with the holder's conduct of a U.S. trade or business, or withholding was reduced or eliminated by an applicable income tax treaty. This information also may be made available under a specific treaty or agreement with the tax authorities in the country in which the non-U.S. holder resides or is established. Backup withholding, currently at a 24% rate, generally will not apply to payments to a non-U.S. holder of dividends on or the gross proceeds of a disposition of our common stock provided the non-U.S. holder furnishes the required certification for its non-U.S. status, such as by providing a valid IRS Form W-8BEN, IRS Form W-8BEN-E or IRS Form W-8ECI, or certain other requirements are met, and if the payor does not have actual knowledge, or reason to know, that the holder is a U.S. person.

Backup withholding is not an additional tax. If any amount is withheld under the backup withholding rules, the non-U.S. holder should consult with a U.S. tax advisor regarding the possibility of and procedure for obtaining a refund or a credit against the non-U.S. holder's U.S. federal income tax liability, if any.

### Withholding on Foreign Entities

Sections 1471 through 1474 of the Code, which are commonly referred to as FATCA, impose a U.S. federal withholding tax of 30% on certain payments made to a "foreign financial institution" (as specially defined under these rules) unless such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities certain information regarding certain U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or an exemption applies. FATCA also generally will impose a U.S. federal withholding tax of 30% on certain payments made to a non-financial foreign entity unless such entity provides the withholding agent a certification identifying certain direct and indirect U.S. owners of the entity or an exemption applies. An intergovernmental agreement between the United States and an applicable foreign country may modify these requirements. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. FATCA currently applies to dividends paid on our common stock and would have applied also to payments of gross proceeds from the sale or other disposition of our common stock. The U.S. Treasury Department has released proposed regulations under FATCA providing for the elimination of the federal withholding tax of 30% applicable to gross proceeds of a sale or other disposition of our common stock. Under these proposed Treasury Regulations (which may be relied upon by taxpayers prior to finalization), FATCA will not apply to gross proceeds from sales or other dispositions of our common stock.

Prospective investors are encouraged to consult with their own tax advisors regarding the possible implications of FATCA on their investment in our common stock.

# UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated April 8, 2021 among us and Jefferies LLC, SVB Leerink LLC and Piper Sandler & Co., as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

| UNDERWRITER | NUMBER OF SHARES |
|---|---|
| Jefferies LLC | 2,343,750 |
| SVB Leerink LLC | 2,187,500 |
| Piper Sandler & Co. | 1,718,750 |
| Total | 6,250,000 |

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

## Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of $0.63 per share of common stock. After the offering, the initial public offering price and concession to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

| | PER SHARE | | TOTAL | |
|---|---|---|---|---|
| | WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES | WITH OPTION TO PURCHASE ADDITIONAL SHARES | WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES | WITH OPTION TO PURCHASE ADDITIONAL SHARES |
| Public offering price | $ 15.00 | $ 15.00 | $93,750,000 | $107,812,500 |
| Underwriting discounts and commissions paid by us | $ 1.05 | $ 1.05 | $ 6,562,500 | $ 7,546,875 |
| Proceeds to us, before expenses | $ 13.95 | $ 13.95 | $87,187,500 | $100,265,625 |

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $3.0 million. We have also agreed to reimburse the underwriters for certain expenses incurred in connection with this offering in an amount up to $40,000.

### Determination of Offering Price

Prior to this offering, there has not been a public market for our common stock. Consequently, the initial public offering price for our common stock was determined by negotiations between us and the representatives. Among the factors considered in these negotiations were prevailing market conditions, our financial information, market valuations of other companies that we and the underwriters believe to be comparable to us, estimates of our business potential, the present state of our development and other factors deemed relevant.

We offer no assurances that the initial public offering price will correspond to the price at which the common stock will trade in the public market subsequent to the offering or that an active trading market for the common stock will develop and continue after the offering.

### Listing

Our common stock has been approved for listing on the Nasdaq Global Market under the symbol "RPHM."

### Stamp Taxes

If you purchase shares of common stock offered in this prospectus, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus.

### Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of 937,500 shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares than the total number set forth on the cover page of this prospectus.

### No Sales of Similar Securities

We, our officers, directors and holders of substantially all of our outstanding capital stock and other securities have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-l(h) under the Exchange Act;
- otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially; or

- publicly announce an intention to do any of the foregoing for a period of 180 days after the date of this prospectus without the prior written consent of Jefferies LLC, SVB Leerink LLC and Piper Sandler & Co.

This restriction terminates after the close of trading of the common stock on and including the 180th day after the date of this prospectus.

Jefferies LLC, SVB Leerink LLC and Piper Sandler & Co. may, in their sole discretion and at any time or from time to time before the termination of the 180-day period, release all or any portion of the securities subject to the lock-up agreements. There are no existing agreements between the underwriters and any of our stockholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

### Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Exchange Act, and certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either “covered” short sales or “naked” short sales.

“Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

“Naked” short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter’s purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on the Nasdaq Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker’s bid, that bid must then be lowered when specified purchase limits are exceeded.

### Electronic Distribution

A prospectus in electronic format may be made available by e-mail or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

### Other Activities and Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

### Notice to Holders

***Australia***

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

- a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the Company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
- a person associated with the Company under Section 708(12) of the Corporations Act; or
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the securities issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

***Canada***

*Resale Restrictions*

The distribution of our shares in Canada is being made only in the provinces of Ontario, Quebec, Alberta and British Columbia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of the shares of common stock in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the securities.

*Representations of Canadian Purchasers*

By purchasing our shares of common stock in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

- the purchaser is entitled under applicable provincial securities laws to purchase the shares without the benefit of a prospectus qualified under those securities laws as it is an “accredited investor” as defined under National Instrument 45-106—Prospectus Exemptions;
- the purchaser is a “permitted client” as defined in National Instrument 31-103—Registration Requirements, Exemptions and Ongoing Registrant Obligations;
- where required by law, the purchaser is purchasing as principal and not as agent; and
- the purchaser has reviewed the text above under Resale Restrictions.

*Conflicts of Interest*

Canadian purchasers are hereby notified that the underwriters proposing to sell into Canada are relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105—Underwriting Conflicts from having to provide certain conflict of interest disclosure in this document.

*Statutory Rights of Action*

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the prospectus (including any amendment thereto) such as this document contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser of these securities in Canada should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

*Enforcement of Legal Rights*

All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside of Canada and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

*Taxation and Eligibility for Investment*

Canadian purchasers of our shares of common stock should consult their own legal and tax advisors with respect to the tax consequences of an investment in the share in their particular circumstances and about the eligibility of the shares for investment by the purchaser under relevant Canadian legislation.

***European Economic Area and United Kingdom***

In relation to each member state of the European Economic Area and the United Kingdom, each, a Relevant State, an offer to the public of any common shares which are the subject of the offering contemplated by this prospectus supplement and the accompanying prospectus may not be made in that Relevant State except that an offer to the public in that Relevant State of any common shares may be made at any time under the following exemptions under the Prospectus Regulation:

- to any legal entity which is a “qualified investor” as defined in the Prospectus Regulation;

- to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Regulation), as permitted under the Prospectus Regulation, subject to obtaining the prior consent of the underwriters or the underwriters nominated by us for any such offer; or
- in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of common shares shall require us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 16 of the Prospectus Regulation.

For the purposes of this provision, the expression “offer to the public” in relation to the common shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and the common shares to be offered so as to enable an investor to decide to purchase or subscribe the common shares, and the expression “Prospectus Regulation” means Regulation (EU)2017/1129.

***Hong Kong***

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong, or SFO, and any rules made under that Ordinance; or in other circumstances which do not result in the document being a “prospectus” as defined in the Companies Ordinance (Cap. 32) of Hong Kong, or CO, or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

***Israel***

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus is being distributed only to, and is directed only at, and any offer of the shares is directed only at, (i) a limited number of persons in accordance with the Israeli Securities Law and (ii) investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and “qualified individuals,” each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

***Japan***

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the Initial Purchaser will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

***Singapore***

This prospectus has not been and will not be lodged or registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is or will be given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

***Switzerland***

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

***Selling Restrictions Addressing Additional United Kingdom Securities Laws***

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of the Prospectus Regulation that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a "relevant person").

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

## LEGAL MATTERS

Cooley LLP, San Diego, California, which has acted as our counsel in connection with this offering, will pass on certain legal matters with respect to U.S. federal law in connection with this offering. Latham & Watkins LLP has acted as counsel to the underwriters in connection with this offering.

## EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements at December 31, 2019 and 2020 and for the years then ended, as set forth in their report. We have included our consolidated financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

## WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all the information set forth in the registration statement, some of which is contained in exhibits to the registration statement as permitted by the rules and regulations of the SEC. For further information with respect to us and our common stock, we refer you to the registration statement, including the exhibits filed as a part of the registration statement. Statements contained in this prospectus concerning the contents of any contract or any other document are not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The SEC also maintains an internet website that contains reports and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

Upon the closing of this offering, we will be subject to the information reporting requirements of the Exchange Act, and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above.

We also maintain a website at www.reneopharma.com, at which, following the closing of this offering, you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained in, or accessible through, our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is only as an inactive textual reference.

**RENEO PHARMACEUTICALS, INC.**

**INDEX TO FINANCIAL STATEMENTS**

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## 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, 2019 and 2020, the related consolidated statements of operations and comprehensive loss, changes in convertible preferred stock and stockholders' deficit, and cash flows for the years then ended, 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, 2019 and 2020, and the results of its operations and its cash flows for the years then ended, 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 19, 2021
except for the last paragraph of Note 1, as to which the date is
April 5, 2021

**RENEO PHARMACEUTICALS, INC.**

**Consolidated Balance Sheets**
(in thousands, except share and par value amounts)

| | DECEMBER 31, | |
|---|---|---|
| | 2019 | 2020 |
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 17,501 | $ 53,613 |
| Short-term investments | 7,386 | — |
| Prepaid expenses and other current assets | 519 | 1,412 |
| Total current assets | 25,406 | 55,025 |
| Property and equipment, net | 79 | 69 |
| Other non-current assets | 20 | 127 |
| Total assets | $ 25,505 | $ 55,221 |
| **Liabilities, convertible preferred stock and stockholders' deficit** | | |
| Current liabilities: | | |
| Accounts payable | $ 542 | $ 908 |
| Accrued expenses | 2,397 | 3,672 |
| Total current liabilities | 2,939 | 4,580 |
| Deferred rent | 41 | 36 |
| Total liabilities | 2,980 | 4,616 |
| Commitments and contingencies (Note 11) | | |
| Series A convertible preferred stock, $0.0001 par value; 24,302,472 shares authorized at December 31, 2019 and December 31, 2020; 24,302,472 shares issued and outstanding at December 31, 2019 and December 31, 2020, liquidation preference of $52,493 and $49,127 at December 31, 2019 and December 31, 2020, respectively | 45,652 | 45,652 |
| Series B convertible preferred stock, $0.0001 par value; zero and 46,881,028 shares authorized at December 31, 2019 and December 31, 2020, respectively; zero and 23,440,514 shares issued and outstanding at December 31, 2019 and December 31, 2020, respectively; liquidation preference of zero and $47,385 as of December 31, 2019 and December 31, 2020, respectively | — | 47,068 |
| Stockholders' deficit: | | |
| Common stock, $0.0001 par value; 43,000,000 and 105,000,000 shares authorized at December 31, 2019 and December 31, 2020, respectively, 2,008,905 and 2,053,070 shares issued and outstanding at December 31, 2019 and December 31, 2020, respectively | — | — |
| Additional paid-in capital | 2,363 | 2,843 |
| Accumulated deficit | (25,493) | (44,958) |
| Accumulated other comprehensive income | 3 | — |
| Total stockholders' deficit | (23,127) | (42,115) |
| Total liabilities, convertible preferred stock and stockholders' deficit | $ 25,505 | $ 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 amounts)

| | YEAR ENDED DECEMBER 31, | |
|---|---|---|
| | 2019 | 2020 |
| Operating expenses: | | |
| Research and development | $ 13,097 | $ 15,944 |
| General and administrative | 2,376 | 3,608 |
| Total operating expenses | 15,473 | 19,552 |
| Loss from operations | (15,473) | (19,552) |
| Other income: | | |
| Change in fair value of Series A convertible preferred stock purchase right liability | 2,581 | - |
| Other income | 456 | 87 |
| Net loss | (12,436) | (19,465) |
| Other comprehensive income: | | |
| Unrealized gain (loss) on short-term investments | 3 | (3) |
| Comprehensive loss | $ (12,433) | $ (19,468) |
| Net loss per share attributable to common stockholders, basic and diluted | $ (6.38) | $ (9.60) |
| Weighted-average shares used in computing net loss per share, basic and diluted | 1,948,170 | 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' Deficit**
(in thousands, except share amounts)

| | CONVERTIBLE PREFERRED STOCK | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Series A | | Series B | | Common Stock | | ADDITIONAL PAID-IN CAPITAL | ACCUMULATED OTHER COMPREHENSIVE INCOME | ACCUMULATED DEFICIT | Total STOCKHOLDERS DEFICIT |
| | SHARES | AMOUNT | Shares | Amount | SHARES | AMOUNT | | | | |
| Balances, December 31, 2018 | 12,728,397 | $ 20,692 | - | $ - | 1,816,347 | $ — | $ 1,275 | $ - | $ (13,057) | $ (11,78 |
| Common shares issued in connection with licensing agreement | - | - | - | - | 179,150 | — | 673 | - | | 67 |
| Issuance of Series A convertible preferred stock, net of issuance cost of $40 | 11,574,075 | 24,960 | - | - | - | — | - | - | | |
| Stock-based compensation | - | - | - | - | - | — | 388 | - | | 38 |
| Stock option exercise | - | - | - | - | 13,408 | — | 27 | - | | 2 |
| Change in unrealized holding gains and losses on short-term investments | - | - | - | - | - | — | - | 3 | | |
| Net loss | - | - | - | - | - | — | - | - | (12,436) | (12,43 |
| Balances, December 31, 2019 | 24,302,472 | $ 45,652 | - | - | 2,008,905 | $ — | $ 2,363 | $ 3 | $ (25,493) | $ (23,12 |
| Issuance of Series B convertible preferred stock, net of issuance cost of $317 | - | - | 23,440,514 | 47,068 | - | - | - | - | - | |
| Stock-based compensation | - | - | - | - | - | - | 393 | - | - | 39 |
| Stock option exercises | - | - | - | - | 44,165 | - | 87 | - | - | 8 |
| Change in unrealized holding gains and losses on short-term investments | - | - | - | - | - | | - | (3) | - | ( |
| Net loss | - | - | - | - | - | - | - | - | (19,465) | (19,46 |
| Balances, December 31, 2020 | 24,302,472 | $ 45,652 | 23,440,514 | $47,068 | 2,053,070 | $ — | $ 2,843 | $ - | $ (44,958) | $ (42,11 |

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, | |
|---|---|---|
| | 2019 | 2020 |
| Cash flows from operating activities | | |
| Net loss | $(12,436) | $(19,465) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Non-cash expense associated with issuance of common shares in connection with license agreement | 673 | - |
| Depreciation and amortization | 34 | 37 |
| Change in fair value of Series A convertible preferred stock purchase right liability | (2,581) | - |
| Amortization/ accretion on short-term investments | (149) | (17) |
| Loss on disposal of property, plant & equipment | - | 2 |
| Stock-based compensation | 388 | 393 |
| Changes in operating assets and liabilities: | | |
| Accounts payable, accrued expenses and other | 1,034 | 1,486 |
| Prepaid expenses and other assets | 525 | (967) |
| Deferred rent | 2 | (5) |
| Net cash used in operating activities | (12,510) | (18,536) |
| Cash flows from investing activities | | |
| Purchase of property and equipment | (7) | (24) |
| Purchase of available-for-sale short-term investments | (19,834) | - |
| Proceeds from maturities of available-for-sale short-term | 12,600 | 7,400 |
| Net cash (used in) provided by investing activities | (7,241) | 7,376 |
| Cash flows from financing activities | | |
| Proceeds from issuance of Series A convertible preferred stock and Series A convertible preferred stock purchase right liability, net of issuance costs | 24,960 | - |
| Proceeds from issuance of Series B convertible preferred stock, net of issuance costs | - | 47,185 |
| Proceeds from exercise of stock options | 26 | 87 |
| Net cash provided by financing activities | 24,986 | 47,272 |
| Net increase in cash and cash equivalents | 5,235 | 36,112 |
| Cash and cash equivalents, beginning of year | 12,266 | 17,501 |
| Cash and cash equivalents, end of year | $ 17,501 | $ 53,613 |
| **Supplemental cash flow information:** | | |
| Property and equipment in accounts payable | $ - | $ 5 |
| Unpaid Series B convertible preferred stock issuance costs | $ - | $ 117 |
| Costs incurred in connection with initial public offering included in accrued expenses | $ - | $ 33 |

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) was incorporated in the state of Delaware on September 22, 2014 (Inception). The Company is 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.

***Liquidity***

The Company has incurred significant losses and negative cash flows from operations. From Inception through December 31, 2020, the Company has raised $99.2 million primarily from private financings to support its drug development efforts. As of December 31, 2020, the Company had cash and cash equivalents of $53.6 million and an accumulated deficit of $45.0 million. The Company had a net loss of $19.5 million and used cash of $18.5 million for operating activities for the year ended December 31, 2020. In accordance with Accounting Standards Update (ASU) 2014-15, *Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a 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 the recent disruptions to, and volatility in, financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. 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.

The Company raised $47.4 million from the sale of 23,440,514 shares of Series B convertible preferred stock in December 2020 and as of December 31, 2020, the Company had $53.6 million in cash and cash equivalents. Along with the closing of the 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 under the same terms and conditions as the initial closing (Milestone Closing). In March 2021, the Company completed the closing of the Milestone Closing of Series B convertible preferred stock and raised $47.4 million (see Note 7). Management believes that the Company's cash and cash equivalents as of December 31, 2020 and proceeds from the sale of Series B convertible preferred stock in March 2021 will be sufficient to fund operations for at least one year from date on which these consolidated financial statements are issued.

***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 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 conversion prices of the convertible preferred stock 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.

## 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).

The consolidated financial statements include the accounts of Reneo Pharmaceuticals, Inc. and its wholly owned subsidiary, Reneo Pharma Ltd located in the United Kingdom (UK). 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, 2019 and 2020, the Company had cash balances deposited at a major financial institution. Cash balances are subject to minimal credit risk as the balances are with high credit quality financial institutions. Cash and cash equivalents include cash in readily available checking, money market accounts and repurchase agreements.

***Short-term Investments***

The Company accounts for short-term investments in accordance with Accounting Standards Codification (ASC) No. 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 balance sheet date.

At December 31, 2019, 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, 2019 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 tested 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, 2019 and 2020.

***Leases***

Leases are accounted for under ASC 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. Upon the occurrence of certain events that are 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 can cause redemption for cash. Therefore, convertible preferred stock is classified as temporary equity (mezzanine) on the consolidated balance sheets as events triggering the liquidation preferences are not solely within the Company's control. The carrying values of the convertible preferred stock will be adjusted to their liquidation preferences if and when it becomes probable that such a liquidation event will occur.

***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, 2020, the Company's tax years since Inception are subject to examination by taxing authorities in the United States and the UK tax returns from 2019 forward are subject to examination.

***Stock-Based Compensation***

Compensation expense related to stock options granted to employees and non-employees is measured at the grant date based on the estimated fair value of the award and is recognized on a straight-line basis over the requisite service period. Forfeitures are recognized as a reduction of stock-based compensation expense as they occur. The Company estimates the fair value of stock option grants using the Black-Scholes option pricing model.

***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 statement of operations and comprehensive loss. For the years ended December 31, 2019 and 2020, total foreign currency gains and losses were not material.

***Series A Convertible Preferred Stock Purchase Right Liability***

In connection with the Company's Series A convertible preferred stock financing, in addition to the initial closings in December 2017 and January 2018, investors agreed to buy, and the Company agreed to sell, additional shares of Series A convertible preferred stock at a fixed price upon either (i) the board of directors' acceptance of the Company management's recommendation to fund following a successful outcome of one of the Company's planned proof of concept clinical studies, as determined in the sole discretion of the board of directors, or (ii) the approval of the holders holding a majority of the outstanding Series A convertible preferred stock. The Company evaluated this purchase right and concluded that it met the definition of a freestanding instrument. Accordingly, the Company determined the fair value of the purchase right liability and recorded it on the balance sheet with the remainder of the proceeds raised being allocated to convertible preferred stock. The convertible preferred stock purchase right liability was revalued at each reporting period with changes in the fair value of the liability recorded as change in fair value of convertible preferred stock purchase right liability in the consolidated statements of operations and comprehensive loss. The convertible preferred stock purchase right liability was revalued at settlement and the resultant fair value was then reclassified to convertible preferred stock at that time.

***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 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 purposes of this calculation, common stock equivalents include the Company's stock options and convertible preferred stock, which are convertible into shares of the Company's common stock. No shares related to the convertible preferred stock were included in the diluted net loss per share calculation for the years ended December 31, 2019 and 2020 because the inclusion of such shares would have had an anti-dilutive effect. The shares to be issued upon exercise of all outstanding stock options were also excluded from the diluted net loss per share calculation for the years ended December 31, 2019 and 2020 because such shares are anti-dilutive.

The following table sets forth the computation of the basic and diluted net loss per share:

| | Year Ended December 31, | |
|---|---|---|
| | 2019 | 2020 |
| Numerator: | | |
| Net loss (in thousands) | $ (12,436) | $ (19,465) |
| Denominator: | | |
| Weighted-average common shares outstanding | 1,948,170 | 2,028,198 |
| Net loss per share, basic and diluted | $ (6.38) | $ (9.60) |

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

| | December 31, | |
|---|---|---|
| | 2019 | 2020 |
| Convertible preferred stock (as converted) | 5,430,957 | 10,669,291 |
| Common stock options | 984,930 | 935,478 |
| Total | 6,415,887 | 11,604,769 |

***New Accounting Pronouncements***

*Recently Adopted Accounting Standards*

In August 2018, the Financial Accounting Standards Board (FASB) issued ASU 2018-13, *Fair Value Measurement* (Topic 820). The new guidance removes, modifies and adds to certain disclosure requirements on fair value measurements in Topic 820. This new guidance became effective for the Company as of January 1, 2020, and its adoption has not had a material impact on the Company's consolidated financial position or results of operations.

*Recent Accounting Pronouncements Not Yet Adopted*

In December 2019, the FASB issued ASU 2019-12, *Simplifying the Accounting for Income Taxes*. The standard simplifies the accounting for income taxes, eliminates certain exceptions within ASC 740, *Income Taxes*, and clarifies certain aspects of the current guidance to promote consistency among reporting entities. The new guidance will be 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 accounting standard update 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 aren't 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 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 January 1, 2022 with early adoption permitted. The Company plans to adopt the ASU on January 1, 2022 and is currently in the process of evaluating the impact of the application of this accounting standard update on its consolidated financial statements and related disclosures.

### 4. 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, that 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 classifies its money market funds and U.S. Treasury bills as categorized as Level 1, using the quoted prices in active markets. Repurchase agreements are valued using level 2 significant other observable inputs. In addition, the Company estimates the fair values of the convertible preferred stock purchase right liability utilizing Level 3 inputs. No assets or liabilities were transferred into or out of level 3 classifications during the years ended December 31, 2019 and 2020. Estimating the fair values of the convertible preferred stock purchase right liability requires the use of significant and subjective inputs that may, and are likely to, change over the duration of the instrument with related changes in internal and external market factors.

The estimated fair value of the convertible preferred stock purchase right liability was determined using a valuation model that considered the probability of occurrence of the Series A Tranche Right Closing (see Note 7), an assumed discount rate, the number of shares and consideration to be received for the Series A Tranche Right Closing, the estimated time period the Series A convertible preferred stock purchase right would be outstanding, and any changes in the fair value of the underlying Series A convertible preferred stock.

The recurring fair value measurement of the Company's assets and liabilities measured at fair value at December 31, 2019 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 |
|---|---|---|---|---|
| ***Cash equivalents*** | | | | |
| Money market investments | $ 11,737 | $ - | $ - | $11,737 |
| Repurchase agreement | - | 4,000 | - | 4,000 |
| ***Short-term investments*** | | | | |
| U.S. Treasury instruments | 7,386 | - | - | 7,386 |
| Total | $ 19,123 | $ 4,000 | $ - | $23,123 |

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 |
|---|---|---|---|---|
| ***Cash equivalents*** | | | | |
| 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 Series A convertible preferred stock purchase right liability (in thousands):

| | TOTAL PREFERRED STOCK PURCHASE RIGHT LIABILITY |
|---|---|
| Balance, January 1, 2019 | $ 2,581 |
| Changes in estimated fair value of convertible preferred stock purchase right liability in connection with second closing of Series A convertible preferred stock (Note 7) | (2,581) |
| Balance, December 31, 2019 | $ - |

## 5. Property and Equipment, Net

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

| | DECEMBER 31, | |
|---|---|---|
| | 2019 | 2020 |
| Computer, software and office equipment | $ 103 | $ 122 |
| Leasehold improvements | 30 | 30 |
| Total property and equipment, gross | 133 | 152 |
| Less: accumulated depreciation and amortization | (54) | (83) |
| Total property and equipment, net | $ 79 | $ 69 |

Depreciation and amortization expense related to property and equipment was $34,000 and $37,000 for the years ended December 31, 2019 and 2020, respectively.

### 6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

| | DECEMBER 31, | |
|---|---|---|
| | 2019 | 2020 |
| Accrued development expenses | $ 955 | $1,443 |
| Accrued clinical expenses | 702 | 1,019 |
| Accrued compensation | 621 | 888 |
| Other accrued expenses | 119 | 322 |
| Total other accrued expenses | $2,397 | $3,672 |

### 7. Convertible Preferred Stock and Stockholders' Deficit

***Series A Convertible Preferred Stock***

In December 2017, the Company and certain investors entered into a Series A convertible preferred stock purchase agreement, whereby the Company issued 3,006,175 shares of Series A convertible preferred stock at $2.16 per share, which constituted the first closing of the first tranche of Series A convertible preferred stock. Out of the 3,006,175 shares issued in December 2017, 1,154,322 shares were issued as a result of conversion of previously issued convertible promissory notes in accordance with the conversion terms, which included a 20% discount on the Series A convertible preferred stock per share price, and the remaining 1,851,853 shares were newly issued for cash consideration of approximately $4 million. In connection with the first closing of the first tranche of Series A convertible preferred stock in December 2017, the Company issued rights to the purchasers for the purchase of an additional 1,843,753 shares of Series A convertible preferred stock under the same terms and conditions upon either (i) the board of directors' acceptance of the Company's management's recommendation to fund following a successful outcome of one of the Company's planned proof of concept clinical studies, as determined in the sole discretion of the board of directors, or (ii) the approval of the holders holding a majority of the outstanding Series A convertible preferred stock (First Closing Tranche Right).

In January 2018, the Company completed the second closing of the first tranche of Series A convertible preferred stock issuance at $2.16 per share. A total of 9,722,222 shares were issued for cash consideration of approximately $21 million. In connection with the second closing of the first tranche of Series A convertible preferred stock in January 2018, the Company issued rights to the purchasers for the purchase of an additional 9,730,322 shares of Series A convertible preferred stock under the same terms and condition upon either (i) the board of directors' acceptance of the Company's management's recommendation to fund following a successful outcome of one of the Company's planned proof of concept clinical studies, as determined in the sole discretion of the board of directors, or (ii) the approval of the holders holding a majority of the outstanding Series A convertible preferred stock (together with the First Closing Tranche Right, Series A Tranche Right).

The Company evaluated the Series A Tranche Right and concluded that it was a freestanding financial instrument that is recorded at fair value. Accordingly, in connection with each of the first and second closing of the first tranche of Series A convertible preferred stock, the Company estimated the fair value of the corresponding tranche right and accounted for the tranche right as a convertible preferred stock purchase right liability. The Company allocated the proceeds raised using the residual method, with the amount first allocated to the convertible preferred stock purchase right liability at its fair value, and the remainder was allocated to the Series A convertible preferred stock. The Series A convertible preferred stock purchase right was recorded at fair value at each reporting period, with changes in fair value recognized as non-operating income or loss in the consolidated statements of operations and comprehensive loss.

In May 2019, the Company issued an additional 11,574,075 shares of Series A convertible preferred stock to the Series A convertible preferred stockholders in accordance with the Series A Tranche Right provisions for total gross proceeds of $25 million (2019 Series A Financing). The Series A Tranche Right was revalued upon settlement in connection with the 2019 Series A Financing, and the Company recorded the change in the fair value of Series A

Tranche Right between January 1, 2019 and closing date of the 2019 Series A Financing as non-operating income/loss in the consolidated statement of operations and comprehensive loss.

For the year ended December 31, 2019, the Company recognized a gain from the change in the fair value of convertible preferred stock purchase right liability of approximately $2.6 million.

***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 under the same terms and conditions upon the board of directors' determination of either (i) that the cash balance of the Company is below $10 million, or (ii) approving the Company's initial public offering of shares of its common stock pursuant to a registration statement under the Securities Act of 1933 (Series B Tranche Right).

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 were issued for aggregate net proceeds of approximately $47.3 million.

The following are key features of the convertible preferred stock:

*Voting Rights*

Each holder of shares of the Series A and Series B convertible preferred stock is entitled to the number of votes equal to the number of shares of common stock into which such shares of Series A and Series B convertible preferred stock could then be converted.

*Dividends*

The holders of Series A and Series B convertible preferred stock are entitled to a non-cumulative dividend of 8% of the original issue price when, as and if declared by board of directors, only out of funds that are legally available.

*Liquidation Preferences*

Holders of the Series A and Series B convertible preferred stock are entitled to receive liquidation preferences equal to the greater of (a) original issue price plus all declared and unpaid dividends or (b) such amount per share as would have been payable had all shares of such series of preferred stock been converted into common stock immediately prior to such liquidation, dissolution, winding up or deemed liquidation event. Only after payment of the full liquidation preference of Series A and Series B convertible preferred stock, the remaining assets of the Company legally available for distribution shall be distributed ratably to the holders of the common stock.

*Conversion Rights*

At the option of the holder, shares of Series A and Series B convertible preferred shares can be converted into fully paid and non-assessable shares of the Company's common stock on a one-for-one basis subject to the reverse stock split. For additional information regarding the reverse stock split, see "Note 1 - Reverse Stock Split".

Upon either (a) the closing of the sale of shares of common stock to the public in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act resulting in at least $75,000,000 of gross proceeds to the Company (Qualified Initial Public Offering) or (b) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of a majority of the outstanding shares of Series A and Series B convertible preferred stock at the time of such vote or consent, voting together as a single class on an as-converted basis, all outstanding shares of Series A and Series B convertible preferred stock shall automatically be converted into shares of common stock, at the applicable ratio at the time of conversion.

*Redemption*

The Series A and Series B convertible preferred stock are not redeemable. However, the Series A and Series B convertible preferred stock include terms such that there are deemed liquidation events that can trigger redemption of the convertible preferred stock that are outside the control of the Company. Accordingly, the Series A and Series B convertible preferred stock are classified outside of permanent equity on the consolidated balance sheets.

***Shares Reserved for Future Issuance***

As of December 31, 2020, the Company had reserved shares of its common stock for future issuance as follows:

| | Shares Reserved |
|---|---|
| Series A convertible preferred stock outstanding (as converted) | 5,430,957 |
| Series B convertible preferred stock outstanding (as converted) | 5,238,334 |
| Common stock options outstanding | 935,478 |
| Available for future grants under the 2014 Equity Incentive Plan | 2,156,744 |
| Total shares of common stock reserved | 13,761,513 |

## 8. Stock-Based Compensation

In 2014, the Company adopted the 2014 Equity Incentive Plan (the 2014 Plan). The 2014 Plan provides for the issuance of incentive stock options to employees of the Company and non-statutory stock options, restricted stock awards, restricted stock unit awards, stock appreciation rights and other stock awards to directors, employees and consultants of the Company. As of December 31, 2020, the 2014 Plan had a reserve of 3,092,222 shares. As of December 31, 2020, there were 2,156,744 shares available for grant under the 2014 Plan.

The options granted under the 2014 Plan will expire no more than ten years from date of grant. The exercise price of each option is determined by the Company's board of directors, although generally options have an exercise price equal to the estimated fair market value of the Company's stock on the date of the option grant. In the case of incentive stock options, the exercise price is required to be no less than 100% of the estimated fair market value of the Company's common stock at the time the option is granted. For holders of more than 10% of the Company's total combined voting power of all classes of stock, incentive stock options may not be granted at less than 110% of the fair market value of the Company's common stock at the date of grant and for a term not to exceed five years. Most option grants generally vest 25% on the first anniversary of the original vesting commencement date, with the balance vesting monthly over the remaining three years.

Under the 2014 Plan, certain employees may be granted the ability to early exercise their options. The shares of common stock issued pursuant to 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 and non-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, 2020, there have not been early exercises of stock options. If and when early exercises take place, cash received in exchange for exercised and unvested shares related to stock options granted will be recorded as a liability for the early exercise of stock options and transferred into common stock and additional paid-in capital as the shares vest.

A summary of the Company's stock option activity and related information is as follows:

| | Options Outstanding | Weighted-Average Exercise Price | Weighted- Average Remaining Contractual Term |
|---|---|---|---|
| Outstanding at December 31, 2019 | 984,930 | $ 2.53 | 8.7 |
| Granted | 8,043 | | |
| Exercised | (44,165) | | |
| Forfeited/cancelled | (13,330) | | |
| Outstanding at December 31, 2020 | 935,478 | $ 2.56 | 7.7 |
| Vested at December 31, 2020 | 629,383 | $ 2.37 | 7.6 |
| Exercisable at December 31, 2020 | 849,405 | $ 2.52 | 7.7 |

Options exercisable at December 31, 2020 include vested options and options eligible for early exercise. All outstanding options as of December 31, 2020 are expected to vest.

In November 2020, the Company hired a new chief executive officer under which the chief executive officer is entitled to receive a special performance bonus in the amount of $7.5 million, payable in cash, common stock or a combination of cash and common stock, 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 bonus award is subject to *ASC 718, Compensation – Stock Compensation* and includes both market and performance conditions. Because the performance conditions are not considered to be probable until the completion of the Company's initial public offering or change in control, no expense has been recorded on the award for the year ended December 31, 2020.

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, | |
|---|---|---|
| | 2019 | 2020 |
| Risk-free interest rate | 1.98% | 1.00% |
| Expected volatility | 71.7% | 71.7% |
| Expected term (in years) | 6.0 | 5.8 |
| Expected dividend yield | -% | -% |

The weighted average grant date fair value of options granted in 2019 and 2020 was $2.24 and $2.51, respectively.

*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.* 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.

Unrecognized compensation expense at December 31, 2020 for both employee and non-employee stock-based compensation expense was $0.6 million, which is expected to be recognized over a weighted-average vesting term of 1.9 years.

Non-cash stock-based compensation expense recorded in the statement of operations and comprehensive loss is as follows (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2019 | 2020 |
| General and administrative | $231 | $228 |
| Research and development | 157 | 165 |
| Total | $388 | $393 |

## 9. License Agreement

In December 2017, the Company entered into a License Agreement with vTv Therapeutics LLC (vTv Therapeutics) (the vTv License Agreement), under which the Company obtained an exclusive, worldwide, sublicensable license under certain vTv Therapeutics intellectual property to develop, manufacture and commercialize PPARd agonists and products containing such PPARd 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 to vTv Therapeutics 309,576 shares of its common stock. The vTv License Agreement was accounted for as an asset acquisition and the upfront cash payment of $3 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.

vTv Therapeutics was also eligible to receive additional common stock of the Company upon future financing event(s) of the Company of up to $50 million, so that vTv Therapeutics' ownership in the Company was maintained at 7% on a fully diluted basis. In January 2018, upon the second closing of the first tranche of the Series A convertible preferred stock financing, the Company issued an additional 87,717 shares of the Company's common stock to vTv Therapeutics. In May 2019, the Company issued an additional 179,150 shares to vTv Therapeutics in connection with the second tranche closing of the Series A convertible preferred stock, following which the Company is no longer obligated to issue more common stock under the vTv License Agreement. The Company accounted for the additional common stock granted to vTv Therapeutics when the shares were obligated to be issued to vTv Therapeutics. For the year ended December 31, 2019, the Company recorded $0.7 million to research and development expenses in connection with the issuance of shares to vTv Therapeutics.

## 10. Income Taxes

The Company's loss before provision for income taxes was generated in the following jurisdictions (in thousands):

| | December 31, | |
|---|---|---|
| | 2019 | 2020 |
| Domestic | $(17,408) | $(21,291) |
| Foreign | 4,972 | 1,826 |
| | $(12,436) | $(19,465) |

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

| | December 31, 2019 | December 31, 2020 |
|---|---|---|
| **Deferred tax assets:** | | |
| NOL carryforwards | $ 669 | $ 6,488 |
| Credit carryforwards | 170 | 663 |
| Compensation accruals | 124 | 179 |
| Other accruals and reserves | 9 | 24 |
| Intangible assets | 3,564 | 3,316 |
| Other | 1 | 1 |
| **Gross deferred tax assets** | 4,537 | 10,671 |
| Less valuation allowance | (4,527) | (10,662) |
| **Total deferred tax assets** | 10 | 9 |
| **Deferred tax liabilities** | | |
| Depreciation | (10) | (9) |
| **Net deferred tax assets (liabilities)** | $ - | $ - |

For the years ended December 31, 2019 and 2020, the Company recorded no provision for income taxes. A reconciliation of income tax expense 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, 2019 and 2020, as follows:

| | December 31, 2019 | December 31, 2020 |
|---|---|---|
| U. S. Federal statutory income tax rate | 21.0% | 21.0% |
| Foreign rate differential | 0.9% | 0% |
| UK R&D true-up | 0% | 6.5% |
| UK permanent items | 0% | 1.8% |
| Other | -1.6% | -0.3% |
| Tax credits, net | 0.8% | 2.2% |
| GILTI inclusion | -9.3% | -0.2% |
| Valuation allowance | -11.8% | -31.2% |
| Total tax provision | 0.0% | 0.0% |

The Company had federal net operating loss (NOL) carryforwards available of approximately $27.1 million as of December 31, 2020, before consideration of limitations under Section 382 of the Internal Revenue Code (Section 382), as further described below. The federal NOLs generated after 2018 of $25.6 million will carry forward indefinitely. NOLs generated prior to 2018 of $1.5 million will begin to expire in 2034. Additionally, the Company had state NOL carryforwards available of $1.6 million as of December 31, 2020. 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 $4.1 million which carryforward indefinitely.

At December 31, 2020, the Company had federal and state tax credit carry forwards of approximately $0.7 million and $0.2 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, 2020. 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.

In response to the COVID-19 pandemic, the Coronavirus Aid, Relief and Economic Security Act (CARES Act) was signed into law in the U.S. in March 2020. The CARES Act adjusted a number of provisions of the tax code, including the eligibility of certain deductions and the treatment of net operating losses and tax credits. The enactment of the CARES Act did not result in any material adjustments to the Company's income tax provision for the year ended December 31, 2020, or to its deferred tax assets as of December 31, 2020.

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, 2020 was $0.2 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, 2020. 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, 2020, a full valuation allowance of $10.7 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):

| | Years Ended December 31, | |
|---|---|---|
| | 2019 | 2020 |
| Beginning balance of unrecognized tax benefits | $ 555 | $ 168 |
| Additions based on tax positions related to the current year | 100 | 90 |
| Reductions for tax positions in prior years | (487) | - |
| Ending balance of unrecognized tax benefits | $ 168 | $ 258 |

The amount of the unrecognized tax benefits that would impact the effective tax rate, absent the valuation allowance, would be $250,000. Due to the full valuation allowance, the impact, however, is zero. At December 31, 2019 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 twelve 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 2019 forward are subject to examination by the UK tax authorities.

## 11. Commitments and contingencies

***Operating Leases***

In June 2018, the Company leased certain office space for its U.S. headquarters 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. The rent expense in the United States for the years ended December 31, 2019 and 2020 totaled $183,000 for both years.

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 rent expense in the UK for the years ended December 31, 2019 and 2020 totaled $24,000 and $25,000 respectively.

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

| YEAR ENDING DECEMBER 31 | |
|---|---|
| 2021 | $214 |
| 2022 | 197 |
| 2023 | 118 |
| Total minimum lease payments | $529 |

***Legal Proceedings***

The Company is currently not a party to any legal proceedings, nor is the Company aware of any threatened or pending litigations. 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, 2019 and 2020, the expense recorded by the Company was immaterial.

## 12. Subsequent Events - Unaudited

In March 2021, the board of directors increased the option pool by 234,158 shares of common stock.

From January 1, 2021 through April 5, 2021, the Company issued stock options to purchase 2,273,285 shares of common stock with exercise prices ranging from $4.88 to $6.35 per share. The estimated fair value of the options is approximately $7.2 million, which will be recognized over the vesting period of approximately 4 years.

***Approval of the 2021 Equity Incentive Plan***

The Company's board of directors adopted the Company's 2021 Equity Incentive Plan (2021 Plan) in March 2021 and the Company's stockholders approved the 2021 Plan in April 2021. The 2021 Plan became effective immediately prior to the execution of the underwriting agreement in connection with the Company's initial public offering. 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. A total of 2,187,524 new shares of common stock were approved to be initially reserved for issuance under the 2021 Plan. In addition, the number of shares of common stock reserved for issuance under the 2021 Plan includes any 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, plus 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. Subject to adjustments as provided in the 2021 Plan, the number of shares of common stock reserved for issuance under the 2021 Plan will automatically

increase on January 1 of each year, beginning on January 1, 2022, and continuing through and including January 1, 2031, by 5% of the total number of shares of common stock outstanding on December 31 of the immediately preceding calendar year; provided, however, that the Company's board of directors may act prior to January 1st of a given year to provide that the increase for such year will be a lesser number of shares of common stock.

***Approval of the 2021 Employee Stock Purchase Plan***

The Company's board of directors adopted the Company's 2021 Employee Stock Purchase Plan (ESPP) in March 2021 and the Company's stockholders approved the ESPP in April 2021. The ESPP became effective immediately prior to the execution of the underwriting agreement in connection with our initial public offering. A total of 243,058 shares of common stock were approved to be initially reserved for issuance under the ESPP. In addition, the number of shares of common stock available for issuance under the ESPP will be automatically increased on the first day of each calendar year during the first ten-years of the term of the ESPP, beginning with January 1, 2022 and ending with January 1, 2031, by an amount equal to the lessor of (i) 1% of the outstanding number of shares of common stock on December 31st of the preceding calendar year, (ii) 729,174 shares of common stock or (iii) such smaller number of shares of common stock as the Company's board of directors may designate prior to the applicable January 1st.

# 6,250,000 Shares


# Common Stock

**PROSPECTUS**

**Jefferies**
**SVB Leerink**
**Piper Sandler**

April 8, 2021