PROSPECTUS SUPPLEMENT (To Prospectus Dated May 9, 2022)

Up to \$100,000,000



Common Stock

We have entered into a sales agreement, or the sales agreement, with Leerink Partners LLC, or Leerink Partners, relating to the sale of shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, under this prospectus supplement and the accompanying prospectus we may offer and sell shares of our common stock, \$0.0001 par value per share, having an aggregate offering price of up to \$100,000,000 from time to time through or to Leerink Partners, acting as our agent.

Our common stock is listed on the Nasdaq Global Market under the symbol "RPHM." On November 10, 2023, the last reported sale price of our common stock on the Nasdaq Global Market was \$6.40 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made by any method deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Leerink Partners will act as our sales agent, using commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms set forth in the sales agreement. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Leerink Partners for sales of common stock sold pursuant to the sales agreement is equal to 3.0% of the gross proceeds of the sales price per share. See "Plan of Distribution" beginning on page S-12 for additional information regarding the compensation to be paid to Leerink Partners. In connection with the sale of the common stock on our behalf, Leerink Partners will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Leerink Partners will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Leerink Partners with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act.

We are an "emerging growth company" as defined by the Jumpstart Our Business Startups Act of 2012, and as such, have elected to comply with reduced public company reporting requirements for this prospectus supplement and the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus and may elect to comply with reduced public company reporting requirements in future filings.

Investing in our common stock involves a high degree of risk. Please read the information contained in and incorporated by reference under the heading "Risk Factors" beginning on page S-5 of this prospectus supplement, and under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

Leerink Partners

The date of this prospectus is November 13, 2023.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to the offering of shares of our common stock having an aggregate offering price of up to \$100,000,000 under the sales agreement. Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated by reference as described under the heading "Incorporation of Certain Information by Reference" in this prospectus supplement and the information in any free writing prospectus that we may authorize for use in connection with this offering. These documents contain important information that you should consider when making your investment decision.

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the common stock we are offering and also adds to, and updates information contained in, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, including the documents incorporated by reference into the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus supplement, we are referring to the combined document consisting of this prospectus supplement and the accompanying prospectus. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference into the accompanying prospectus that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date, for example, a document incorporated by reference into this prospectus supplement or accompanying prospectus, the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained in, or incorporated by reference into this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we may authorize for use in connection with this offering. We have not, and Leerink Partners has not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we may authorize for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we may authorize for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement titled "Where You Can Find More Information" and "Incorporation of Certain Information by Reference."

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where such offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of our common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of our common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement and the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference into this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we may authorize for use in connection with this offering, including the information contained in and incorporated by reference under the heading "Risk Factors" beginning on page S-5 of this prospectus supplement, and under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement.

Unless the context requires otherwise, references in this prospectus supplement to "Reneo," "the company," "we," "us," "our" or similar terms refer to Reneo Pharmaceuticals, Inc. and its wholly owned subsidiary.

Company Overview

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

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

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

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

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

We have received orphan drug designations for mavodelpar in the United States for PMM and LC-FAOD. Additionally, we have received orphan drug designations for mavodelpar for mitochondrial encephalomyopathy, lactic acidosis, and neurological stroke-like episodes, a form of PMM, and long-chain 3-hydroxy acyl-CoA dehydrogenase, or LCHAD, a form of LC-FAOD in Europe. We have received Fast Track designation for mavodelpar for the treatment of patients with PMM and LC-FAOD due to LCHAD deficiency, one of the predominant LC-FAOD genotypes.

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, or the JOBS Act. We may take advantage of certain exemptions from various public company reporting requirements, including 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, or 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 any golden parachute payments. We may take advantage of these exemptions until December 31, 2026 or until we are no longer an "emerging growth company," whichever is earlier. We will cease to be an emerging growth company prior to the end of such period if certain earlier events occur, including if we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, our annual gross revenues exceed \$1.235 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period.

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

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company, which would allow us to take advantage of many of the same exemptions available to emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation. We will be able to take advantage of the scaled disclosures available to smaller reporting companies 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 in Delaware in September 2014. Our principal executive offices are located at 18575 Jamboree Road, Suite 275-S, Irvine, California 92612, and our telephone number is (858) 283-0280. Our corporate website address is www.reneopharma.com. Our website and the information contained on, or that can be accessed through, our website will not be deemed to be incorporated by reference in, and are not considered part of, this prospectus supplement or the accompanying prospectus. Our design logo, "Reneo," and our other registered and common law trade names, trademarks and service marks are the property of Reneo Pharmaceuticals, Inc.

The Offering

Common stock offered by us

In accordance with the terms of the sales agreement, we may offer and sell shares of our

common stock from time to time through or to Leerink Partners having an aggregate

offering price of up to \$100,000,000.

Common stock to be outstanding after this offering Up to 49,497,166 shares (as more fully described in the notes following this table),

assuming sales of 15,625,000 shares of our common stock in this offering at an assumed offering price of \$6.40 per share, which was the last reported sale price of our common stock on the Nasdaq Global Market on November 10, 2023. The actual number of shares issued will vary depending on how many shares of our common stock we choose to sell

and the prices at which such sales occur.

Plan of Distribution "At the market offering" that may be made from time to time through or to Leerink

Partners as our sales agent or principal. See "Plan of Distribution" on page S-12 of this

prospectus supplement.

Use of Proceeds We currently intend to use the net proceeds from this offering, if any, to fund the

development and commercialization of our programs (if approved), and for general corporate purposes, including working capital, operating expenses and capital expenditures. See "Use of Proceeds" on page S-9 of this prospectus supplement.

Risk Factors Investing in our common stock involves a high degree of risk. Please read the information

contained in and incorporated by reference under the heading "Risk Factors" beginning on page S-5 of this prospectus supplement, and under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement, before deciding whether 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 set forth above is based on 33,872,166 shares of our common stock outstanding as of September 30, 2023, which does not reflect our repurchase of 576,443 shares of our common stock from vTv Therapeutics LLC, or vTv Therapeutics, in October 2023, and excludes:

- 6,095,807 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2023, at a weighted-average exercise price of \$4.71 per share;
- 441,500 shares of our common stock issuable upon the vesting and settlement of restricted stock units outstanding as of September 30, 2023;
- 1,300,869 shares of our common stock reserved for future issuance under our 2021 Equity Incentive Plan, or 2021 Plan, as of
 September 30, 2023, as well as any automatic annual increases in the number of shares of common stock reserved for issuance under
 our 2021 Plan and any shares underlying outstanding stock awards granted under our 2014 Equity Incentive Plan, or 2014 Plan, that
 expire or are repurchased, forfeited, cancelled or withheld; and
- 546,341 shares of our common stock reserved for issuance under our 2021 Employee Stock Purchase Plan, or ESPP, as of September 30, 2023, as well as any automatic annual increases in the number of shares of common stock reserved for future issuance under our ESPP.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and in our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as updated or superseded by the risks and uncertainties described in our subsequent filings under the Exchange Act, each of which is incorporated by reference into this prospectus supplement and the accompanying prospectus in their entirety, and all of the other information in this prospectus supplement and the accompanying prospectus, including our financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus. If any of these risks is realized, our business, financial condition, results of operations and prospects could be harmed. In that event, the trading price of our common stock could decline and you could lose part or all of your investment. Additional risks and uncertainties that are not yet identified or that we think are immaterial may also harm our business, operating results and financial condition and could result in a complete loss of your investment.

Additional Risks Related to This Offering

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 to us from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our drug candidates. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing instruments.

You will suffer immediate dilution of your investment.

The offering prices per share in this offering may exceed the net tangible book value per share of our common stock. Assuming that an aggregate of 15,625,000 shares of our common stock are sold at a price of \$6.40 per share pursuant to this prospectus supplement, which was the last reported sale price of our common stock on the Nasdaq Global Market on November 10, 2023, for aggregate gross proceeds of approximately \$100.0 million, after deducting commissions and estimated aggregate offering expenses payable by us, you would experience immediate dilution of \$\$2.12 per share, representing the difference between our as adjusted net tangible book value per share as of September 30, 2023 after giving effect to this offering at the assumed offering price. The exercise of outstanding stock options or the vesting and settlement of outstanding restricted stock units may result in further dilution of your investment. See the section titled "Dilution" below for a more detailed illustration of the dilution you would incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share paid by any investor in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by any investor in this offering, and investors purchasing shares or other securities in the future could have rights superior to you. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by any investor in this offering.

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. Any return to stockholders will therefore be limited to the appreciation of their stock.

It is not possible to predict the aggregate proceeds resulting from sales made under the sales agreement.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver a placement notice to Leerink Partners at any time throughout the term of the sales agreement. The number of shares that are sold through Leerink Partners after delivering a placement notice will fluctuate based on a number of factors, including the market price of our common stock during the sales period, any limits we may set with Leerink Partners in any applicable placement notice and the demand for our common stock. Because the price per share of each share sold pursuant to the sales agreement will fluctuate over time, it is not currently possible to predict the aggregate proceeds to be raised in connection with sales under the sales agreement.

The common stock offered hereby will be sold in "at the market offerings" and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and accordingly may experience different levels of dilution and different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices and number of shares sold in this offering. In addition, subject to the final determination by our board of directors or any restrictions we may place in any applicable placement notice, there is no minimum or maximum sales price for shares to be sold in this offering. Investors may experience a decline in the value of the shares they purchase in this offering as a result of sales made at prices lower than the prices they paid.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference in this prospectus supplement and the accompanying prospectus contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, and the Private Securities Litigation Reform Act of 1995, as amended, that involve substantial risks and uncertainties. These forward-looking statements speak only as of the date of this prospectus supplement, the accompanying prospectus or the documents incorporated by reference in this prospectus supplement and accompanying prospectus, as applicable, and are subject to a number of risks, uncertainties and assumptions described under the sections in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "project," "positioned," "potential," "seek," "should," "target," "will," "would" or the negative or plural of those terms, and similar expressions intended to identify statements about the future, although not all forward-looking statements contain these words. These forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these statements.

These forward-looking statements are based on our management's current beliefs, expectations and assumptions about future events, conditions and results and on information currently available to us. These statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain.

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 supplement, 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.

Forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus include, but are not limited to, statements about:

- our ability to obtain and maintain regulatory approval for mavodelpar (REN001) in any indication or any of our future product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- · the commercialization of mavodelpar, if approved in any indication;
- our ability to develop and maintain sales and marketing capabilities, whether alone or with potential future collaborators;

- our plans to research, develop and commercialize mayodelpar, including the timing of our ongoing clinical trials of mayodelpar;
- our expectations regarding the size of target patient populations for mavodelpar, if approved for commercial use, and any additional product candidates we may develop;
- the size and growth potential of the markets for mavodelpar, and our ability to serve those markets;
- the rate and degree of market acceptance of mavodelpar, as well as third-party payor coverage and reimbursement for mavodelpar;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our expectations regarding our ability to obtain, maintain, enforce and defend our intellectual property protection for our product candidates;
- regulatory and legal developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- our ability to obtain funding for our operations; and
- the accuracy of our estimates regarding expenses, capital requirements and needs for additional financing.

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 our 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 supplement. See the section titled "Where You Can Find More Information" in this prospectus supplement.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$100,000,000 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the sales agreement with Leerink Partners as a source of financing.

We currently intend to use the net proceeds from this offering to fund the development and commercialization of our programs (if approved) and for general corporate purposes, including working capital, operating expenses and capital expenditures. We may also use a portion of the net proceeds to acquire or invest in businesses and products that are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus.

The amounts and timing of our use of any net proceeds from this offering will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any partnering efforts, technological advances and the competitive environment for our products and product candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from the sale of the securities offered by us hereunder. Accordingly, our management will have broad discretion in the application of the net proceeds and investors will be relying upon the judgment of our management regarding the application of these proceeds. We reserve the right to change the use of these proceeds.

We intend to invest the net proceeds to us from the sale of securities offered hereby that are not used as described above in short-term, investment-grade, interest-bearing instruments.

DILUTION

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

As of September 30, 2023, we had a historical net tangible book value of \$114.9 million, or \$3.39 per share of common stock based on 33,872,166 shares of common stock outstanding, which does not reflect our repurchase of 576,443 shares of our common stock from vTv Therapeutics in October 2023. Our historical net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of common stock outstanding at September 30, 2023.

After giving effect to the sale of our common stock under the sales agreement in the aggregate amount of \$100.0 million at an assumed offering price of \$6.40 per share, the last reported sale price of our common stock on the Nasdaq Global Market on November 10, 2023 and after deducting commissions and estimated aggregate offering expenses payable by us, our net tangible book value as of September 30, 2023 would have been \$211.7 million, or \$4.28 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.89 per share to our existing stockholders and an immediate dilution in net tangible book value of \$2.12 per share to new investors. We determine dilution by subtracting our 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:

	\$6.40
\$3.39	
\$0.89	
	\$4.28
	\$4.28 \$2.12

The table above assumes for illustrative purposes that an aggregate of 15,625,000 shares of our common stock are sold under the sales agreement at a price of \$6.40 per share, the last reported sale price of our common stock on the Nasdaq Global Market on November 10, 2023, for aggregate gross proceeds of \$100.0 million. The shares subject to the sales agreement are being sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$6.40 per share, assuming all of our common stock in the aggregate amount of \$100.0 million is sold at that price, would increase our as adjusted net tangible book value per share after the offering to \$4.47 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$2.93 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$6.40 per share, assuming all of our common stock in the aggregate amount of \$100.0 million is sold at that price, would decrease our as adjusted net tangible book value per share after the offering to \$4.04 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$1.36 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

The above discussion and table are based on 33,872,166 shares of our common stock outstanding as of September 30, 2023, which does not reflect our repurchase of 576,443 shares of our common stock from vTv Therapeutics in October 2023, and excludes:

• 6,095,807 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2023, at a weighted-average exercise price of \$4.71 per share;

- 441,500 shares of our common stock issuable upon the vesting and settlement of restricted stock units outstanding as of September 30, 2023:
- 1,300,869 shares of our common stock reserved for future issuance under our 2021 Plan as of September 30, 2023, as well as any automatic annual increases in the number of shares of common stock reserved for issuance under our 2021 Plan and any shares underlying outstanding stock awards granted under our 2014 Plan that expire or are repurchased, forfeited, cancelled or withheld; and
- 546,341 shares of our common stock reserved for issuance under our ESPP as of September 30, 2023, as well as any automatic annual increases in the number of shares of common stock reserved for future issuance under our ESPP.

To the extent that stock options outstanding as of September 30, 2023 have been or are exercised, outstanding restricted stock units as of September 30, 2023 have or become vested and settled, or other shares are issued, investors purchasing shares in this offering could experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations, including for potential acquisition or in-licensing opportunities, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Leerink Partners under which we may issue and sell up to \$100,000,000 of shares of our common stock from time to time through Leerink Partners as our sales agent. Sales of our common stock, if any, will be made by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act, including sales made directly on or through the Nasdaq Global Market, on or through any other existing trading market for the common stock or to or through a market maker.

Leerink Partners will offer our common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Leerink Partners. We will designate the maximum number or amount of common stock to be sold through Leerink Partners on a daily basis or otherwise determine such maximum number or amount together with Leerink Partners. Subject to the terms and conditions of the sales agreement, Leerink Partners will use commercially reasonable efforts consistent with its normal trading and sales practices to sell on our behalf all of the common stock requested to be sold by us. We may instruct Leerink Partners not to sell common stock if the sales cannot be effected at or above a minimum price designated by us in any such instruction. Leerink Partners or we may suspend the offering of our common stock being made through Leerink Partners under the sales agreement upon proper notice to the other party. Leerink Partners and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party's sole discretion at any time. The offering of our common stock pursuant to the sales agreement will otherwise terminate upon the termination of the sales agreement as provided therein.

The compensation payable to Leerink Partners as sales agent will be 3.0% of the gross proceeds of any shares of common stock sold through it pursuant to the sales agreement. We have also agreed to reimburse Leerink Partners for certain actual outside legal expenses incurred by Leerink Partners in connection with this offering, including Leerink Partners' counsel fees in an amount up to \$75,000, plus certain ongoing fees of its legal counsel. In accordance with FINRA Rule 5110 these reimbursed fees and expenses are deemed sales compensation to Leerink Partners in connection with this offering. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Leerink Partners under the sales agreement, will be approximately \$275,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory or self-regulatory organization in connection with the sales of our common stock, will equal our net proceeds for the sale of such common stock.

Leerink Partners will provide written confirmation to us no later than the next succeeding trading day on the Nasdaq Global Market after each day on which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number or amount of shares sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us from such sales.

We will report at least quarterly the number of shares of common stock sold through Leerink Partners under the sales agreement, the net proceeds to us and the compensation paid by us to Leerink Partners in connection with the sales of common stock during the relevant period.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the second trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sale of the common stock on our behalf pursuant to the sales agreement, Leerink Partners may be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation paid to Leerink Partners may be deemed to be underwriting commissions or discounts. We have agreed in the

sales agreement to provide indemnification and contribution to Leerink Partners with respect to certain liabilities, including liabilities under the Securities Act or the Exchange Act. As sales agent, Leerink Partners will not engage in any transactions that stabilize our common stock.

Our common stock is listed and traded on the Nasdaq Global Market under the symbol "RPHM." The transfer agent and registrar for our common stock is Equiniti Trust Company, LLC. The transfer agent's address is 6201 15th Avenue, Brooklyn, New York 11219.

Leerink Partners and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received, and may in the future receive, customary fees.

LEGAL MATTERS

Cooley LLP, New York, New York, has passed upon the validity of the common stock offered by this prospectus supplement. Leerink Partners is being represented in connection with this offering by Latham & Watkins LLP, San Diego, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2022, as set forth in their report (which contains an explanatory paragraph describing conditions that raise substantial doubt about our ability to continue as a going concern as described in Note 1 to the consolidated financial statements), which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus supplement and the accompanying prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date on the front page of this prospectus supplement, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of the securities offered by this prospectus supplement and the accompanying prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including Reneo Pharmaceuticals, Inc. The address of the SEC website is www.sec.gov.

Copies of certain information filed by us with the SEC are also available on our website at www.reneopharma.com. Information contained in or accessible through our website does not constitute a part of this prospectus supplement or the accompanying prospectus and is not incorporated by reference into this prospectus supplement or the accompanying prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus supplement and the accompanying prospectus. Information in this prospectus supplement supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement, while information that we file later with the SEC will automatically update and supersede the information in this prospectus supplement. We also incorporate by reference into this prospectus supplement and the registration statement of which this prospectus supplement is a part the documents listed below and any future filings made by us with the SEC (other than Current Reports or portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items and other portions of documents that are furnished, but not filed, pursuant to applicable rules promulgated by the SEC) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and prior to the termination of the offering of the common stock covered by this prospectus supplement and the accompanying prospectus:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, filed with the SEC on March 27, 2023;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2022 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed) filed with the SEC on April 26, 2023;
- our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2023, June 30, 2023 and September 30, 2023, filed with the SEC on May 11, 2023, August 10, 2023 and November 13, 2023, respectively;
- our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on March 14, 2023, May 3, 2023, May 5, 2023, June 7, 2023, October 10, 2023 and October 30, 2023; and
- the description of our Common Stock in our registration statement on <u>Form 8-A</u> filed with the SEC on April 6, 2021, including any
 amendments or reports filed for the purpose of updating such description.

We will provide to each person, including any beneficial owner, to whom a prospectus supplement is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus supplement and the registration statement of which this prospectus supplement is a part but not delivered with the prospectus supplement and the accompanying prospectus, including exhibits which are specifically incorporated by reference into such documents. You should direct any requests for documents by writing us at 18575 Jamboree Road, Suite 275-S, Irvine, California 92612, or by telephoning us at (858) 283-0280.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

PROSPECTUS



\$200,000,000

Common Stock Preferred Stock Debt Securities Warrants

From time to time, we may offer up to \$200,000,000 of any combination of the securities described in this prospectus in one or more offerings. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable antidilution provisions.

This prospectus provides a general description of the securities we may offer. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

This prospectus may not be used to consummate a sale of any securities unless accompanied by a prospectus supplement.

Our common stock is traded on the Nasdaq Global Market under the symbol "RPHM." On April 28, 2022, the last reported sales price of our common stock was \$2.34 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on the Nasdaq Global Market or any securities market or other exchange of the securities, if any, covered by the applicable prospectus supplement. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell our securities registered on the registration statement of which this prospectus is a part in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below \$75.0 million. We have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to and including the date of this prospectus.

We will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts or options to purchase additional securities will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

We are an "emerging growth company" as defined by the Jumpstart Our Business Startups Act of 2012, and as such, have elected to comply with reduced public company reporting requirements for this prospectus and the documents incorporated by reference herein and may elect to comply with reduced public company reporting requirements in future filings.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" on page 6 of this prospectus as well as those contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is May 9, 2022

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total aggregate offering price of \$200,000,000. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading "Incorporation of Certain Information by Reference," before investing in any of the securities offered.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

Neither we, nor any agent, underwriter or dealer has authorized any person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus prepared by or on behalf of us or to which we have referred you. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus, any applicable supplement to this prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading "Where You Can Find More Information."

PROSPECTUS SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Unless the context requires otherwise, references in this prospectus to "Reneo," "the company," "we," "us," "our" or similar terms refer to Reneo Pharmaceuticals, Inc. and its wholly owned subsidiary.

Company Overview

Reneo is a clinical-stage pharmaceutical company focused on the development and commercialization of therapies for patients with rare genetic mitochondrial diseases, which are often associated with the inability of mitochondria to produce adenosine triphosphate. Our lead product candidate, REN001, is a potent and selective agonist of the peroxisome proliferator-activated receptor delta, or PPARd. REN001 has been shown to increase transcription of genes involved in mitochondrial function and increase fatty acid oxidation, and may increase production of new mitochondria.

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

Increases in PPARd activity also correlate with a shift in muscle tissue towards oxidative, fat-consuming type I fibers that are associated with endurance as opposed to glycolytic, type II fibers. In preclinical and clinical studies, increased PPARd activity through transgenic overexpression or pharmacological activation increases muscular strength and endurance across a variety of functional measures. REN001 was studied in healthy volunteers with one leg immobilized to produce muscle atrophy. Compared to placebo, administration of REN001 resulted in statistically significant increases in expression of genes involved in mitochondrial oxidative phosphorylation, and statistically significant improvements in muscle strength. REN001 was also studied in an open-label trial in patients with primary mitochondrial myopathies, or PMM. In this trial, administration of REN001 improved function, reduced symptoms, and increased expression of genes involved in mitochondrial activity.

As a PPARd agonist, REN001 may benefit patients with genetic mitochondrial myopathies who experience weakness, fatigue, or deterioration in muscle due to impaired mitochondrial energy production. We are currently developing REN001 in rare genetic diseases that typically present with myopathy and have high unmet medical needs, including PMM and long-chain fatty acid oxidation disorders. Patients with these diseases are unable to perform many everyday activities, can experience cardiomyopathy and other organ dysfunction, and typically have a reduced life expectancy.

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, or the JOBS Act. We may take advantage of certain exemptions from various public company reporting requirements, including 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, or 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 any golden parachute payments. We may take advantage of these exemptions until December 31, 2026 or until we are no longer an "emerging growth company," whichever is earlier. We will cease to be an emerging growth company prior to the end of such period if certain earlier events occur, including if we become a "large accelerated filer" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, or 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 the scaled disclosures available to smaller reporting companies 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 in Delaware in September 2014. Our principal executive offices are located at 18575 Jamboree Road, Suite 275-S, Irvine, California 92612, and our telephone number is (858) 283-0280. Our corporate website address is www.reneopharma.com. Our website and the information contained on, or that can be accessed through, our website will not be deemed to be incorporated by reference in, and are not considered part of, this prospectus. Our design logo, "Reneo," and our other registered and common law trade names, trademarks and service marks are the property of Reneo Pharmaceuticals, Inc.

The Securities We May Offer

We may offer shares of our common stock, shares of our preferred stock, various series of debt securities and warrants to purchase any of such securities, up to a total aggregate offering price of \$200,000,000 from time to time in one or more offerings under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of the relevant offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- · maturity, if applicable;
- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;

- redemption, conversion, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking, if applicable;
- restrictive covenants, if any;
- · voting or other rights, if any; and
- important U.S. federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

We may sell the securities directly to investors or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- · details regarding options to purchase additional securities, if any; and
- the estimated net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. Holders of our common stock are entitled to one vote per share for the election of directors and on all other matters that require stockholder approval. Subject to any preferential rights of any then outstanding preferred stock, in the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the assets remaining after payment of liabilities and the liquidation preferences of any then outstanding preferred stock. Our common stock does not carry any preemptive rights enabling a holder to subscribe for, or receive shares of, our common stock or any other securities convertible into shares of common stock, or any redemption rights.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are

offering before the issuance of the related series of preferred stock. We urge you to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into our common stock or preferred stock. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. A form of indenture has been filed as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental warrant agreements and forms of warrant certificates will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in our Annual Report on Form 10-K for the year ended December 31, 2021, as updated by our annual, quarterly and other reports and documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section below titled "Special Note Regarding Forward-Looking Statements."

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act, and the Private Securities Litigation Reform Act of 1995, as amended, that involve substantial risks and uncertainties. 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; and our expected future financing needs, 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 futur

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 or the documents incorporated by reference in this prospectus. as applicable, and are subject to a number of risks, uncertainties and assumptions described under the sections in this prospectus and the documents incorporated by reference herein entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this prospectus and the documents incorporated by reference herein. 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 forwardlooking 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 More 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.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Except as described in any prospectus supplement or any related free writing prospectus that we may authorize to be provided to you, we currently intend to use the net proceeds from the sale of the securities offered hereby for general corporate purposes, including working capital, operating expenses and capital expenditures. We may also use a portion of the net proceeds to acquire or invest in businesses and products that are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus. We intend to invest the net proceeds to us from the sale of securities offered hereby that are not used as described above in short-term, investment-grade, interest-bearing instruments.

DESCRIPTION OF CAPITAL STOCK

General

The following description summarizes the terms of our capital stock. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description of the matters set forth in this "Description of Capital Stock," you should refer to our amended and restated certificate of incorporation and amended and restated bylaws, which are included as exhibits to the registration statement of which this prospectus forms a part, and to the applicable provisions of the Delaware General Corporation Law.

Our amended and restated certificate of incorporation authorizes us to issue 200,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share. Our board of directors is authorized, without stockholder approval except as required by the listing standards of The Nasdaq Stock Market LLC, to issue additional shares of our capital stock. In addition, under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock.

Common Stock

Voting Rights

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

Economic Rights

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

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

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

No Preemptive or Similar Rights

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

Preferred Stock

Undesignated Preferred Stock

Under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of 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.

Additional Series of Preferred Stock

We will incorporate by reference as an exhibit to the registration statement, which includes this prospectus, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering. This description and the applicable prospectus supplement will include:

- the title and stated value;
- the number of shares authorized;
- · the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date, and method of calculation for dividends;
- · whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;

- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

When we issue shares of preferred stock under this prospectus, the shares will fully be paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

Registration Rights

We are party to an amended and restated investors' rights agreement, dated December 9, 2020, 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 will expire in April 2026, or with respect to any particular stockholder, such time that such stockholder (a) holds less than 1% of our outstanding securities and (b) can sell all of its shares without any restriction on volume or manner of sale in any three-month period under Rule 144 of the Securities Act or any successor rule under the Securities Act.

Demand Registration Rights

Certain holders of shares of our common stock are entitled to certain demand registration rights. With certain exceptions, at any time, 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

Certain holders of shares of our common stock are entitled to certain piggyback registration rights. 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

Certain holders of shares of our common stock are 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.

Anti-Takeover Provisions

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

Certificate of Incorporation and Bylaws

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

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

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

Section 203 of the Delaware General Corporation Law

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

Choice of Forum

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware 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 bylaws provide that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation and our amended and restated bylaws.

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.

Exchange Listing

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

Transfer Agent and Registrar

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

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as "discount securities," which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with "original issue discount," or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- · the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- · our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple
 thereof:
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our
 obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt
 securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;

- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request;
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;

- to comply with the provisions described above under "Description of Debt Securities—Consolidation, Merger or Sale;"
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of
 the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such
 additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the
 indenture:
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under "Description of Debt Securities—General" to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- · hold monies for payment in trust;
- · recover excess money held by the trustee;

- compensate and indemnify the trustee; and
- · appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depositary named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and free writing prospectuses, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be issued independently or together with common stock, preferred stock or debt securities offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement and any applicable free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, if any, including a form of warrant certificate, that describes the terms of the particular series of warrants we are offering. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to the particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms relating to a series of warrants being offered, including:

- the title of such securities;
- the offering price or prices and aggregate number of warrants offered;
- the currency or currencies for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- if applicable, the minimum or maximum amount of such warrants which may be exercised at any one time;
- in the case of warrants to purchase common stock, the number of shares of common stock purchasable upon the exercise of one warrant and the price at which, and the currency in which, these shares may be purchased upon such exercise;
- in the case of warrants to purchase preferred stock, the number of shares of preferred stock purchasable upon the exercise of one warrant and the price at which, and the currency in which, these shares may be purchased upon such exercise;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at which, and currency in which, this principal amount of debt securities may be purchased upon such exercise;

- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- the terms of any rights to force the exercise of the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special U.S. federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase common stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any;
- in the case of warrants to purchase preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any; or
- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture,

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent in connection with the exercise of the warrant.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements, and any claim, controversy or dispute arising under or related to the warrants or warrant agreements, will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee or depositary maintain for this purpose as the "holders" of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as "indirect holders" of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Global securities will be registered in the name of the depositary or its participants. Consequently, for global securities, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in "street name." Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depositary will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any such trustee or depositary will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee or third party employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the legal holder, we have no further responsibility for the payment or notice even if that legal holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of an indenture, or for other purposes. In such an event, we would seek approval only from the legal holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- · whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the
 future:
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under "—Special Situations When a Global Security Will Be Terminated." As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued as a global security, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only as global securities, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law
 to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in the global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in the global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in the global security, nor will we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, a global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own names, so that they will be direct holders. We have described the rights of holders and street name investors above.

A global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and neither we nor any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities covered hereby from time to time pursuant to underwritten public offerings, direct sales to the public, negotiated transactions, block trades or a combination of these methods. A distribution of these securities offered by this prospectus may also be effected through the issuance of derivative securities, including without limitation, warrants. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We may also sell equity securities covered by this registration statement in an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price, either:

- on or through the facilities of the Nasdaq Global Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- to or through a market maker other than on the Nasdaq Global Market or such other securities exchanges or quotation or trading services.

Such at-the-market offerings, if any, may be conducted by underwriters acting as principal or agent.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of any underwriters, dealers or agents, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any options pursuant to which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any option to purchase additional securities. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to

time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions and other compensation we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any agents or underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities. There is currently no market for any of the offered securities, other than our common stock which is listed on the Nasdaq Global Market. We have no current plans for listing of the preferred stock, debt securities or warrants on any securities exchange or quotation system; any such listing with respect to any particular preferred stock, debt securities or warrants will be described in the applicable prospectus supplement or other offering materials, as the case may be.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Rule 103 of Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any agents and underwriters who are qualified market makers on the Nasdaq Global Market may engage in passive market making transactions in the securities on the Nasdaq Global Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, certain legal matters in connection with the offering and the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon by Cooley LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2021, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including Reneo Pharmaceuticals, Inc. The address of the SEC website is www.sec.gov.

Copies of certain information filed by us with the SEC are also available on our website at www.reneopharma.com. Information contained in or accessible through our website does not constitute a part of this prospectus and is not incorporated by reference into this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We also incorporate by reference into this prospectus the documents listed below and any future filings made by us with the SEC (other than Current Reports or portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items and other portions of documents that are furnished, but not filed, pursuant to applicable rules promulgated by the SEC) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the filing and concurrent effectiveness of the registration statement but prior to the termination of all offerings covered by this prospectus:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, filed with the SEC on March 23, 2022;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed) filed with the SEC on April 22, 2022;
- our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on <u>January 24, 2022</u>, <u>February 2, 2022</u> and <u>March 7, 2022</u>; and
- the description of our Common Stock in our registration statement on Form 8-A filed with the SEC on April 6, 2021, including any
 amendments or reports filed for the purpose of updating such description.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. You should direct any requests for documents by writing us at 18575 Jamboree Road, Suite 275-S, Irvine, California 92612, or by telephoning us at (858) 283-0280.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

Up to \$100,000,000



Common Stock PROSPECTUS SUPPLEMENT Leerink Partners

November 13, 2023