

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Filed Pursuant to Rule 424(b)(5)  
Registration No. 333-264091

Subject to Completion, dated December 7, 2022

**PRELIMINARY PROSPECTUS SUPPLEMENT**  
**(To Prospectus dated April 1, 2022)**

\$250,000,000



**Common Stock**

We are offering \$250,000,000 of our common stock.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "RXDX." On December 6, 2022, the last reported sales price of our common stock on the Nasdaq Global Select Market was \$36.06 per share of common stock.

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

**Investing in our common stock involves risks. See "[Risk Factors](#)" beginning on page S-5 of this prospectus supplement and the documents incorporated by reference into this prospectus supplement.**

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

	Per share	Total
Public offering price	\$	\$
Underwriting discounts and commissions <sup>(1)</sup>	\$	\$
Proceeds to Prometheus, before expenses	\$	\$

(1) We have agreed to reimburse the underwriters for certain FINRA-related expenses. See "Underwriting" for additional information regarding compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to an additional \$37,500,000 of shares of common stock from us at the public offering price, less the underwriting discounts and commissions.

The underwriters expect to deliver the shares of common stock to purchasers on or about December , 2022.

**Goldman Sachs & Co. LLC**                      **SVB Securities**                      **Jefferies**                      **Guggenheim Securities**

The date of this prospectus supplement is December , 2022.

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## ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus dated April 1, 2022 are part of a registration statement that we filed with the Securities and Exchange Commission (SEC) utilizing a “shelf” registration process. This prospectus supplement and the accompanying prospectus relate to the offer by us of shares of our common stock to certain investors. We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying prospectus or any document incorporated by reference herein prior to the date of this prospectus supplement, you should rely on this prospectus supplement. However, 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 in this prospectus supplement or the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates. You should read this prospectus supplement, the accompanying prospectus, the documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering when making your investment decision. You should also read and consider the information in the documents we have referred you to under the headings “Where You Can Find More Information; Information Incorporated by Reference.”

We have not, and the underwriters have not, authorized anyone to provide you with information that is different from that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by or on behalf of us in connection with this offering. We are offering to sell and seeking offers to buy shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement, the accompanying prospectus, the documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering are accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement or of any sale of our common stock.

In this prospectus supplement, unless the context otherwise indicates, the terms “Prometheus,” the “Company,” “we,” “our” and “us” or similar terms refer to Prometheus Biosciences, Inc.

We use our trademarks in this prospectus supplement as well as trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus supplement appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

## PROSPECTUS SUPPLEMENT SUMMARY

*This summary provides an overview of selected information contained elsewhere in or incorporated by reference in this prospectus supplement and the accompanying prospectus and does not contain all the information you should consider before investing in our common stock. Therefore, you should read the entire prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the “Risk Factors” section, and other documents or information included or incorporated by reference in this prospectus supplement and the accompanying prospectus before making any investment decision.*

### **Prometheus Biosciences, Inc.**

We are a clinical-stage biotechnology company pioneering a precision medicine approach to the discovery, development, and commercialization of novel therapeutic and companion diagnostic products for the treatment of immune-mediated diseases, starting first with inflammatory bowel disease (IBD). We leverage our proprietary precision medicine platform, Prometheus360™, which includes one of the world’s largest gastrointestinal (GI) bioinformatics databases and sample biobanks, to identify novel therapeutic targets and develop therapeutic candidates to engage those targets. In parallel, we are developing genetic-based companion diagnostic tests designed to identify patients more likely to respond to our therapeutic candidates. We have generated a robust pipeline of therapeutic development programs for the treatment of immune-mediated diseases.

Our lead product candidate, PRA023, is a humanized IgG1 monoclonal antibody (mAb) that has been shown to block the tumor necrosis factor (TNF)-like ligand 1A (TL1A), a target associated with both intestinal inflammation and fibrosis. PRA023 has the potential to substantially improve outcomes for moderate-to-severe IBD patients, especially those predisposed to increased TL1A expression. PRA023’s dual mechanism of action, targeting both inflammation and fibrosis, also provides a strong rationale for investigating the potential applicability of TL1A antagonism in areas outside IBD including indications in dermatology, pulmonary or hepatobiliary disease.

In July 2021, we advanced PRA023 into a global Phase 2 randomized placebo-controlled clinical trial in patients with moderate-to-severe UC (ARTEMIS-UC) and an open-label Phase 2a clinical trial in patients with moderate-to-severe Crohn’s disease (CD) (APOLLO-CD), each utilizing our genetics-based companion diagnostic candidate (CDx) designed to identify patients who are predisposed to increased expression of TL1A and therefore potentially more likely to respond to PRA023.

In June 2022, we completed enrollment for APOLLO-CD, which was statistically powered to evaluate the safety and efficacy of PRA023 in approximately 50 patients. In July 2022, we completed enrollment of the initial cohort (Cohort 1) for ARTEMIS-UC, which was statistically powered to evaluate the safety and efficacy of PRA023 in approximately 120 patients, and began enrollment in the expansion cohort (Cohort 2), which is designed to further evaluate the treatment effect of PRA023 in approximately 40 additional patients who are companion diagnostic positive.

In March 2022, we initiated a Phase 2 clinical trial for PRA023 in Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD). The U.S. Food and Drug Administration (FDA) granted fast track designation for PRA023 for the treatment of SSc-ILD in January 2022. Topline results from our Phase 2 trial of PRA023 in Systemic Sclerosis-Associated Interstitial Lung Disease (ATHENA-SSc-ILD) are expected in the first half of 2024.

Our second product candidate, PRA052, is an anti-CD30L mAb. The CD30L-CD30 co-stimulatory pathway has been implicated in IBD by genetic, preclinical, and human translational data. In preclinical studies, CD30L antagonism was observed to improve multiple animal models of colitis. PRA052 is designed to have high affinity and specificity for CD30L and to block both transmembrane and soluble CD30L. We filed an investigational new drug application (IND) for PRA052 in the third quarter of 2022 and the FDA cleared us to proceed. We initiated a Phase 1 single ascending dose/multiple ascending dose clinical trial in normal healthy volunteers in the fourth quarter of 2022 and expect results in the fourth quarter of 2023. We are also developing a proprietary genetics-based companion diagnostic test for PRA052 to identify patients that are more likely to respond to CD30L inhibition.

### **Recent Developments**

In December 2022, we reported results from our ARTEMIS-UC Phase 2 and APOLLO-CD Phase 2a studies of PRA023 demonstrating strong efficacy and favorable safety results in both studies. Based on the totality of the data in these two studies, we intend to advance PRA023 into Phase 3 studies for UC and CD in 2023.

#### *Topline Results from the ARTEMIS-UC Phase 2 Study*

Our Phase 2 ARTEMIS-UC clinical trial was a 12-week, double-blind, placebo-controlled, randomized study to evaluate the efficacy and safety of PRA023 in patients with moderately to severely active UC who have failed conventional or advanced therapy. PRA023 met the primary and all ranked secondary endpoints including clinical, endoscopic, histologic, and patient-reported outcome measures in the initial cohort (Cohort 1) of the trial. All 68 of the 68 PRA023-treated patients completed the Cohort 1 study, compared to 60 of the 67 patients in the placebo group. The topline results for the key endpoints were as follows:

- 26.5% of patients on PRA023 reached the primary endpoint of clinical remission (per modified Mayo Score), compared to 1.5% on placebo, for a placebo-adjusted clinical remission rate of 25.0% on the primary endpoint ( $p < 0.0001$ );
- 36.8% of patients on PRA023 reached the secondary endpoint of endoscopic improvement (Mayo endoscopy subscore of  $\leq 1$ ), compared to 6.0% on placebo, for a placebo-adjusted endoscopic improvement rate of 30.8% on the secondary endpoint ( $p < 0.0001$ ); and
- All secondary endpoints met with statistical significance.

PRA023 was well tolerated in Cohort 1, with no treatment-emergent serious adverse events (SAEs), adverse events (AEs) leading to discontinuation, severe AEs, opportunistic infections or infusion reactions reported in the PRA023 treatment group. The only AE that occurred in more than two patients and at a higher frequency in the PRA023 group compared to placebo was COVID-19 (5 out of 68 [7.4%] and 3 out of 67 patients [4.5%], respectively).

Based upon confidence in our precision approach and speed to market, we conducted an interim CDx analysis of Cohort 1 to evaluate the effectiveness of the CDx candidate in ARTEMIS-UC. Although from limited patient numbers, data from the subset of patients who tested positive on the CDx in Cohort 1 ( $N=32$ ) demonstrated a placebo-adjusted clinical remission rate of 37.5%, compared with the placebo-adjusted remission rate of 25.0% for all-comers. The expansion cohort (Cohort 2) will continue to enroll, and we expect results in the second quarter of 2023.

*Results from the APOLLO-CD Phase 2a Study*

Our Phase 2a APOLLO-CD clinical trial was a 12-week open-label study that enrolled 55 patients with moderate-to-severely active CD with endoscopically active disease who had failed conventional or biologic therapy. The study enrolled a highly refractory patient population with 70.9% of patients previously treated with at least one biologic therapy and 52.7% treated with two or more biologic therapies. The results on the key endpoints were as follows:

- 26.0% of patients on PRA023 achieved endoscopic response (p=0.002 compared to 12% prespecified historical placebo rate); and
- 49.1% of patients on PRA023 achieved clinical remission (p<0.001 compared to 16% prespecified historical placebo rate).

PRA023 was well tolerated in the APOLLO-CD study. There were no treatment-emergent SAEs, AEs leading to discontinuation, or severe AEs assessed as related to PRA023 by the investigator. There were no opportunistic infections or infusion reactions reported. AEs that occurred in more than two patients included COVID-19, urinary tract infection, CD, anemia, nasopharyngitis and fatigue.

The predictive power of our prespecified genetic markers was validated using an alternative Crohn's-specific CDx algorithm which showed 45.0% (9/20) endoscopic response relative to all-comers of 26% (13/50). While the original algorithm provided limited benefit on some of the endpoints, the alternative algorithm demonstrated enhanced performance across both clinical and endoscopic outcomes. We plan to advance this alternative algorithm in registrational studies for CD. In addition, a compelling reduction in markers of inflammation and fibrosis was observed between pre-treatment and post-treatment with PRA023, as measured by circulating cytokine levels, immunohistochemistry and gene expression in disease tissue.

**Corporate Information**

We were originally founded as a Delaware corporation on October 26, 2016, under the name Precision IBD, Inc. On October 3, 2019, we changed our name to Prometheus Biosciences Inc. Our principal executive offices are located at 3050 Science Park Road, San Diego, California 92121, and our telephone number is 858-422-4300. Our website address is [www.prometheusbiosciences.com](http://www.prometheusbiosciences.com). The information on, or accessible through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

## THE OFFERING

Common stock offered by us	\$250.0 million of shares
Option to purchase additional shares	We have granted the underwriters an option exercisable for a period of 30 days after the date of this prospectus supplement to purchase up to \$37.5 million of additional shares of our common stock.
Common stock to be outstanding immediately after this offering	shares (or shares if the underwriters exercise in full their option to purchase additional shares of our common stock in full)
Use of proceeds	We intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments to fund the development of PRA023, PRA052 and our other research and development programs, and for working capital and general corporate purposes. See "Use of Proceeds".
Risk factors	You should read the "Risk Factors" section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to invest in our common stock.
Nasdaq Global Select Market symbol	"RXDX"

The number of shares of common stock to be outstanding immediately after this offering is based on 41,848,181 shares outstanding as of September 30, 2022, including 6,127 shares subject to forfeiture or our right of repurchase, and excludes:

- 7,314,511 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2022, at a weighted average exercise price of \$15.62 per share;
- 112,886 shares of common stock issuable upon the settlement of restricted stock units outstanding as of September 30, 2022;
- 3,205,633 shares of common stock reserved for future issuance under our 2021 Incentive Award Plan and our 2021 Employee Stock Purchase Plan as of September 30, 2022; and
- 14,884 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2022, at a weighted-average exercise price of \$7.558 per share.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding options and no exercise by the underwriters of their option to purchase up to an additional shares of our common stock.

## RISK FACTORS

*You should consider carefully the risks described below and discussed under the section captioned “Risk Factors” contained in our Annual Report on Form 10-K for the year ended December 31, 2021 as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended (the Exchange Act), which are incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, together with other information in this prospectus supplement, the accompanying prospectus and the information and documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our common stock. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.*

### Risks Relating to This Offering

**If you purchase shares of our common stock sold in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares. In addition, we may issue additional equity or convertible debt securities in the future, which may result in additional dilution to investors.**

The offering price per share of common stock in this offering is considerably more than the net tangible book value per share of our outstanding common stock. As a result, investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the value of our tangible assets after subtracting liabilities. Based upon the public offering price of \$ \_\_\_\_\_ per share, new investors will incur immediate dilution of \$ \_\_\_\_\_ per share based on the net tangible book value as of September 30, 2022. For a more detailed discussion of the foregoing, see “Dilution.” To the extent outstanding stock options are exercised, there will be further dilution to new investors. In addition, to the extent we need to raise additional capital in the future and we issue additional shares of common stock or securities convertible or exchangeable for our common stock, our then existing stockholders may experience dilution and the new securities may have rights senior to those of our common stock offered in 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 from this offering, including for any of the purposes described in “Use of Proceeds,” and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. We expect to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments to fund the development of PRA023, PRA052 and our other research and development programs, and for working capital and general corporate purposes. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short- and immediate-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.



## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Exchange Act. All statements other than statements of historical facts contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein are forward-looking statements, including statements regarding future results of operations and financial position, business strategy, research and development plans, the anticipated timing, costs, design and conduct of our ongoing and planned preclinical studies and clinical trials for our product candidates, our plans to use our Prometheus360 product platform to expand our pipeline of product candidates and develop marketable products, the anticipated timing and costs of our development of companion diagnostics, the potential benefits from our collaboration arrangements with third parties and our plans to enter into additional arrangements, the timing and likelihood of regulatory filings and approvals for our product candidates and companion diagnostics, our ability to commercialize our product candidates, if approved, the impact of COVID-19 on our business, the pricing and reimbursement of our product candidates, if approved, and testing products, the potential to develop future product candidates, the timing and likelihood of success, plans and objectives of management for future operations, and future results of anticipated product development efforts, and the anticipated use of proceeds from this offering, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

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 supplement, the accompanying prospectus and the documents incorporated by reference herein 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 supplement and are subject to a number of risks, uncertainties and assumptions, which we discuss in greater detail in the documents incorporated by reference herein, including under the heading “Risk Factors” and elsewhere in this prospectus supplement. 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. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

## USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately \$                    million from the sale of                    shares of common stock offered by us in this offering, or approximately \$                    million if the underwriters exercise in full their option to purchase up to an additional                    shares of common stock, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments to fund the development of PRA023, PRA052 and our other research and development programs, and for working capital and general corporate purposes.

The amounts and timing of our actual expenditures will depend on numerous factors, including the factors described under “Risk Factors” in this prospectus supplement and in the documents incorporated by reference herein, as well as the amount of cash used in our operations. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short- and intermediate-term, investment-grade, interest-bearing securities.

## 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 and the net tangible book value per share of our common stock after this offering. As of September 30, 2022, our net tangible book value was \$232.5 million, or \$5.56 per share, based on 41,848,181 shares of our common stock outstanding as of September 30, 2022. Our net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities, divided by the total number of shares of our common stock outstanding as of September 30, 2022.

After giving effect to our sale in this offering of \_\_\_\_\_ shares of common stock at the public offering price of \$ \_\_\_\_\_ per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of September 30, 2022 would have been approximately \$ \_\_\_\_\_ million, or \$ \_\_\_\_\_ per share of common stock. This represents an immediate increase in net tangible book value of \$ \_\_\_\_\_ per share to our existing stockholders and immediate dilution of \$ \_\_\_\_\_ per share to new investors purchasing our common stock in this offering. The following table illustrates this per share dilution to the new investors purchasing common shares in this offering.

Public offering price per share	\$
Net tangible book value per share at September 30, 2022	\$5.56
Increase per share attributable to investors purchasing shares in this offering	_____
As adjusted net tangible book value per share, after giving effect to this offering	_____
Dilution per share to investors purchasing our common stock in this offering	\$ _____

If the underwriters exercise in full their option to purchase up to an additional \_\_\_\_\_ shares of our common stock at the public offering price of \$ \_\_\_\_\_ per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value after this offering would be \$ \_\_\_\_\_ per share, representing an immediate increase in net tangible book value of \$ \_\_\_\_\_ per share to our existing stockholders and immediate dilution of \$ \_\_\_\_\_ per share to new investors purchasing common stock in this offering.

The foregoing tables and calculations (other than net tangible book value calculations) are based on 41,848,181 shares outstanding as of September 30, 2022, including 6,127, shares subject to forfeiture or our right of repurchase, and excludes:

- 7,314,511 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2022, at a weighted average exercise price of \$15.62 per share;
- 112,886 shares of common stock issuable upon the settlement of restricted stock units outstanding as of September 30, 2022;
- 3,205,633 shares of common stock reserved for future issuance under our 2021 Incentive Award Plan and our 2021 Employee Stock Purchase Plan as of September 30, 2022; and
- 14,884 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2022, at a weighted-average exercise price of \$7.558 per share.

To the extent that outstanding options are exercised, you may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital by issuing equity or convertible debt securities, your ownership will be further diluted.

## UNDERWRITING

We and the representatives for the underwriters for the offering named below will enter into an underwriting agreement with respect to the common stock being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of our common stock set forth opposite its name below. Goldman Sachs & Co. LLC, SVB Securities LLC and Jefferies LLC are the representatives of the underwriters.

Underwriter	Number of Shares
Goldman Sachs & Co. LLC	
SVB Securities LLC	
Jefferies LLC	
Guggenheim Securities, LLC	
Total	

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the option to purchase additional shares described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Sales of a substantial number of such shares upon expiration of the lock-up and market stand-off agreements, the perception that such sales may occur, or early release of these agreements, could cause our market price to fall or make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

*Option to Purchase Additional Shares.* We have granted to the underwriters an option to purchase up to \_\_\_\_\_ additional shares of our common stock at the public offering price, less the underwriting discounts and commissions. This option is exercisable for a period of 30 days. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

*Discounts and Commissions.* The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Per Share	Total Without Option to Purchase Additional Shares	With Full Option to Purchase Additional Shares
Public offering price	\$	\$	\$
Underwriting discounts and commissions	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

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We estimate that the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$285,000 and are payable by us. We also have agreed to reimburse the underwriters for up to \$25,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

The underwriters propose to offer the shares of our common stock to the public at the public offering price set forth on the cover of this prospectus supplement. The underwriters may offer the shares of our common stock to securities dealers at the public offering price less a concession not in excess of \$ \_\_\_\_\_ per share. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

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

*Stabilization.* In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions permit bids to purchase shares of our common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.
- Overallotment transactions involve sales by the underwriters of shares of our common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in the option to purchase additional shares. The underwriters may close out any short position by exercising their option to purchase additional shares and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the option to purchase additional shares. If the underwriters sell more shares than could be covered by exercise of the option to purchase additional shares and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.
- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on Nasdaq, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

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*Passive Market Making.* In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M under the Exchange Act, during a period before the commencement of offers or sales of common stock and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, such bid must then be lowered when specified purchase limits are exceeded.

*Lock-Up Agreements.* Pursuant to certain "lock-up" agreements, we and certain of our directors and executive officers have agreed that, without the prior written consent of Goldman Sachs & Co. LLC, SVB Securities LLC and Jefferies LLC, we or such other person will not, during the period ending 90 days after the day of this prospectus supplement, (i) directly or indirectly, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock, or (ii) enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of the common stock, whether any such swap or transaction described in clause (i) or (ii) above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we have agreed not to publicly announce an intention to effect any such swap, agreement or other transaction or file or confidentially submit any registration statement under the Securities Act with respect to any of the foregoing, and our directors and officers have agreed not to exercise any right with respect to the registration of any such securities.

The restrictions described above do not apply to us in respect of: (i) the sale of the shares to the underwriters; (B) any shares of common stock issued upon the exercise of an option or warrant or the conversion of a convertible security outstanding on the date of this offering; (iii) any shares of common stock issued or options to purchase common stock granted pursuant to existing employee benefit plans; (iv) any shares of common stock issued pursuant to any existing non-employee director stock plan or dividend reinvestment plan; (v) the filing of any registration statement on Form S-8 or a successor form thereto; or (vi) shares of common stock, or securities convertible into, exercisable for, or which are otherwise exchangeable for, common stock, in commercial, licensing or collaborations transactions, acquisitions or other similar strategic transactions, provided that the aggregate number of shares of common stock, or securities convertible into, exercisable for, or which are otherwise exchangeable for, common stock (on an as-converted, as-exercised or as-exchanged basis, as the case may be) that we may sell or issue or agree to sell or issue pursuant to this clause (vi) shall not exceed 5% of the total number of shares of common stock issued and outstanding immediately following the completion of this offering and the recipient of any such shares or securities shall enter into a lock-up agreement with the underwriters.

The restrictions described above do not apply to directors or executive officers in respect of transfers by any such person: (i) as bona fide gifts, (ii) to any trust for the direct or indirect benefit of such person or his or her immediate family; (iii) to such person's affiliates or to any investment fund or other entity controlled or managed by such person; (iv) pursuant to a court or regulatory agency order, a qualified domestic relations order or in connection with a divorce settlement; (v) by will or intestate succession upon the death of such person; (vi) if the undersigned is a trust, to a trustor, trustee (or co-trustee) or beneficiary of the trust or to the estate of the beneficiary of such trustor; (vii) to the Company in satisfaction of any tax withholding obligation; (viii) to the Company in connection with the termination of such person's services to the Company; (ix) in connection with the exercise or exchange by such person of any option or warrant to acquire any shares of common stock or options to purchase shares of common stock, in each case for cash or on a "cashless" or "net exercise" basis, pursuant to any stock option, stock bonus or other stock plan or arrangement; (x) upon the completion of a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all holders of the Company's

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securities involving a change of control of the Company; (xi) transactions relating to common stock or other securities convertible into or exercisable or exchangeable for common stock acquired in this offering or in open market transactions after completion of the offering; and (xii) the sale of common stock pursuant to an existing 10b5-1 trading plan.

*Electronic Offer, Sale and Distribution of Shares.* A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus supplement or the registration statement of which this prospectus supplement forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

### *Other Relationships.*

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses. Jefferies LLC is the sales agent under our sales agreement, dated April 1, 2022. Under the sales agreement, we may offer and sell, from time to time, shares of our common stock through Jefferies LLC through an “at the market offering,” as defined in Rule 415(a)(4) promulgated under the Securities Act.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

### *Selling Restrictions*

Other than in the United States, no action has been taken by us, or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not

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constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

*European Economic Area.* In relation to each Member State of the European Economic Area and the United Kingdom (each a "Relevant State"), no shares of common stock (the "Shares") have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the Shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that offers of Shares may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

- (a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the Representatives for any such offer; or
- (c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of Shares shall require the Company or any Representative to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

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

*United Kingdom.* No shares or pre-funded warrants have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the shares or pre-funded warrants which has been approved by the Financial Conduct Authority, except that the shares or pre-funded warrants may be offered to the public in the United Kingdom at any time:

- (a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the Representative for any such offer; or
- (c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of the shares or pre-funded warrants shall require us or any underwriter to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the U.K. Prospectus Regulation. For the purposes of this provision, the expression an "offer to the public" in relation to the shares or pre-funded warrants in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares or pre-funded warrants to be offered so as to enable an investor to decide to purchase or subscribe for any shares or pre-funded warrants and the expression "U.K. Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as



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defined in the U.K. Prospectus Regulation) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the “Order,” and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”) or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares or pre-funded warrants in the United Kingdom within the meaning of the FSMA. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons. Any person in the UK who is not a relevant person must not act on or rely upon this document or any of its contents.

### **Canada**

The securities may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption form, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

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

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

### **Switzerland**

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

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

### **Dubai International Financial Centre (“DIFC”)**

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority (“DFSA”). This document is intended for distribution only to persons

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of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for this document. The securities to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this document you should consult an authorized financial advisor.

In relation to its use in the DIFC, this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the securities may not be offered or sold directly or indirectly to the public in the DIFC.

### **United Arab Emirates**

The shares have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus supplement does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus supplement has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

### **Australia**

This prospectus supplement:

- does not constitute a disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth) (the "Corporations Act");
- has not been, and will not be, lodged with the Australian Securities and Investments Commission ("ASIC"), as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document for the purposes of the Corporations Act; and
- may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, available under section 708 of the Corporations Act ("Exempt Investors").

The shares may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the shares may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any shares may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the shares, you represent and warrant to us that you are an Exempt Investor.

As any offer of shares under this document will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the shares you undertake to us that you will not, for a period of 12 months from the date of issue and sale of the shares, offer, transfer, assign or otherwise alienate those shares to investors in Australia except in

circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

### **Hong Kong**

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) (“Companies (Winding Up and Miscellaneous Provisions) Ordinance”) or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (“Securities and Futures Ordinance”), or (ii) to “professional investors” as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

### **Singapore**

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the “SFA”)) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation’s securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore (“Regulation 32”)

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries’ rights and interest (howsoever described) in that trust shall not be

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transferable for 6 months after that trust has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

### ***Japan***

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

### ***Israel***

In the State of Israel this prospectus supplement shall not be regarded as an offer to the public to purchase shares of common stock or pre-funded warrants under the Israeli Securities Law, 5728—1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728—1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions, or the Addressed Investors, or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728—1968, subject to certain conditions, or the Qualified Investors. The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728—1968. We have not and will not distribute this prospectus supplement or make, distribute or direct an offer to subscribe for our common stock or pre-funded warrants to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request, as a condition to be offered common stock or pre-funded warrants, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728—1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock or pre-funded warrants; (iv) that the shares of common stock or pre-funded warrants that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728—1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728—1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

## LEGAL MATTERS

Latham & Watkins LLP, San Diego, California, will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Prometheus Biosciences, Inc. Latham & Watkins LLP and certain attorneys in the firm who have rendered, and will continue to render, legal services to us, own shares of our common stock representing in the aggregate less than one percent of the shares of our common stock outstanding. The underwriters are being represented in connection with this offering by Davis Polk & Wardwell LLP, New York, New York.

## EXPERTS

The consolidated financial statements as of December 31, 2021 and 2020 and for the years then ended incorporated by reference in this prospectus supplement and in the registration statement have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

## WHERE YOU CAN FIND MORE INFORMATION; INFORMATION INCORPORATED BY REFERENCE

### ***Available Information***

We have filed with the SEC a registration statement on Form S-3 under the Securities Act, of which this prospectus supplement forms a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement and the accompanying prospectus certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus supplement and the accompanying prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

We file reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

Our website address is [www.prometheusbiosciences.com](http://www.prometheusbiosciences.com). The information on, or accessible through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

### ***Incorporation by Reference***

The SEC's rules allow us to "incorporate by reference" information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement and the accompanying prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus supplement or a previously filed document incorporated by reference will

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be deemed to be modified or superseded for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained in this prospectus supplement, the accompanying prospectus, or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus supplement and the accompanying prospectus incorporate by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 9, 2022;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022, June 30, 2022 and September 30, 2022 filed with the SEC on [May 12, 2022](#), [August 11, 2022](#) and [November 9, 2022](#), respectively;
- the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on April 1, 2022; and
- our Current Reports on Form 8-K filed with the SEC on [April 1, 2022](#), [May 20, 2022](#), [June 8, 2022](#), [July 26, 2022](#), [October 3, 2022](#) and December 7, 2022;
- the description of our Common Stock contained in our registration statement on [Form 8-A](#), filed with the SEC on March 9, 2021, and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and the accompanying prospectus and deemed to be part of this prospectus supplement and the accompanying prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus supplement and the accompanying prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Prometheus Biosciences, Inc.  
Attention: Corporate Secretary  
3050 Science Park Road  
San Diego, California 92121  
(858) 422-4300

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus supplement or the accompanying prospectus.

PROSPECTUS



**Common Stock**

**Preferred Stock**

**Debt Securities**

**Warrants**

**Units**

We may offer and sell the securities identified above, and selling securityholders that may be named in a prospectus supplement, if any, may offer and sell common stock, in each case, from time to time in one or more offerings. This prospectus provides you with a general description of the securities. We will not receive any proceeds from the sale of our common stock by the selling securityholders.

Each time we or any of the selling securityholders offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and, if applicable, the selling securityholders, as well as the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement, together with the documents we incorporate by reference, before you invest in any of our securities.

We or any selling securityholder may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods, on a continuous or delayed basis. In addition, the selling securityholders may offer and sell shares of our common stock from time to time, together or separately. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

**INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "[RISK FACTORS](#)" ON PAGE 5 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.**

Our common stock is listed on the Nasdaq Global Select Market under the symbol "RXDX." On March 31, 2022 the last reported sale price of our common stock on the Nasdaq Global Select Market was \$37.76 per share.

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

**The date of this prospectus is April 1, 2022.**

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act, using a “shelf” registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings, and the selling securityholders to be named in a supplement to this prospectus may sell common stock from time to time in one or more offerings. Each time that we or the selling securityholders offer and sell securities, we or the selling securityholders will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific 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 or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.”

Neither we, nor the selling securityholders, have authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We and the selling securityholders take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the selling securityholders will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus and the documents incorporated herein by reference, these estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” contained in this prospectus, the applicable prospectus supplement and any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

When we refer to “Prometheus,” “we,” “our,” “us” and the “Company” in this prospectus, we mean Prometheus Biosciences, Inc., unless otherwise specified. When we refer to “you,” we mean the holders of the applicable series of securities.

We use our trademarks in this prospectus as well as trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

## **WHERE YOU CAN FIND MORE INFORMATION**

We file reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information about issuers, including us, who file electronically with the SEC. The address of that website is [www.sec.gov](http://www.sec.gov).

Our website address is [www.prometheusbiosciences.com](http://www.prometheusbiosciences.com). The information on our website, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided above. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

## INCORPORATION BY REFERENCE

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act in this prospectus, between the date of this prospectus and the termination of the offering of the securities described in this prospectus. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed "filed" with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 9, 2022;
- the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on April 1, 2022; and
- the description of our Common Stock contained in our registration statement on [Form 8-A](#), filed with the SEC on March 9, 2021, and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Prometheus Biosciences, Inc.  
Attention: Corporate Secretary  
3050 Science Park Road  
San Diego, California 92121  
(858) 422-4300

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus or any accompanying prospectus supplement.

## THE COMPANY

We are a clinical-stage biotechnology company pioneering a precision medicine approach to the discovery, development, and commercialization of novel therapeutic and companion diagnostic products for the treatment of immune-mediated diseases, starting first with inflammatory bowel disease, or IBD. We leverage our proprietary precision medicine platform, Prometheus360™, which includes one of the world's largest gastrointestinal, or GI, bioinformatics database and sample biobank, to identify novel therapeutic targets and develop therapeutic candidates to engage those targets. In parallel, we are developing companion diagnostic tests designed to identify patients more likely to respond to our therapeutic candidates. We have generated a robust pipeline of therapeutic development programs for the treatment of immune-mediated diseases.

Our lead product candidate, PRA023, is a humanized IgG1 monoclonal antibody, or mAb, that has been shown to block the tumor necrosis factor, or TNF,-like ligand 1A, or TL1A, a target associated with both intestinal inflammation and fibrosis. PRA023's dual mechanism of action, targeting both inflammation and fibrosis, provides strong support for investigating the potential applicability of TL1A modification in areas outside IBD including indications in dermatology, pulmonary or hepatobiliary disease. We have advanced PRA023 into a Phase 2 randomized placebo-controlled clinical trial in patients with moderate-to-severe Ulcerative Colitis, or UC, an open-label Phase 2a clinical trial in patients with moderate-to-severe Crohn's disease, or CD, and a Phase 2 randomized placebo-controlled clinical trial in patients with systemic sclerosis-associated interstitial lung disease, or SSc-ILD. We will continue to explore additional potential indications for PRA023.

We were originally founded as a Delaware corporation on October 26, 2016, under the name Precision IBD, Inc. On October 3, 2019, we changed our name to Prometheus Biosciences, Inc. Our principal executive offices are located at 3050 Science Park Road, San Diego, California 92121, and our telephone number is 858-422-4300.

## RISK FACTORS

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K we file after the date of this prospectus, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. All statements other than statements of historical facts contained in this prospectus and the documents incorporated by reference herein, including statements regarding our future results of operations and financial position, business strategy, research and development plans, the anticipated timing, costs, design and conduct of our ongoing and planned preclinical studies and clinical trials for our product candidates, our plans to use our Prometheus360 product platform to expand our pipeline of product candidates and develop marketable products, the anticipated timing and costs of our development of companion diagnostics, the potential benefits from our collaboration arrangements with third parties and our plans to enter into additional arrangements, the timing and likelihood of regulatory filings and approvals for our product candidates and companion diagnostics, our ability to commercialize our product candidates, if approved, the impact of COVID-19 on our business, the pricing and reimbursement of our product candidates, if approved, and testing products, the potential to develop future product candidates, the timing and likelihood of success, plans and objectives of management for future operations, and future results of anticipated product development efforts, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

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 and the documents incorporated by reference herein are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions, which we discuss in greater detail in the documents incorporated by reference herein, including under the heading “Risk Factors” and elsewhere in this prospectus. 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. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

### **USE OF PROCEEDS**

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement. We will not receive any of the proceeds from the sale of common stock being offered by any of the selling securityholders.

### **DIVIDEND POLICY**

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors our board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

## DESCRIPTION OF CAPITAL STOCK

### General

The following description summarizes some of the terms of our common stock. Because it is only a summary, it does not contain all the information that may be important to you and is subject to and qualified in its entirety by reference to our amended and restated certificate of incorporation, and amended and restated bylaws, which are filed as exhibits to our most recent Annual Report on Form 10-K and are incorporated by reference herein. We encourage you to read our certificate of incorporation and our bylaws for additional information.

Our authorized capital stock consists of 400,000,000 shares of common stock, \$0.0001 par value per share, and 40,000,000 shares of preferred stock, \$0.0001 par value per share.

### Common Stock

As of March 31, 2022, there were 39,103,107 shares of our common stock outstanding and held of record by 31 stockholders. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the outstanding shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose, other than any directors that holders of any preferred stock we may issue may be entitled to elect. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Our amended and restated certificate of incorporation and amended and restated bylaws also provide that our directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon. In addition, the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon is required to amend or repeal, or to adopt any provision inconsistent with, several of the provisions of our amended and restated certificate of incorporation. See below under the heading “Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws.”

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared by the board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the assets legally available for distribution to stockholders after the payment of or provision for all of our debts and other liabilities, subject to the prior rights of any preferred stock then outstanding. Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking funds provisions applicable to the common stock. All outstanding shares of common stock are duly authorized, validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

### Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar’s address is 150 Royall Street, Canton, Massachusetts 02021.

### Preferred Stock

As of March 31, 2022, there were no shares of our preferred stock outstanding. Under the terms of our amended and restated certificate of incorporation, our board of directors has the authority, without further action by our stockholders, to issue up to 40,000,000 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 dividend, voting and other rights,

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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, deterring or preventing a change in our control and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock.

Prior to the issuance of shares of each series, the board of directors is required by the General Corporation Law of the State of Delaware, or the DGCL, and our amended and restated certificate of incorporation to adopt resolutions and file a certificate of designation with the Secretary of State of the State of Delaware. The certificate of designation fixes for each class or series the designations, powers, preferences, rights, qualifications, limitations and restrictions, including dividend rights, conversion rights, redemption privileges and liquidation preferences.

We will describe in a prospectus supplement relating to the class or series of preferred stock being offered the following terms:

- the title and stated value of the preferred stock;
- the number of shares of the preferred stock offered, the liquidation preference per share and the offering price of the preferred stock;
- the dividend rate(s), period(s) or payment date(s) or method(s) of calculation applicable to the preferred stock;
- whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock will accumulate;
- the procedures for any auction and remarketing, if any, for the preferred stock;
- the provisions for a sinking fund, if any, for the preferred stock;
- the provision for redemption, if applicable, of the preferred stock;
- any listing of the preferred stock on any securities exchange;
- the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock, including the conversion price or manner of calculation and conversion period;
- voting rights, if any, of the preferred stock;
- a discussion of any material or special U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs; and
- any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

Unless we specify otherwise in the applicable prospectus supplement, the preferred stock will rank, relating to dividends and upon our liquidation, dissolution or winding up:

- senior to all classes or series of our common stock and to all of our equity securities ranking junior to the preferred stock;



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- on a parity with all of our equity securities the terms of which specifically provide that the equity securities rank on a parity with the preferred stock; and
- junior to all of our equity securities the terms of which specifically provide that the equity securities rank senior to the preferred stock.

The term equity securities does not include convertible debt securities.

### **Registration Rights**

As of March 31, 2022, holders of 5,008,508 shares of our common stock, are entitled to the following rights with respect to the registration of such shares for public resale under the Securities Act, pursuant to the registration rights agreement by and among us and certain investors. The registration of shares of common stock as a result of the following rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.

#### **Demand Registration Rights**

*Form S-1.* If at any time the holders of at least a majority of the registrable securities request in writing that we effect a registration with respect to all or a part of the registrable securities then outstanding where the aggregate price to the public of the offering is \$10.0 million or more, we may be required to provide notice to all holders of registrable securities and to use commercially reasonable efforts to effect such registration; provided, however, that we will not be required to effect such a registration if, among other things, within the preceding 12 months, we have already effected two registrations for the holders of registrable securities in response to these demand registration rights.

*Form S-3.* If at any time the holders of the registrable securities request in writing that we effect a registration with respect to all or a part of the registrable securities then outstanding where the price to the public of the offering is \$5.0 million or more, we may be required to provide notice to all holders of registrable securities and to use commercially reasonable efforts to effect such registration; provided, however, that we will not be required to effect such a registration if, among other things, within the preceding 12 months, we have already effected two registrations on Form S-3 for the holders of registrable securities.

If the holders requesting registration intend to distribute their shares by means of an underwriting, the underwriter of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

#### **Piggyback Registration Rights**

If at any time we propose to register any shares of our common stock under the Securities Act, subject to certain exceptions, the holders of registrable securities will be entitled to notice of the registration and to include their shares of registrable securities in the registration. If our proposed registration involves an underwriting, the managing underwriter of such offering will have the right to limit the number of shares to be underwritten for reasons related to the marketing of the shares.

#### **Indemnification**

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

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### **Expenses**

Ordinarily, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling securityholders, blue sky fees and expenses and the expenses of any special audits incident to the registration.

### **Termination of Registration Rights**

The registration rights terminate in March 2028.

### **Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws**

Some provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

### **Undesignated Preferred Stock**

The ability of our board of directors, without action by the stockholders, to issue up to 40,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

### **Stockholder Meetings**

Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board of directors, chief executive officer or president, or by a resolution adopted by a majority of our board of directors.

### **Requirements for Advance Notification of Stockholder Nominations and Proposals**

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

### **Elimination of Stockholder Action by Written Consent**

Our amended and restated certificate of incorporation and amended and restated bylaws eliminate the right of stockholders to act by written consent without a meeting.

### **Staggered Board of Directors**

Our board of directors is divided into three classes. The directors in each class serve for a three-year term, with one class being elected each year by our stockholders. This system of electing directors may tend to discourage a third party from attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

### **Removal of Directors**

Our amended and restated certificate of incorporation provides that no member of our board of directors may be removed from office except for cause and, in addition to any other vote required by law, upon the approval of not less than two thirds of the total voting power of all of our outstanding voting stock then entitled to vote in the election of directors.

### **Stockholders Not Entitled to Cumulative Voting**

Our amended and restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

### **Delaware Anti-Takeover Statute**

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed to be “interested stockholders” from engaging in a “business combination” with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an “interested stockholder” is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation’s voting stock. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

### **Choice of Forum**

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative form, 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 asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders, creditors or other constituents; (iii) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our amended and restated certificate of incorporation or amended and restated bylaws; (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (v) any action asserting a claim governed by the internal affairs doctrine. The provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, our amended and restated certificate of incorporation will also provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause or causes of action arising under the Securities Act, including all causes of action asserted against any defendant to such complaint. For the avoidance of doubt, this provision is intended to benefit and may be enforced by us, our officers and directors, the underwriters to any offering giving rise to such complaint, and any other professional entity whose profession

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gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying the offering. In any case, stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. Our amended and restated certificate of incorporation also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision.

### **Amendment of Charter Provisions**

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least two thirds of the total voting power of all of our outstanding voting stock.

The provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board of directors and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

## DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement or free writing prospectus, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

### General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;
- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

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- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be U.S. dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;
- if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, and premium, if any, and interest on, the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide

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you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement. If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

### **Transfer and Exchange**

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company (DTC or the Depository), or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a “book-entry debt security”), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a “certificated debt security”) as set forth in the applicable prospectus supplement. Except as set forth under the heading “Global Debt Securities and Book-Entry System” below, book-entry debt securities will not be issuable in certificated form.

**Certificated Debt Securities.** You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder. Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see “Global Securities.”

### **Covenants**

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

### **No Protection in the Event of a Change of Control**

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

### **Consolidation, Merger and Sale of Assets**

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a “successor person”) unless:

- we are the surviving corporation or the successor person (if other than Prometheus) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and
- immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

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Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

### **Events of Default**

“Event of Default” means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or Prometheus and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Prometheus; or
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.



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The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture, unless the trustee receives indemnity satisfactory to it against any cost, liability or expense that might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the trustee, 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. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each holder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

### **Modification and Waiver**

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading “Consolidation, Merger and Sale of Assets;”
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or Events of Default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depository;
- to make any change that does not adversely affect the rights of any holder of debt securities;

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- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a Default or Event of Default in the payment of the principal of, or premium or interest on, any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of, or premium or interest on, any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, and premium and interest on, those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on, any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

### **Defeasance of Debt Securities and Certain Covenants in Certain Circumstances**

*Legal Defeasance.* The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of

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money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on, and any mandatory sinking fund payments in respect of, the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

*Defeasance of Certain Covenants.* The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading “Consolidation, Merger and Sale of Assets” and certain other covenants set forth in the indenture, as well as any additional covenants that may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (“covenant defeasance”).

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on, and any mandatory sinking fund payments in respect of, the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and
- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

### **No Personal Liability of Directors, Officers, Employees or Securityholders**

None of our past, present or future directors, officers, employees or securityholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

**Governing Law**

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum. (Section 10.10)

## DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. The following summary of material provisions of the warrants and warrant agreements is subject to, and qualified in its entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;
- the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;
- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;
- the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;
- the terms of any rights to redeem or call the warrants;
- the date on which the right to exercise the warrants will commence and the date on which the right will expire;
- U.S. federal income tax consequences applicable to the warrants; and
- any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled to:

- vote, consent or receive dividends;
- receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or
- exercise any rights as stockholders of Prometheus.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth 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.

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any

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other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

## DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain U.S. federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

## GLOBAL SECURITIES

### Book-Entry, Delivery and Form

Unless we indicate differently in any applicable prospectus supplement or free writing prospectus, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of DTC and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depository to its nominee or by the nominee to the depository, or by the depository or its nominee to a successor depository or to a nominee of the successor depository.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a “banking organization” within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a “clearing corporation” within the meaning of the New York Uniform Commercial Code; and
- a “clearing agency” registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants’ accounts, thereby eliminating the need for physical movement of securities certificates. “Direct participants” in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC’s records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants’ records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC’s partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC’s records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.



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So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depository and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depository or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below and unless if otherwise provided in the description of the applicable securities herein or in the applicable prospectus supplement, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in "street name." Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility; disbursement of payments to direct participants is the responsibility of DTC; and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depository with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depository is not obtained, securities certificates are required to be printed and delivered.

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As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

- DTC notifies us that it is unwilling or unable to continue as a depository for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depository is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;
- we determine, in our sole discretion, not to have such securities represented by one or more global securities; or
- an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depository directs. It is expected that these directions will be based upon directions received by the depository from its participants with respect to ownership of beneficial interests in the global securities.

### ***Euroclear and Clearstream***

If so provided in the applicable prospectus supplement, you may hold interests in a global security through Clearstream Banking S.A., which we refer to as "Clearstream," or Euroclear Bank S.A./N.V., as operator of the Euroclear System, which we refer to as "Euroclear," either directly if you are a participant in Clearstream or Euroclear or indirectly through organizations which are participants in Clearstream or Euroclear. Clearstream and Euroclear will hold interests on behalf of their respective participants through customers' securities accounts in the names of Clearstream and Euroclear, respectively, on the books of their respective U.S. depositories, which in turn will hold such interests in customers' securities accounts in such depositories' names on DTC's books.

Clearstream and Euroclear are securities clearance systems in Europe. Clearstream and Euroclear hold securities for their respective participating organizations and facilitate the clearance and settlement of securities transactions between those participants through electronic book-entry changes in their accounts, thereby eliminating the need for physical movement of certificates.

Payments, deliveries, transfers, exchanges, notices and other matters relating to beneficial interests in global securities owned through Euroclear or Clearstream must comply with the rules and procedures of those systems. Transactions between participants in Euroclear or Clearstream, on one hand, and other participants in DTC, on the other hand, are also subject to DTC's rules and procedures.

Investors will be able to make and receive through Euroclear and Clearstream payments, deliveries, transfers and other transactions involving any beneficial interests in global securities held through those systems only on days when those systems are open for business. Those systems may not be open for business on days when banks, brokers and other institutions are open for business in the United States.

Cross-market transfers between participants in DTC, on the one hand, and participants in Euroclear or Clearstream, on the other hand, will be effected through DTC in accordance with the DTC's rules on behalf of Euroclear or Clearstream, as the case may be, by their respective U.S. depositories; however, such cross-market transactions will require delivery of instructions to Euroclear or Clearstream, as the case may be, by the counterparty in such system in accordance with the rules and procedures and within the established deadlines (European time) of such system. Euroclear or Clearstream, as the case may be, will, if the transaction meets its settlement requirements, deliver instructions to its U.S. depository to take action to effect final settlement on its behalf by delivering or receiving interests in the global securities through DTC, and making or receiving payment in accordance with normal procedures for same-day fund settlement. Participants in Euroclear or Clearstream may not deliver instructions directly to their respective U.S. depositories.

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Due to time zone differences, the securities accounts of a participant in Euroclear or Clearstream purchasing an interest in a global security from a direct participant in DTC will be credited, and any such crediting will be reported to the relevant participant in Euroclear or Clearstream, during the securities settlement processing day (which must be a business day for Euroclear or Clearstream) immediately following the settlement date of DTC. Cash received in Euroclear or Clearstream as a result of sales of interests in a global security by or through a participant in Euroclear or Clearstream to a direct participant in DTC will be received with value on the settlement date of DTC but will be available in the relevant Euroclear or Clearstream cash account only as of the business day for Euroclear or Clearstream following DTC's settlement date.

### ***Other***

The information in this section of this prospectus concerning DTC, Clearstream, Euroclear and their respective book-entry systems has been obtained from sources that we believe to be reliable, but we do not take responsibility for this information. This information has been provided solely as a matter of convenience. The rules and procedures of DTC, Clearstream and Euroclear are solely within the control of those organizations and could change at any time. Neither we nor the trustee nor any agent of ours or of the trustee has any control over those entities and none of us takes any responsibility for their activities. You are urged to contact DTC, Clearstream and Euroclear or their respective participants directly to discuss those matters. In addition, although we expect that DTC, Clearstream and Euroclear will perform the foregoing procedures, none of them is under any obligation to perform or continue to perform such procedures and such procedures may be discontinued at any time. Neither we nor any agent of ours will have any responsibility for the performance or nonperformance by DTC, Clearstream and Euroclear or their respective participants of these or any other rules or procedures governing their respective operations.

**SELLING SECURITYHOLDERS**

Information about selling securityholders, where applicable, will be set forth in a prospectus supplement, in a post-effective amendment or in other filings we make with the SEC under the Exchange Act that are incorporated by reference.

## PLAN OF DISTRIBUTION

We or any of the selling securityholders may sell the offered securities from time to time:

- through underwriters or dealers;
- through agents;
- directly to one or more purchasers; or
- through a combination of any of these methods of sale.

We will identify the specific plan of distribution, including any underwriters, dealers, agents or direct purchasers and their compensation in the applicable prospectus supplement.

## **LEGAL MATTERS**

Latham & Watkins LLP, San Diego, California, will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Prometheus Biosciences, Inc. Latham & Watkins LLP and certain attorneys in the firm who have rendered, and will continue to render, legal services to us, own shares of our common stock representing in the aggregate less than one percent of the shares of our common stock outstanding. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

## **EXPERTS**

The consolidated financial statements as of December 31, 2021 and 2020 and for the years then ended incorporated by reference in this prospectus and in the registration statement have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

\$250,000,000



Common Stock

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**PROSPECTUS SUPPLEMENT**  
December , 2022

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**Goldman Sachs & Co. LLC**  
**SVB Securities**  
**Jefferies**  
**Guggenheim Securities**

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