

PROSPECTUS SUPPLEMENT
(To Prospectus dated May 7, 2024)

\$300,000,000



Common Stock

We have entered into a sales agreement, or Sales Agreement, with TD Securities (USA) LLC, or TD Cowen, dated May 7, 2024, relating to the sale of shares of our common stock, par value \$0.0001 per share, offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the Sales Agreement, under this prospectus supplement we may offer and sell shares of our common stock having an aggregate offering price of up to \$300,000,000, from time to time through or to TD Cowen, acting as our agent or principal. The Sales Agreement replaces our previous sales agreement, dated June 1, 2021 and amended on May 9, 2023, with Cowen and Company, LLC, an affiliate of TD Cowen.

Our common stock trades on The Nasdaq Global Select Market under the trading symbol "MDGL." On May 3, 2024, the last reported sale price of our common stock on The Nasdaq Global Select Market was \$229.84 per share.

Sales of our common stock, if any, under this prospectus supplement will be made in sales deemed to be "at the market offerings" as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, or the Securities Act.

TD Cowen is not required to sell any specific amount of securities, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between TD Cowen and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The aggregate compensation payable to TD Cowen for sales of common stock sold pursuant to this prospectus supplement and the Sales Agreement will be an amount equal to up to 3.0% of the gross proceeds of the shares of common stock sold pursuant to this prospectus supplement and the Sales Agreement. In connection with the sale of the common stock on our behalf, TD Cowen will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of TD Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to TD Cowen with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should carefully consider the risks described under the heading "[Risk Factors](#)" beginning on page S-9 of this prospectus supplement and under similar headings in other 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 determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

TD Cowen

May 7, 2024

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EXPLANATORY NOTE

On June 1, 2021, we entered into the original sales agreement with Cowen and Company, LLC, an affiliate of TD Cowen, as amended on May 9, 2023, pursuant to which we could offer and sell up to an aggregate amount of \$400 million of our common stock. The terms of such offering of shares of our common stock were contained in prospectus supplements filed under our former shelf registration statement on Form S-3ASR (Reg. No. 333-256666) filed on June 1, 2021 and May 9, 2023 (the “Prior Prospectus Supplements”) We sold 1,333,594 shares of our common stock having an aggregate offering price of \$225.1 million pursuant to the original sales agreement, as amended. The Sales Agreement and this prospectus supplement replace the original sales agreement and Prior Prospectus Supplements and register the offering and sale of our common stock having an aggregate offering price of up to \$300 million under the Sales Agreement and this prospectus supplement.

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a “shelf” registration process and consists of two parts. The first part is the prospectus supplement, including the documents incorporated by reference herein, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference therein, provides more general information. In general, when we refer only to the prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under the heading “Where You Can Find More Information.” These documents contain information you should carefully consider when deciding whether to invest in our common stock.

This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent there is a conflict between the information contained in this prospectus supplement and the accompanying prospectus, you should rely on information contained in this prospectus supplement, provided that if any statement in, or incorporated by reference into, one of these documents is inconsistent with a statement in another document having a later date, the statement in the document having the later date modifies or supersedes the earlier statement. Any statement so modified will be deemed to constitute a part of this prospectus only as so modified, and any statement so superseded will be deemed not to constitute a part of this prospectus.

You should rely only on the information contained in this prospectus supplement, the accompanying prospectus, any document incorporated by reference herein or therein, or any free writing prospectuses we may provide to you in connection with this offering. Neither we nor TD Cowen have authorized anyone to provide you with any different information. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may provide to you. The information contained in this prospectus supplement, the accompanying prospectus, and in the documents incorporated by reference herein or therein is accurate only as of the date such information is presented. Our business, financial condition, results of operations and prospects may have changed since that date.

This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the shares of common stock to which it relates, nor do this prospectus supplement and the accompanying prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

Unless otherwise indicated, information contained in or incorporated by reference into this prospectus concerning our industry and the markets in which we operate, including market opportunity, market position and competitive landscape, is based on information from our management’s estimates, as well as from industry publications, surveys and studies conducted by third parties. Management estimates are derived from publicly available

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information, our knowledge of our industry, and assumptions based on such information and knowledge, which we believe to be reasonable. In addition, while we believe that information contained in the industry publications, surveys and studies has been obtained from reliable sources, the accuracy and completeness of such information is not guaranteed, and we have not independently verified any of the data contained in these third-party sources.

This prospectus supplement and the accompanying prospectus, and any documents incorporated by reference herein or therein, include statements that are based on various assumptions and estimates that are subject to numerous known and unknown risks and uncertainties. Some of these risks and uncertainties are described under the heading “Risk Factors” beginning on page S-9 of this prospectus supplement and in the section titled “Risk Factors” in our most recent Annual Report on Form 10-K, which are incorporated by reference into the prospectus. These and other important factors could cause our future results to be materially different from the results expected as a result of, or implied by, these assumptions and estimates. You should read the information contained in this prospectus supplement and the accompanying prospectus, and the documents incorporated by reference herein and therein, completely and with the understanding that future results may be materially different and worse from what we expect. See the information included under the heading “Special Note Regarding Forward-Looking Statements.”

We note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreement, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless otherwise indicated or the context otherwise requires, the terms “Company,” “Madrigal Pharmaceuticals,” “we,” “us” and “our” refer to Madrigal Pharmaceuticals, Inc., a Delaware corporation, and its predecessors and consolidated subsidiaries.

SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus supplement, the accompanying prospectus and the documents we incorporate by reference herein and therein include forward-looking statements within the meaning of the federal securities laws, which statements are: subject to substantial risks and uncertainties; based on our beliefs and assumptions and on information currently available to us; and subject to factors beyond our control. These forward-looking statements are intended to qualify for the safe harbor from liability established by the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical fact are forward-looking statements. Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding forward-looking statements, future performance or events; include all statements that are not historical facts; and can be identified by terms such as "accelerate," "achieve," "allow," "anticipates," "appear," "be," "believes," "can," "continue," "confidence," "could," "demonstrates," "design," "estimates," "expectation," "expects," "forecasts," "future," "goal," "help," "hopeful," "inform," "informed," "intends," "may," "might," "on track," "planned," "planning," "plans," "positions," "potential," "powers," "predicts," "predictive," "projects," "seeks," "should," "will," "will achieve," "will be," "would" or similar expressions and the negatives of those terms.

In particular, this prospectus supplement, and the documents we incorporate by reference in this prospectus supplement, contain forward-looking statements relating to, among other things:

- The initiation of the commercial launch of Rezdiffra™ (resmetirom) for the treatment of adults with noncirrhotic non-alcoholic steatohepatitis ("NASH") with moderate to advanced liver fibrosis in the United States;
- Anticipated or estimated future results, including the risks and uncertainties associated with our future operating performance and financial position, and our projected resources and sufficiency of capital to fund our operating expenses;
- Our possible or assumed future results of operations and expenses, business strategies and plans (including potential ex-U.S. commercialization or partnering opportunities), capital needs and financing plans, including incurrence of indebtedness and compliance with debt covenants under the Loan and Security Agreement with Hercules Capital, Inc., as agent and lender, market trends, market sizing, competitive position, industry environment and potential growth opportunities, among other things;
- Post-approval requirements and commitments, including verification of a clinical benefit in confirmatory trials;
- Our ability to delay certain research activities and related clinical expenses as necessary;
- Our clinical trials, including the anticipated timing of disclosure, presentations of data from, or outcomes from our trials;
- Research and development activities, and the timing and results associated with the future development of Rezdiffra / resmetirom, including projected market size, sector leadership, and patient treatment estimates for NASH and non-alcoholic fatty liver disease ("NAFLD") patients;
- The timing and completion of projected future clinical milestone events, including enrollment, additional studies, top-line data and open label projections;
- Rezdiffra's potential to be a cost-effective specialty therapy for NASH patients with significant liver fibrosis (consistent with fibrosis stages 2 and 3);
- Projections or objectives for obtaining full approval for resmetirom for NASH patients with significant fibrosis (or non-cirrhotic NASH patients) and NASH patients with compensated cirrhosis, including all statements concerning potential clinical benefit to support approval and/or potential approval;
- Estimates of patients diagnosed with NASH;

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- Our primary and key secondary study endpoints for resmetirom, and the potential for achieving such endpoints and projections, including NASH resolution, safety, fibrosis treatment, cardiovascular effects and lipid treatment with resmetirom;
- The relationship between NASH progression and adverse patient outcomes;
- The estimated clinical burden of uncontrolled NASH;
- Analyses for patients with NASH with significant fibrosis concerning potential progression to cirrhosis, decompensated cirrhosis, liver transplant or death, and cardiovascular risks, comorbidities and outcomes;
- Optimal dosing levels for resmetirom and projections regarding potential NASH or NAFLD and potential patient benefits with resmetirom, including future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment and/or biomarker effects with resmetirom;
- Our ability to address the unmet needs of patients suffering from NASH with significant fibrosis;
- The potential efficacy and safety of resmetirom for non-cirrhotic NASH patients and cirrhotic NASH patients;
- The potential for resmetirom to become the best-in-class treatment option for patients with NASH and significant fibrosis;
- Strategies, objectives and commercial opportunities, including potential prospects or results;
- Potential ex-U.S. commercialization or partnering opportunities;
- The ability to develop clinical evidence demonstrating the utility of non-invasive tools and techniques to screen and diagnose NASH and/or NAFLD patients;
- The predictive power of liver fat reduction with resmetirom, as measured by non-invasive tests, on NASH resolution and/or fibrosis reduction or improvement, and potential NASH or NAFLD patient risk profile benefits with resmetirom;
- The predictive power of liver fat, liver volume changes or MAST scores for NASH and/or NAFLD patients;
- The predictive power of NASH resolution and/or fibrosis reduction with resmetirom or improvement using non-invasive tests, including the use of ELF, FibroScan, MRE and/or MRI-PDFF;
- The predictive power of non-invasive tests generally, including for purposes of diagnosing NASH, monitoring patient response to resmetirom, or recruiting and conducting a NASH clinical trial;
- Market demand for and acceptance of our products;
- Research, development and commercialization of new products;
- The potential for resmetirom to be an effective treatment for other disease indications;
- Obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections;
- Risks associated with meeting the objectives of our clinical studies, including, but not limited to our ability to achieve enrollment objectives concerning patient numbers (including an adequate safety database), outcomes objectives and/or timing objectives for our studies, any delays or failures in enrollment, the occurrence of adverse safety events, and the risks of successfully conducting trials that are substantially larger, and have patients with different disease states, than our past trials;
- The potential impact of cyber attacks and other security incidents on our operations or business;
- Our continued reliance on third-party contract manufacturers for the manufacture of our products and product candidates, including resmetirom;

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- Risks related to the effects of resmetirom’s mechanism of action and our ability to accomplish our business and business development objectives and realize the anticipated benefit of any such transactions; and
- Assumptions underlying any of the foregoing.

We caution you that the foregoing list may not include all of the forward-looking statements made in this prospectus supplement. Although management presently believes that the expectations reflected in such forward-looking statements are reasonable, it can give no assurance that such expectations will prove to be correct and you should be aware that actual results could differ materially from those contained in the forward-looking statements.

Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to: our clinical and commercial development of resmetirom; the challenges with the commercial launch of a new product, particularly for a company that does not have commercial experience; enrollment and trial outlook uncertainties, generally, based on blinded, locked or limited trial data; our potential inability to raise sufficient capital to fund our ongoing operations as currently planned or to obtain financings on terms similar to those we have arranged in the past; our ability to meet post-approval commitments and requirements, including completion of enrollment of—and ability to obtain positive data from—any confirmatory studies required by the FDA; our ability to service our indebtedness and otherwise comply with our debt covenants; outcomes or trends from competitive studies; future topline data timing or results; the risks of achieving potential benefits in studies that includes substantially more patients, and patients with different disease states, than our prior studies; our ability to prevent and/or mitigate cybersecurity attacks, unauthorized exfiltration of data or other security incidents; limitations associated with early stage or non-placebo controlled study data; the timing and outcomes of clinical studies of resmetirom; and the uncertainties inherent in clinical testing; and uncertainties concerning analyses or assessments outside of a controlled clinical trial. Undue reliance should not be placed on forward-looking statements, which speak only as of the date they are made. Madrigal undertakes no obligation to update any forward-looking statements to reflect new information, events or circumstances after the date they are made, or to reflect the occurrence of unanticipated events. Please refer to Madrigal’s submissions filed or furnished with the U.S. Securities and Exchange Commission for more detailed information regarding these risks and uncertainties and other factors that may cause actual results to differ materially from those expressed or implied.

We specifically discuss these risks and uncertainties in greater detail in the section appearing in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on February 28, 2024, and in Part II, Item 1A of our Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, filed with the SEC on May 7, 2024. You should read these documents and the other documents that we file or have filed with the SEC, with the understanding that our actual future results may be materially different from the results expressed or implied by these forward-looking statements. See “Incorporation of Certain Information by Reference” in this prospectus supplement.

Moreover, we operate in an evolving environment. New risks and uncertainties emerge from time to time and it is not possible for our management to predict all risks and uncertainties, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual future results to be materially different from those expressed or implied by any forward-looking statements.

Except as required by applicable law, we assume no obligation to update any forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future. We qualify all of our forward-looking statements by these cautionary statements.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. For a more complete understanding of our company and this offering, you should read this entire prospectus supplement and the accompanying prospectus carefully, including information under the heading “Risk Factors” in this prospectus supplement and the information incorporated by reference herein, including information under the heading “Risk Factors” contained in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on February 28, 2024, and in Part II, Item 1A of our Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, filed with the SEC on May 7, 2024, as well as in our other filings with the SEC.

Overview

We are a biopharmaceutical company focused on delivering novel therapeutics for nonalcoholic steatohepatitis (“NASH”), also known as metabolic dysfunction-associated steatohepatitis (“MASH”), a liver disease with high unmet medical need. In March 2024, we announced that Rezdiffra™ (resmetirom) has been granted accelerated approval by the U.S. Food and Drug Administration (“FDA”) in conjunction with diet and exercise for the treatment of adults with noncirrhotic NASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). Continued approval for this indication may be contingent upon verification and description of clinical benefit in ongoing confirmatory trials.

We initiated the commercial launch of Rezdiffra in the second quarter of 2024. In support of our commercialization efforts we have employed a national sales force consisting of approximately 150 to 200 sales representatives. As used herein, “Rezdiffra” refers to resmetirom approved by the FDA for the treatment of adults with NASH with moderate to advanced liver fibrosis, and “resmetirom” refers to, where applicable, Rezdiffra as well as resmetirom for the treatment of indications beyond NASH with moderate to advanced liver fibrosis.

Rezdiffra is a once-daily, oral THR-β agonist designed to target key underlying causes of NASH. NASH is a more advanced form of nonalcoholic fatty liver disease (“NAFLD”). NASH is a leading cause of liver-related mortality and an increasing burden on healthcare systems globally. Additionally, patients with NASH, especially those with more advanced metabolic risk factors (hypertension, concomitant type 2 diabetes), are at increased risk for adverse cardiovascular events and increased morbidity and mortality.

Once patients progress to NASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), the risk of adverse liver outcomes increases dramatically. NASH is rapidly becoming the leading cause of liver transplantation in the U.S.

NASH is also known as MASH following a change in disease nomenclature introduced by hepatology medical societies in 2023.

General Information

We were incorporated in Delaware in September 2011. Our principal executive offices are located at 200 Barr Harbor Drive, Suite 200, West Conshohocken, Pennsylvania 19428. Our telephone number is (267) 824-2827. Our website address is www.madrigalpharma.com. The contents of our website are not incorporated into, and do not form a part of, this prospectus supplement or the registration statement of which it forms a part.

The Offering

The following summary contains basic information about our common stock and the offering and is not intended to be complete. It does not contain all of the information that may be important to you. For a more complete understanding of our common stock, you should read the section entitled “Description of Capital Stock” in the accompanying prospectus.

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| Common stock offered by us | Shares of our common stock having an aggregate offering price of up to \$300,000,000. |
| Common stock to be outstanding after this offering assuming the sale of all shares in this offering ⁽¹⁾ | Up to 22,073,230 shares, assuming sales of 1,388,567 shares of our common stock in the offering at a price of \$216.05 per share, which was the closing price of our common stock on The Nasdaq Global Select Market on May 2, 2024. The actual number of shares issued will vary depending on the sales price under this offering. |
| Manner of Offering | “At the market offering” that may be made from time to time on The Nasdaq Global Select Market or other existing trading market for our common stock through our sales agent, TD Cowen. See “Plan of Distribution” on page S-19 of this prospectus supplement for more information. |
| Use of Proceeds | We intend to use the net proceeds from the sale of shares of common stock offered under this prospectus supplement primarily for our commercial activities in connection with the launch of Rezdifra in the U.S. and general corporate purposes, including, without limitation, research and development expenditures, ongoing clinical trial expenditures, manufacture and supply of drug substance and drug products, potential ex-U.S. commercialization or partnering opportunities, potential acquisitions or licensing of new technologies, capital expenditures and working capital. See “Use of Proceeds” on page S-12 of this prospectus supplement for more information. |
| Nasdaq Global Select Market Symbol | MDGL |
| Risk Factors | Your investment in our common stock involves substantial risks. You should read carefully the “Risk Factors” included and incorporated by reference in this prospectus supplement and the accompanying prospectus, including the risk factors incorporated by reference from our filings with the SEC. |
| (1) The common stock outstanding after the offering is based on 20,684,663 shares of our common stock outstanding as of March 31, 2024, and excludes the following: | |
| | <ul style="list-style-type: none">• 1,969,797 shares of our common stock issuable upon conversion of our Series A Convertible Preferred Stock and 400,000 shares of our common stock issuable upon conversion of our Series B Convertible Preferred Stock outstanding as of March 31, 2024; |

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- 2,458,227 shares of our common stock issuable upon the exercise of options outstanding as of March 31, 2024, having a weighted average exercise price of \$88.18 per share, and 530,671 shares of our common stock issuable upon the vesting of restricted stock units (less 252,753 shares of our common stock issued upon the exercise of options subsequent to March 31, 2024 through May 2, 2024, at a weighted average exercise price of \$32.15 per share);
- an aggregate of 479,607 shares of our common stock reserved for future issuance as of March 31, 2024 under our 2015 Stock Plan and 2023 Inducement Plan;
- 19,454 shares of our common stock issuable upon the exercise of warrants issued to Hercules Capital, Inc. (“Hercules”) under warrant agreements between us and Hercules (the “Warrant Agreements”), as of March 31, 2024; and
- 3,605,790 shares of our common stock issuable upon the exercise of pre-funded warrants at an exercise price of a \$0.0001 per share, as of March 31, 2024.

RISK FACTORS

Before making an investment decision, you should carefully consider the risks described below and discussed in the section titled “Risk Factors” in our most recent Annual Report on Form 10-K, as well as the risks, uncertainties and additional information set forth in our SEC reports on Forms 10-K, 10-Q and 8-K, including after the date of this prospectus supplement, and in other documents incorporated by reference in this prospectus supplement and the accompanying prospectus. We expect to update these Risk Factors from time to time in the periodic and current reports that we file with the SEC after the date of this prospectus supplement. These updated Risk Factors will be incorporated by reference in this prospectus supplement.

Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business, financial condition results of operations and prospects. Certain statements below are forward-looking statements. See the information included under the heading “Special Note Regarding Forward-Looking Statements.”

Risks Relating to Ownership of Our Common Stock

The price of our common stock has been, and may continue to be, volatile.

Historically, the market price of our common stock has fluctuated over a wide range, and it is likely that the price of our common stock will continue to be volatile in the future. The closing price of our common stock has ranged from \$120.40 to \$312.00 per share during the period from January 1, 2023 to May 1, 2024. The market price of our common stock could be impacted due to a variety of factors, including: global market or financial developments; prevailing macroeconomic conditions, including potential recession or economic downturns; US market events (including the potential for unusual market trading activity following external short interest developments or social media activity); the outbreak of war or hostilities; NASH therapeutic company developments and/or FDA developments, regardless of whether occurring generally and/or specifically as to our commercial activities, clinical trials and development programs; industry-wide events; and the following events or developments:

- the losses we may incur;
- developments in patent or other proprietary rights owned or licensed by us, our collaborative partners or our competitors;
- the progress and results of our clinical trials;
- public concern as to the safety and efficacy of products developed by us or others; and
- litigation.

In addition, due to one or more of the foregoing factors in one or more future quarters, our results of operations may fall below the expectations of securities analysts and investors. In that event, the market price of our common stock could materially decline.

A small number of our stockholders beneficially own a substantial amount of our common stock and have substantial control over us; therefore, your ability to influence corporate matters may be limited.

Certain stockholders affiliated and associated with our officers and directors collectively beneficially owned approximately 22.8% of our common stock as of April 22, 2024 and acting together, may have the ability to substantially affect matters submitted to our stockholders for approval. This concentration of ownership may have the effect of delaying, deferring or preventing a strategic transaction, even if such a transaction would benefit other stockholders.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our charter and bylaws may delay or prevent a merger, acquisition or other change of control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions include a classified board of directors. In addition, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits, with some exceptions, stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. Although we believe these provisions together provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if such an offer may be considered beneficial by some stockholders.

Future sales and issuances of our common stock or rights to purchase common stock could result in additional dilution of the percentage ownership of our stockholders and could cause our share price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

We do not anticipate paying cash dividends on our common stock, and accordingly, stockholders must rely on stock appreciation for any return on their investment.

We have never declared or paid any cash dividend on our common stock and do not anticipate paying cash dividends on our common stock in the future. As a result, the only currently anticipated return to stockholders would be appreciation in the price of our common stock, which may never occur. Investors seeking cash dividends should not invest in our common stock.

Risks Related to This Offering

If you purchase shares of our common stock in this offering, you will experience immediate dilution in the net tangible book value of your shares.

The shares sold in this offering, if any, will be sold from time to time at various prices. However, the expected offering price per share of our common stock may be higher than the net tangible book value per share of our outstanding common stock. Assuming that an aggregate of 1,388,567 shares of our common stock are sold at a price of \$216.05 per share, the last reported sales price of our common stock on The Nasdaq Global Select Market on May 2, 2024, after deducting commissions and estimated aggregate offering expenses payable by us, you will experience immediate dilution of \$164.36 per share, representing the difference between our as-adjusted net tangible book value per share as of March 31, 2024 after giving effect to this offering and the assumed offering price of \$216.05 per share. To the extent outstanding options and warrants (including pre-funded warrants) are exercised or the Series A Convertible Preferred Stock and the Series B Convertible Preferred Stock is converted, you will incur further dilution. See “Dilution” below for a more detailed illustration of the dilution you would incur if you participate in this offering.

The actual number of shares we will issue under the Sales Agreement, at any one time or in total, is uncertain.

Subject to certain limitations in the Sales Agreement and compliance with applicable law, we have the discretion to deliver a placement notice to TD Cowen at any time throughout the term of the Sales Agreement. The number

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of shares that are sold by TD Cowen after delivering a placement notice will fluctuate based on the market price of our common stock during the sales period and limits we set with TD Cowen. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares that will be ultimately issued.

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

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold. There is no minimum or maximum sales price in this offering. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

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

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled “Use of Proceeds,” and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. We intend to use the net proceeds from the sale of shares of common stock offered under this prospectus supplement primarily for our commercial activities in connection with the launch of Rezdiffra in the U.S. and general corporate purposes, including, without limitation, research and development expenditures, ongoing clinical trial expenditures, manufacture and supply of drug substance and drug products, potential ex-U.S. commercialization or partnering opportunities, potential acquisitions or licensing of new technologies, capital expenditures and working capital. The failure by our management to apply these funds effectively could harm our business. Pending their use to fund operations, we may invest the net proceeds from this offering short-term, interest-bearing instruments, including obligations of U.S. government agencies, U.S. Treasury debt securities, corporate debt securities and money market funds. 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.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate gross sales proceeds of up to \$300,000,000 from time to time (before deducting sales agent commissions and expenses) pursuant to this prospectus supplement. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that, in the future, we will sell any shares under or fully utilize the Sales Agreement with TD Cowen as a source of financing.

We intend to use the net proceeds from the sale of shares of common stock offered under this prospectus supplement primarily for our commercial activities in connection with the launch of Rezdiffra in the U.S. and general corporate purposes, including, without limitation, research and development expenditures, ongoing clinical trial expenditures, manufacture and supply of drug substance and drug products, potential ex-U.S. commercialization or partnering opportunities, potential acquisitions or licensing of new technologies, capital expenditures and working capital.

The expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures will depend on numerous factors, including the progress of our commercial activities, clinical trials and other development efforts and other factors described under “Risk Factors” in this prospectus supplement, the accompanying base prospectus and the documents incorporated by reference herein and therein, 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 timing and application of the net proceeds. Pending the use of the net proceeds described above, we may invest the net proceeds from this offering in a variety of capital preservation investments, including short-term, interest-bearing instruments, including obligations of U.S. government agencies, U.S. Treasury debt securities, corporate debt securities and money market funds.

DIVIDEND POLICY

We do not currently anticipate declaring or paying cash dividends on our capital stock in the foreseeable future. We currently intend to retain all of our future earnings, if any, to finance the operation and expansion of our business. Any future determination relating to our dividend policy will be made at the discretion of our board of directors and will depend on a number of factors, including future earnings, capital requirements, future prospects, contractual restrictions and covenants and other factors that our board of directors may deem relevant.

DILUTION

If you invest in our common stock, your interest will be diluted to the extent of the difference between the price per share you pay in this offering and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering. Our net tangible book value at March 31, 2024 was approximately \$844.2 million, or \$40.81 per share, based on 20,684,663 shares of our common stock then outstanding. Net tangible book value per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares outstanding as of March 31, 2024.

After giving effect to the sale of our common stock in this offering in the aggregate amount of \$300 million at an assumed offering price of \$216.05 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on May 2, 2024, and after deducting commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2023 would have been approximately \$1,140.9 million, or \$51.69 per share of common stock. This represents an immediate increase in pro forma net tangible book value of \$10.88 per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of \$164.36 per share to new investors in this offering. Dilution per share to new investors in this offering is calculated as the difference between the assumed public offering price per share and the pro forma as adjusted net tangible book value per share after this offering.

The following table illustrates this calculation on a per share basis. The as adjusted information is illustrative only and will adjust based on the actual price to the public, the actual number of shares sold and other terms of the offering determined at the time shares of our common stock are sold pursuant to this prospectus supplement. The as adjusted information assumes that all of our common stock in the aggregate amount of \$300 million is sold at the assumed offering price of \$216.05 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on May 2, 2024. The shares sold in this offering, if any, will be sold from time to time at various prices.

| | |
|--|-----------------|
| Assumed public offering price per share | \$216.05 |
| Net tangible book value per share as of March 31, 2024 | \$40.81 |
| Increase in pro forma net tangible book value per share after this offering | <u>\$10.88</u> |
| Pro forma as adjusted net tangible book value per share as of March 31, 2024, after giving effect to this offering | <u>\$ 51.69</u> |
| Dilution per share to new investors participating in this offering | <u>\$164.36</u> |

The common stock outstanding after the offering is based on 20,684,663 shares of our common stock outstanding as of March 31, 2024, and excludes the following:

- 1,969,797 shares of our common stock issuable upon conversion of our Series A Convertible Preferred Stock and 400,000 shares of our common stock issuable upon conversion of our Series B Convertible Preferred Stock outstanding as of March 31, 2024;
- 2,458,227 shares of our common stock issuable upon the exercise of options outstanding as of March 31, 2024, having a weighted average exercise price of \$88.18 per share, and 530,671 shares of our common stock issuable upon the vesting of restricted stock units (less 252,753 shares of our common stock issued upon the exercise of options subsequent to March 31, 2024 through May 2, 2024, at a weighted average exercise price of \$32.15 per share);
- an aggregate of 479,607 shares of our common stock reserved for future issuance as of March 31, 2024 under our 2015 Stock Plan and 2023 Inducement Plan and

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- 19,454 shares of our common stock issuable upon the exercise of warrants issued to Hercules under the Warrant Agreements, as of March 31, 2024; and
- 3,605,790 shares of our common stock issuable upon the exercise of pre-funded warrants at an exercise price of a \$0.0001 per share, as of March 31, 2024.

An increase of \$10.00 per share in the price at which the shares are sold from the assumed offering price of \$216.05 per share shown in the table above would result in pro forma adjusted net tangible book value per share after the offering of \$51.83 per share and dilution in pro forma adjusted net tangible book value per share to new investors in this offering of \$174.22 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$10.00 per share in the price at which the shares are sold from the assumed offering price of \$216.05 per share shown in the table above would result in pro forma adjusted net tangible book value per share after the offering of \$51.53 per share and dilution in pro forma adjusted net tangible book value per share to new investors in this offering of \$154.52 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

To the extent options or warrants (including pre-funded warrants) are exercised or our Series A Convertible Preferred Stock or Series B Convertible Preferred Stock is converted into common stock, or we issue additional shares of common stock or other securities convertible into or exercisable for common stock in the future, there may be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

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

The following is a general discussion of the material U.S. federal income tax consequences applicable to non-U.S. holders (as defined herein) with respect to the purchase, ownership and disposition of our common stock issued or acquired pursuant to this offering. All prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock. In general, a non-U.S. holder means a beneficial owner of our common stock (other than a partnership or an entity or arrangement treated as a partnership for U.S. federal income tax purposes) that is not, for U.S. federal income tax purposes:

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

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, or the Code, existing U.S. Treasury Regulations promulgated thereunder, published administrative pronouncements and rulings of the U.S. Internal Revenue Service, or the IRS, and judicial decisions, all as in effect as of the date of this prospectus supplement. These authorities are subject to change and to differing interpretation, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus supplement.

We assume in this discussion that a non-U.S. holder holds our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances, nor does it address any alternative minimum tax, Medicare contribution tax or investment income, estate or gift tax consequences, or any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as holders that own, or are deemed to own, more than 5% of our capital stock (except to the extent specifically set forth below), corporations that accumulate earnings to avoid U.S. federal income tax, tax-exempt organizations, banks, financial institutions, insurance companies, brokers, dealers or traders in securities, commodities or currencies, tax-qualified retirement plans, holders who hold or receive our common stock pursuant to the exercise of employee stock options or otherwise as compensation, holders holding our common stock as part of a hedge, straddle or other risk reduction strategy, conversion transaction or other integrated investment, "qualified foreign pension funds" as defined in Section 897(1)(2) of the Code, persons subject to special tax accounting under Section 451(b) of the Code, holders deemed to sell our common stock under the constructive sale provisions of the Code, controlled foreign corporations, passive foreign investment companies and certain former U.S. citizens or long-term residents.

In addition, this discussion does not address the tax treatment of partnerships (or entities or arrangements that are treated as partnerships for U.S. federal income tax purposes) or persons that hold their common stock through partnerships. If a partnership, including any entity or arrangement treated as a partnership for U.S. federal income tax purposes, holds our common stock, the U.S. federal income tax treatment of a partner in such partnership will generally depend upon the status of the partner and the activities of the partnership. Such partners and partnerships should consult their tax advisors regarding the tax consequences of the purchase, ownership and disposition of our common stock.

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There can be no assurance that a court or the IRS will not challenge one or more of the tax consequences described in this prospectus supplement, and we have not obtained, nor do we intend to obtain, a ruling or opinion of counsel with respect to the U.S. federal income tax consequences to a non-U.S. holder of the purchase, ownership or disposition of our common stock.

Distributions on Our Common Stock

Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such non-U.S. holder's adjusted tax basis in the common stock. Any remaining excess will be treated as capital gain from the sale or exchange of such common stock, subject to the tax treatment described below in "Gain on Sale, Exchange or Other Disposition of Our Common Stock."

Except as otherwise described below, dividends paid to a non-U.S. holder will generally be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. A non-U.S. holder who claims the benefit of an applicable income tax treaty generally will be required to satisfy certain certification and other requirements. Such non-U.S. holders must generally provide us and/or our paying agent, as applicable, with a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E (or applicable successor form) claiming an exemption from or reduction in withholding under an applicable income tax treaty. Such certificate must be provided before the payment of dividends and must be updated periodically. If tax is withheld in an amount in excess of the amount applicable under an income tax treaty, a refund of the excess amount may generally be obtained by a non-U.S. holder by timely filing an appropriate claim for refund with the IRS. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under an applicable income tax treaty. Dividends will also be subject to the discussion below regarding backup withholding and foreign accounts.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements prior to the distribution date (generally including provision of a valid IRS Form W-8ECI (or applicable successor form) certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States). However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty.

Gain on Sale, Exchange or Other Disposition of Our Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, in general, a non-U.S. holder will not be subject to any U.S. federal income tax on any gain realized upon such non-U.S. holder's sale, exchange or other disposition of our common stock unless:

- the gain is effectively connected with a U.S. trade or business of the non-U.S. holder and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed base maintained in the United States by such non-U.S. holder, in which case the non-U.S. holder generally will be taxed at the graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock" also may apply;

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- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the net gain derived from the disposition, which may be offset by U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States); or
- our common stock constitutes a U.S. real property interest because we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation." Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. Even if we are or become a U.S. real property holding corporation, provided that our common stock is regularly traded, as defined by applicable U.S. Treasury Regulations, on an established securities market, our common stock will be treated as a U.S. real property interest only with respect to a non-U.S. holder that holds more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. If we are a U.S. real property holding corporation and either our common stock is not regularly traded on an established securities market or a non-U.S. holder holds, or is treated as holding, more than 5% of our outstanding common stock, directly or indirectly, during the applicable testing period, such non-U.S. holder will generally be taxed on any gain in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply. If we are a U.S. real property holding corporation and our common stock is not regularly traded on an established securities market, a non-U.S. holder's proceeds received on the disposition of our common stock will also generally be subject to withholding at a rate of 15%. Prospective investors are encouraged to consult their own tax advisors regarding the possible consequences to them if we are, or were to become, a U.S. real property holding corporation. No assurance can be provided that our common stock is or will in the future be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the dividends on our common stock paid to such non-U.S. holder and the tax withheld, if any, with respect to such dividends. A non-U.S. holder will have to comply with specific certification procedures to establish that the non-U.S. holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. A non-U.S. holder generally will not be subject to U.S. backup withholding with respect to payments of dividends on our common stock if it certifies its non-U.S. status by providing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI (or applicable successor form), or otherwise establishes an exemption; provided we do not have actual knowledge or reason to know such non-U.S. holder is a U.S. person (as defined in the Code). Dividends paid to non-U.S. holders subject to the U.S. withholding tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding. Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the non-U.S. holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner

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similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder may be allowed as a credit against the non-U.S. holder's U.S. federal income tax liability, if any, and may entitle such non-U.S. holder to a refund, provided the required information is timely furnished to the IRS.

FATCA

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a U.S. federal withholding tax of 30% on dividends and, subject to the proposed Treasury Regulations discussed below, the gross proceeds of a disposition of our common stock paid to a "foreign financial institution" (as specifically defined for this purpose) and certain other non-U.S. entities unless various U.S. information reporting and due diligence requirements (generally relating to ownership by U.S. persons of interests in or accounts with those entities) have been satisfied, or an exemption applies. An intergovernmental agreement between the United States and an applicable foreign country may modify these requirements. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of taxes withheld under FATCA. The U.S. Treasury released proposed Treasury Regulations which, if finalized in their present form, would eliminate the federal withholding tax of 30% applicable to the gross proceeds of a sale or other disposition of our common stock. Taxpayers may generally rely on the proposed regulations until final regulations are issued. Non-U.S. holders should consult their tax advisors regarding the effects of FATCA on their investment in our common stock.

THIS SUMMARY IS NOT INTENDED TO BE TAX ADVICE. EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS TAX ADVISOR REGARDING THE PARTICULAR U.S. FEDERAL, STATE AND LOCAL AND NON-U.S. TAX CONSEQUENCES OF PURCHASING, OWNING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAWS.

PLAN OF DISTRIBUTION

We previously entered into the original sales agreement with Cowen and Company LLC, an affiliate of TD Cowen, dated June 1, 2021, and amended on May 9, 2023, under which we could issue and sell from time to time an aggregate of up to \$400 million of our common stock through or to TD Cowen as our sales agent or principal. As of the date of this prospectus supplement, we had sold an aggregate of \$225.1 million of our common stock pursuant to the original sales agreement.

On May 7, 2024 we entered into the Sales Agreement to replace the original sales agreement. In accordance with the terms of the Sales Agreement we may offer and sell from time to time under this prospectus supplement up to \$300,000,000 of our common stock through or to TD Cowen as our sales agent or principal. Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an “at the market offering” as defined in Rule 415 under the Securities Act including sales made directly on or through the Nasdaq Global Select Market or any other existing trading market for shares of our common stock. Sales pursuant to the sales agreement may be made through an affiliate of TD Cowen.

TD Cowen will offer our common stock subject to the terms and conditions of the Sales Agreement on a daily basis or as otherwise agreed upon by us and TD Cowen. We will designate the maximum amount of common stock to be sold through TD Cowen on a daily basis or otherwise determine such maximum amount together with TD Cowen. Subject to the terms and conditions of the Sales Agreement, TD Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct TD Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. TD Cowen or we may suspend the offering of our common stock being made through TD Cowen under the Sales Agreement upon proper notice to the other party. TD Cowen and we each have the right, by giving written notice as specified in the Sales Agreement, to terminate the Sales Agreement in each party’s sole discretion at any time.

The aggregate compensation payable to TD Cowen as sales agent equals up to 3.0% of the gross sales price of the shares sold through it pursuant to this prospectus supplement and the Sales Agreement. We have also agreed to reimburse TD Cowen up to \$75,000 of TD Cowen’s actual outside legal expenses incurred by TD Cowen in connection with this offering. We estimate that the total expenses of the offering payable by us, excluding commissions payable to TD Cowen under the Sales Agreement, will be approximately \$250,000.

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

TD Cowen will provide written confirmation to us following the close of trading on The Nasdaq Global Select Market on each day in which common stock is sold through it as sales agent under the Sales Agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through TD Cowen under the Sales Agreement and the net proceeds to us in connection with the sales of common stock.

Until May 28, 2024, settlement for sales of common stock will occur, unless the parties agree otherwise, on the second business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. After May 28, 2024, settlement for sales of common stock will occur, unless the parties agree otherwise, on the first business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

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In connection with the sales of our common stock on our behalf, TD Cowen will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to TD Cowen will be deemed to be underwriting commissions or discounts. We have agreed in the Sales Agreement to provide indemnification and contribution to TD Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, TD Cowen will not engage in any transactions that stabilizes our common stock.

Our common stock is listed on The Nasdaq Global Select Market and trades under the symbol “MDGL.” The transfer agent of our common stock is Computershare Trust Company, N.A.

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

LEGAL MATTERS

The validity of the securities offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Hogan Lovells US LLP, Washington, D.C. Certain legal matters will be passed upon for TD Cowen by Duane Morris LLP, New York, New York.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report On Internal Control Over Financial Reporting) incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2023 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's requirement for additional financing to fund future operations as described in Note 3 to the financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have on file with the SEC an effective "shelf" registration statement on Form S-3 relating to the securities that may be offered and sold hereunder. The full registration statement, including exhibits thereto, contains additional relevant information about us and these securities that, as permitted by the rules and regulations of the SEC, we have not included in this prospectus supplement or the accompanying prospectus. You should read the full registration statement for further information about us and these securities.

Any statement made in this prospectus supplement or the accompanying prospectus concerning the contents of any contract, agreement or other document is only a summary of the actual contract, agreement or other document. If we have filed any contract, agreement or other document as an exhibit to the registration statement, then you should read the exhibit for a more complete understanding of the document or matter involved.

We maintain a website at www.madrigalpharma.com. We make our SEC filings available on our website, free of charge, as soon as reasonably practicable after such materials are filed with, or furnished to, the SEC. Information presented or accessed through our website is not incorporated into, or made a part of, this prospectus supplement or the accompanying prospectus.

Our SEC filings are available from the SEC's Internet site at <http://www.sec.gov>, which contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC.

In addition, our common stock is listed on The Nasdaq Global Select Market and similar information concerning us can be inspected and copied at the offices of The Nasdaq Stock Market, One Liberty Plaza, 165 Broadway, New York, NY 10006.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form S-3 filed by us with the SEC on May 7, 2024. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement, certain parts of which are omitted in accordance with the rules and regulations of the SEC. For further information about us and the securities offered by this prospectus supplement and the accompanying prospectus, we refer you to the registration statement and its exhibits and schedules which may be obtained as described herein.

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The SEC's rules allow us to "incorporate by reference" information into this prospectus supplement and the accompanying 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 considered to be part of this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus incorporate by reference the documents listed below that we have previously filed with the SEC:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, as filed with the SEC on [February 28, 2024](#);
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, as filed with the SEC on [May 7, 2024](#);
- our Definitive Proxy Statement on Schedule 14A filed on [April 29, 2024](#);
- our Current Reports on Form 8-K, as filed with the SEC on [January 8, 2024](#), [February 28, 2024](#) (filed under Item 5.02) and [March 15, 2024](#), [March 20, 2024](#) and [April 2, 2024](#);
- the description of our common stock contained in our Registration Statement on Form 8-A, filed with the SEC on [January 26, 2007](#), as amended by the description of our common stock contained in [Exhibit 4.3](#) to our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, as filed with the SEC on February 23, 2023, and including any amendment or report filed for the purpose of updating such description.

We also incorporate by reference into this prospectus supplement and the accompanying prospectus all documents filed by us with the SEC pursuant to Sections 12(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of any offering of securities made by this prospectus supplement and the accompanying prospectus. Nothing in this prospectus supplement or the accompanying prospectus shall be deemed to incorporate information furnished but not filed with the SEC (including without limitation, information furnished under Item 2.02 or Item 7.01 of Form 8-K, and any exhibits relating to such information).

Any statement contained in this prospectus supplement or the accompanying prospectus or in a document incorporated or deemed to be incorporated by reference in this prospectus supplement or the accompanying prospectus shall be deemed to be modified or superseded for purposes of this prospectus supplement or the accompanying prospectus to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference modifies or supersedes the statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement and the accompanying prospectus.

You may request a copy of the filings incorporated herein by reference, including exhibits to such documents that are specifically incorporated by reference, at no cost, by writing or calling us at the following address or telephone number:

Mardi C. Dier
Chief Financial Officer
Madrigal Pharmaceuticals, Inc.
Four Tower Bridge
200 Barr Harbor Drive, Suite 200
West Conshohocken, Pennsylvania 19428
(267) 824-2827

Statements contained in this prospectus supplement and the accompanying prospectus as to the contents of any contract or other documents are not necessarily complete, and in each instance investors are referred to the copy of the contract or other document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference and the exhibits and schedules thereto.

PROSPECTUS

Madrigal Pharmaceuticals, Inc.



Common Stock
Preferred Stock
Warrants
Debt Securities
Units

From time to time, we may offer and sell, in one or more offerings, common stock, preferred stock, warrants, debt securities or units consisting of any combination of the other securities described in this prospectus. The preferred stock, warrants or debt securities may be convertible into or exercisable or exchangeable for common stock, preferred stock or other securities. We may offer any combination of the securities, in separate series or classes and in amounts, at prices and on terms described in one or more supplements to this prospectus. In addition, this prospectus may be used to offer securities for certain selling stockholders.

This prospectus describes some of the general terms that may apply to the securities we and/or any selling stockholder may offer and sell and the general manner in which they may be offered. Each time we and/or any selling stockholder offer securities pursuant to this prospectus, we will provide one or more supplements to this prospectus or free writing prospectuses that contain specific information about the offering and the terms of any securities being sold. You should carefully read this prospectus, any prospectus supplement and any free writing prospectus, as well as any documents incorporated in any of the foregoing by reference, before you invest in our securities. This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement. The prospectus supplement or any related free writing prospectus may also add, update, supplement, change or clarify information contained in this prospectus.

Our common stock is traded on the Nasdaq Global Select Market under the symbol "MDGL."

We or any selling stockholder may offer and sell our securities to or through one or more agents, underwriters, dealers or other third parties or directly to one or more purchasers on a continuous or delayed basis. If agents, underwriters or dealers are used to sell our securities, we or any selling stockholder will name them and describe their compensation in a prospectus supplement. The price to the public of our securities and the net proceeds we expect to receive from the sale of such securities will also be set forth in a prospectus supplement. We will not receive any proceeds from the sale of securities by selling stockholders.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD REVIEW CAREFULLY THE RISKS AND UNCERTAINTIES REFERENCED UNDER THE HEADING "[RISK FACTORS](#)" ON PAGE 7 OF THIS PROSPECTUS AS WELL AS THOSE CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND ANY RELATED FREE WRITING PROSPECTUS, AND IN THE OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS OR THE APPLICABLE PROSPECTUS SUPPLEMENT.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is May 7, 2024.

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We are responsible for the information contained and incorporated by reference in this prospectus, in any accompanying prospectus supplement, and in any related free writing prospectus we prepare or authorize. We have not authorized anyone to give you any other information, and we take no responsibility for any other information that others may give you. If you are in a jurisdiction where offers to sell, or solicitations of offers to purchase, the securities offered by this documentation are unlawful, or if you are a person to whom it is unlawful to direct these types of activities, then the offer presented in this document does not extend to you. The information contained in this document speaks only as of the date of this document, unless the information specifically indicates that another date applies. Our business, financial condition, results of operations and prospectus may have changed since those dates.

ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement that we filed with the 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. Under this shelf registration process, we and/or selling stockholders may offer any security, or any combination of the securities, described in this prospectus from time to time in one or more offerings. This prospectus only provides you with a general description of the securities we and/or selling stockholders may offer. Each time we and/or selling stockholders offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the specific terms of the 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. This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement. Each such prospectus supplement and any free writing prospectus that we may authorize to be provided to you may also add, update, supplement, change or clarify information contained in this prospectus or in documents incorporated by reference into this prospectus. We urge you to carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the headings “Where You Can Find Additional Information” and “Incorporation of Certain Information by Reference” before you invest in our securities.

Neither we nor any selling stockholder have authorized anyone to provide you with information in addition to or different from that contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus. We take no responsibility for, and can provide no assurances as to the reliability of, any information not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we or a selling stockholder may authorize to be provided to you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

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

Unless otherwise mentioned or unless the context requires otherwise, throughout this prospectus, any applicable prospectus supplement and any related free writing prospectus, the words “Madrigal,” “we,” “us,” “our,” the “company” or similar references refer to Madrigal Pharmaceuticals, Inc. and its subsidiaries; and the term “securities” refers collectively to our common stock, preferred stock, warrants, debt securities, units consisting of any combination of the securities described in this prospectus, and any combination of the foregoing.

This prospectus and the information incorporated herein by reference contains references to trademarks, service marks and trade names owned by us or other companies. Solely for convenience, trademarks, service marks and trade names referred to in this prospectus and the information incorporated herein, including logos, artwork, and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, service marks and trade names. We do not intend our use or display of other companies’ trade names, service marks or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. We are subject to the information requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. The SEC maintains a website that contains these documents, which may be accessed through the SEC's Electronic Data Gathering, Analysis and Retrieval system, or EDGAR, via electronic means, including the SEC's home page (www.sec.gov).

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated, and those future filings may modify or supersede some of the information included or incorporated in this prospectus. You should review all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus. This prospectus incorporates by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the completion of the offering of securities described in this prospectus:

- our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2023, as filed with the SEC on February 28, 2024;
- our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2024, as filed with the SEC on May 7, 2024;
- our Definitive Proxy Statement on [Schedule 14A](#) filed on April 29, 2024;
- our Current Reports on Form 8-K, as filed with the SEC on [January 8, 2024](#), [February 28, 2024](#) (filed under Item 5.02), [March 15, 2024](#), [March 20, 2024](#) and [April 2, 2024](#);
- the description of our common stock contained in our Registration Statement on Form 8-A, filed with the SEC on [January 26, 2007](#), as amended by the description of our common stock contained in [Exhibit 4.3](#) to our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2022, as filed with the SEC on February 23, 2023, and including any amendment or report filed for the purpose of updating such description.

We do not, however, incorporate by reference in this prospectus or any prospectus supplement any documents or portions thereof that are not deemed "filed" with the SEC, including any information furnished pursuant to Item 2.02 or Item 7.01 of our Current Reports on Form 8-K unless, and except to the extent, specified in such reports.

You may request a copy of these filings, at no cost, by contacting us, either orally or in writing, at:

Mardi C. Dier
Chief Financial Officer
Madrigal Pharmaceuticals, Inc.
Four Tower Bridge
200 Barr Harbor Drive, Suite 200
West Conshohocken, Pennsylvania 19428
(267) 824-2827

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You may also access these documents, free of charge on the SEC's website at www.sec.gov or on our website at www.madrigalpharma.com. The reference to our website is intended to be an inactive textual reference only. The information contained in, or that can be accessed through, our website is not part of this prospectus.

This prospectus is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

Neither we nor any selling stockholder have authorized anyone to provide you with information other than what is incorporated by reference or provided in this prospectus or any prospectus supplement.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference herein contain statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These forward-looking statements are based on our beliefs and assumptions and on information currently available to us, but are subject to factors beyond our control. Forward-looking statements reflect management's current knowledge, assumptions, judgment and expectations regarding future performance or events; include all statements that are not historical facts; and can be identified by terms such as "accelerate," "achieve," "allow," "anticipates," "appear," "be," "believes," "can," "continue," "confidence," "could," "demonstrates," "design," "estimates," "expectation," "expects," "forecasts," "future," "goal," "help," "hopeful," "inform," "informed," "intends," "may," "might," "on track," "planned," "planning," "plans," "positions," "potential," "powers," "predicts," "predictive," "projects," "seeks," "should," "will," "will achieve," "will be," "would" or similar expressions and the negatives of those terms. We believe that it is important to communicate our future expectations to our investors. However, there may be events in the future that we are not able to accurately predict or control and that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements.

Investors are cautioned not to unduly rely on forward-looking statements because they relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- The initiation of the commercial launch of Rezdiffra™ (resmetirom) for the treatment of adults with noncirrhotic non-alcoholic steatohepatitis ("NASH") with moderate to advanced liver fibrosis in the United States;
- Anticipated or estimated future results, including the risks and uncertainties associated with our future operating performance and financial position, and our projected resources and sufficiency of capital to fund our operating expenses;
- Our possible or assumed future results of operations and expenses, business strategies and plans (including potential ex-U.S. commercialization or partnering opportunities), capital needs and financing plans, including incurrence of indebtedness and compliance with debt covenants under the Loan and Security Agreement with Hercules Capital, Inc., as agent and lender, market trends, market sizing, competitive position, industry environment and potential growth opportunities, among other things;
- Post-approval requirements and commitments, including verification of a clinical benefit in confirmatory trials;
- Our ability to delay certain research activities and related clinical expenses as necessary;
- Our clinical trials, including the anticipated timing of disclosure, presentations of data from, or outcomes from our trials;
- Research and development activities, and the timing and results associated with the future development of Rezdiffra / resmetirom, including projected market size, sector leadership, and patient treatment estimates for NASH and non-alcoholic fatty liver disease ("NAFLD") patients;
- The timing and completion of projected future clinical milestone events, including enrollment, additional studies, top-line data and open label projections;
- Rezdiffra's potential to be a cost-effective specialty therapy for NASH patients with significant liver fibrosis (consistent with fibrosis stages 2 and 3);
- Projections or objectives for obtaining full approval for resmetirom for NASH patients with significant fibrosis (or non-cirrhotic NASH patients) and NASH patients with compensated cirrhosis, including all statements concerning potential clinical benefit to support approval and/or potential approval;

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- Estimates of patients diagnosed with NASH;
- Our primary and key secondary study endpoints for resmetirom, and the potential for achieving such endpoints and projections, including NASH resolution, safety, fibrosis treatment, cardiovascular effects and lipid treatment with resmetirom;
- The relationship between NASH progression and adverse patient outcomes;
- The estimated clinical burden of uncontrolled NASH;
- Analyses for patients with NASH with significant fibrosis concerning potential progression to cirrhosis, decompensated cirrhosis, liver transplant or death, and cardiovascular risks, comorbidities and outcomes;
- Optimal dosing levels for resmetirom and projections regarding potential NASH or NAFLD and potential patient benefits with resmetirom, including future NASH resolution, safety, fibrosis treatment, cardiovascular effects, lipid treatment and/or biomarker effects with resmetirom;
- Our ability to address the unmet needs of patients suffering from NASH with significant fibrosis;
- The potential efficacy and safety of resmetirom for non-cirrhotic NASH patients and cirrhotic NASH patients;
- The potential for resmetirom to become the best-in-class treatment option for patients with NASH and significant fibrosis;
- Strategies, objectives and commercial opportunities, including potential prospects or results;
- Potential ex-U.S. commercialization or partnering opportunities;
- The ability to develop clinical evidence demonstrating the utility of non-invasive tools and techniques to screen and diagnose NASH and/or NAFLD patients;
- The predictive power of liver fat reduction with resmetirom, as measured by non-invasive tests, on NASH resolution and/or fibrosis reduction or improvement, and potential NASH or NAFLD patient risk profile benefits with resmetirom;
- The predictive power of liver fat, liver volume changes or MAST scores for NASH and/or NAFLD patients;
- The predictive power of NASH resolution and/or fibrosis reduction with resmetirom or improvement using non-invasive tests, including the use of ELF, FibroScan, MRE and/or MRI-PDFP;
- The predictive power of non-invasive tests generally, including for purposes of diagnosing NASH, monitoring patient response to resmetirom, or recruiting and conducting a NASH clinical trial;
- Market demand for and acceptance of our products;
- Research, development and commercialization of new products;
- The potential for resmetirom to be an effective treatment for other disease indications;
- Obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections;
- Risks associated with meeting the objectives of our clinical studies, including, but not limited to our ability to achieve enrollment objectives concerning patient numbers (including an adequate safety database), outcomes objectives and/or timing objectives for our studies, any delays or failures in enrollment, the occurrence of adverse safety events, and the risks of successfully conducting trials that are substantially larger, and have patients with different disease states, than our past trials;

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- The potential impact of cyber attacks and other security incidents on our operations or business;
- Our continued reliance on third-party contract manufacturers for the manufacture of our products and product candidates, including resmetirom;
- Risks related to the effects of resmetirom's mechanism of action and our ability to accomplish our business and business development objectives and realize the anticipated benefit of any such transactions; and
- Assumptions underlying any of the foregoing.

Given these uncertainties, you should not place undue reliance on these forward-looking statements. These forward-looking statements speak only as of the date on which the statements were made and are not guarantees of future performance. Except as may be required by applicable law, we do not undertake or intend to update any forward-looking statements after the date of this prospectus or the respective dates of documents incorporated by reference herein that include forward-looking statements.

RISK FACTORS

You should carefully consider the risks described in the documents incorporated by reference in this prospectus and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described in the documents incorporated herein by reference, including our most recent annual report on Form 10-K which is on file with the SEC and is incorporated herein by reference, and other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

ABOUT THE COMPANY

We are a biopharmaceutical company focused on delivering novel therapeutics for nonalcoholic steatohepatitis (“NASH”), also known as metabolic dysfunction-associated steatohepatitis (“MASH”), a liver disease with high unmet medical need. In March 2024, we announced that Rezdiffra™ (resmetirom) has been granted accelerated approval by the U.S. Food and Drug Administration (“FDA”) in conjunction with diet and exercise for the treatment of adults with noncirrhotic NASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). Continued approval for this indication may be contingent upon verification and description of clinical benefit in ongoing confirmatory trials.

Rezdiffra is a once-daily, oral THR-b agonist designed to target key underlying causes of NASH. NASH is a more advanced form of nonalcoholic fatty liver disease (“NAFLD”). NASH is a leading cause of liver-related mortality and an increasing burden on healthcare systems globally. Additionally, patients with NASH, especially those with more advanced metabolic risk factors (hypertension, concomitant type 2 diabetes), are at increased risk for adverse cardiovascular events and increased morbidity and mortality.

We were incorporated in Delaware in September 2011. Our principal executive offices are located at 200 Barr Harbor Drive, Suite 200, West Conshohocken, Pennsylvania 19428 and our telephone number at that address is (267) 824-2827. We maintain a website at www.madrigalpharma.com. The information on, or that can be accessed through, our website does not constitute part of this prospectus, and you should not rely on any such information in making the decision whether to purchase our securities.

DESCRIPTION OF CAPITAL STOCK

The following is a summary of all material characteristics of our capital stock as set forth in our restated certificate of incorporation, our restated bylaws, our Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock and our Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock. Our common stock is the only class of our securities registered under Section 12 of the Exchange Act, and is listed on The Nasdaq Stock Market LLC. The summary does not purport to be complete and is qualified in its entirety by reference to our certificate of incorporation and bylaws, copies of which are incorporated by reference as exhibits to the registration statement of which this prospectus forms a part.

Description of Common Stock

We are authorized to issue 200,000,000 shares of common stock, par value \$0.0001 per share. The following summary of certain provisions of our common stock does not purport to be complete. You should refer to our restated certificate of incorporation and our restated bylaws, both of which are incorporated by reference as exhibits to the registration statement of which this prospectus forms a part. The summary below is also qualified by provisions of applicable law.

General

Holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, and do not have cumulative voting rights. Subject to preferences that may be applicable to any outstanding shares of preferred stock, holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our board of directors out of funds legally available for dividend payments. The holders of common stock have no preferences or rights of conversion, exchange, pre-emption or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. In the event of any liquidation, dissolution or winding-up of our affairs, holders of common stock will be entitled to share ratably in our assets that are remaining after payment or provision for payment of all of our debts and obligations and after liquidation payments to holders of outstanding shares of preferred stock, if any.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company N.A., whose address is Meidinger Tower, 462 South 4th Street, Louisville, KY 40202 and whose telephone number is (502) 301-6088.

Nasdaq Global Select Market

Our common stock is listed for quotation on The Nasdaq Global Select Market under the symbol "MDGL."

Dividends

We have never declared any cash dividends on our common stock and we do not anticipate paying any cash dividends on our common stock in the foreseeable future.

Description of Preferred Stock

We are authorized to issue 5,000,000 shares of preferred stock, par value \$0.0001 per share. As of March 31, 2024, we had (i) 1,969,797 shares of preferred stock, designated Series A Convertible Preferred Stock, outstanding held by two stockholders of record, and (ii) 400,000 shares of preferred stock, designated Series B Convertible Preferred Stock, outstanding held by two stockholders of record. No other shares of our preferred stock were outstanding or designated. The following summary of certain provisions of our preferred stock does

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not purport to be complete. You should refer to our restated certificate of incorporation, our restated bylaws, our Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock and our Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock, each of which have been filed with the SEC. The summary below is also qualified by provisions of applicable law.

General

Our board of directors may, without further action by our stockholders, from time to time, direct the issuance of shares of preferred stock in series and may, at the time of issuance, determine the rights, preferences and limitations of each series, including voting rights, dividend rights and redemption and liquidation preferences. Satisfaction of any dividend preferences of outstanding shares of preferred stock would reduce the amount of funds available for the payment of dividends on shares of our common stock. Holders of shares of preferred stock may be entitled to receive a preference payment in the event of any liquidation, dissolution or winding-up of our company before any payment is made to the holders of shares of our common stock. In some circumstances, the issuance of shares of preferred stock may render more difficult or tend to discourage a merger, tender offer or proxy contest, the assumption of control by a holder of a large block of our securities or the removal of incumbent management. Upon the affirmative vote of our board of directors, without stockholder approval, we may issue shares of preferred stock with voting and conversion rights which could adversely affect the holders of shares of our common stock.

Series A Convertible Preferred Stock

Each share of the Series A Convertible Preferred Stock is convertible into shares of the common stock at any time at the holder's option at a one-to-one ratio, subject to adjustment. A holder of Series A Convertible Preferred Stock, however, will be prohibited from converting shares of the Series A Convertible Preferred Stock into shares of our common stock if, as a result of such conversion, the holder, together with its affiliates, would own more than 4.99% of the shares of our common stock or any other class of any equity security of ours (other than an exempted security) that is registered pursuant to Section 12 of the Exchange Act, which may be increased or decreased to any other percentage at the holder's election on 61 days' notice delivered to the Company.

Upon our liquidation, dissolution or winding-up, whether voluntary or involuntary, after the satisfaction in full of our debts and the payment of any liquidation preference owed to the holders of shares of our capital stock ranking prior to the Series A Convertible Preferred Stock upon liquidation, the holders of the Series A Convertible Preferred Stock shall participate *pari passu* with the holders of our common stock and the holders of our Series B Convertible Preferred Stock (on an as-if-converted-to-common-stock basis) in our net assets. Shares of the Series A Convertible Preferred Stock will generally have no voting rights, except as required by law. Shares of the Series A Convertible Preferred Stock will be entitled to receive dividends *pari passu* with the shares of the Series B Convertible Preferred Stock, and before shares of any other class or series of our capital stock (other than dividends in the form of our common stock) equal to the dividend payable on each share of our common stock, on an as-converted basis.

Series B Convertible Preferred Stock

Each share of the Series B Convertible Preferred Stock is convertible into shares of the common stock at any time at the holder's option at a one-to-one ratio, subject to adjustment as provided in the Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock. A holder of Series B Convertible Preferred Stock, however, will be prohibited from converting shares of the Series B Convertible Preferred Stock into shares of our common stock if, as a result of such conversion, the holder, together with its affiliates, would own more than 4.99% of the shares of our common stock or any other class of any equity security of ours (other than an exempted security) that is registered pursuant to Section 12 of the Exchange Act, which may be increased or decreased up to 19.99% at the holder's election on 61 days' notice delivered to the Company.

Upon our liquidation, dissolution or winding-up, whether voluntary or involuntary, after the satisfaction in full of our debts and the payment of any liquidation preference owed to the holders of shares of our capital stock ranking prior to the Series B Convertible Preferred Stock upon liquidation, the holders of the Series B Convertible Preferred Stock shall participate pari passu with the holders of our common stock and the holders of the Series A Convertible Preferred Stock (on an as-if-converted-to-common-stock basis) in our net assets. Shares of the Series B Convertible Preferred Stock will generally have no voting rights, except as required by law. Shares of the Series B Convertible Preferred Stock will be entitled to receive dividends pari passu with the shares of the Series A Convertible Preferred Stock, and before shares of any other class or series of capital stock of the Company (other than dividends in the form of the Common Stock) equal to the dividend payable on each share of our common stock, on an as-converted basis.

Anti-Takeover Provisions of our Certificate of Incorporation and Bylaws

In addition to the board of directors' ability to issue shares of preferred stock, our restated certificate of incorporation and restated bylaws contain other provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of our company unless such takeover or change in control is approved by our board of directors.

These provisions, summarized below, are expected 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 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.

Classified board of directors; removal of directors for cause. Our restated certificate of incorporation and restated bylaws provide for our board of directors to be divided into three classes serving staggered terms. At each annual meeting of stockholders, directors elected to succeed those directors whose terms have expired are elected for a three-year term of office. All directors elected to our classified board of directors will serve until the election and qualification of their respective successors or their earlier resignation or removal. The board of directors is authorized to create new directorships and to fill such positions so created and is permitted to specify the class to which any such new position is assigned. The person filling such position would serve for the term applicable to that class. The board of directors (or its remaining members, even if less than a quorum) also is empowered to fill vacancies on the board of directors occurring for any reason for the remainder of the term of the class of directors in which the vacancy occurred. Members of the board of directors may only be removed for cause and only by the affirmative vote of 80% of our outstanding voting stock. These provisions are likely to increase the time required for stockholders to change the composition of the board of directors. For example, in general, at least two annual meetings will be necessary for stockholders to effect a change in a majority of the members of the board of directors. The provision for a classified board could prevent a party who acquires control of a majority of our outstanding common stock from obtaining control of our board of directors until our second annual stockholders meeting following the date the acquirer obtains the controlling stock interest. The classified board provision could have the effect of discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us and could increase the likelihood that incumbent directors will retain their positions.

Advance notice provisions for stockholder proposals. Our restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors, as well as procedures for including proposed nominations at special meetings at which directors are to be elected. Stockholders at our annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board or by a stockholder who was a stockholder of record on the record date for the meeting,

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who is entitled to vote at the meeting and who has given to our secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting, and who has complied with the procedures and requirements set forth in the bylaws. Although our bylaws do not give our board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, our bylaws may have the effect of precluding the conduct of some business at a meeting if the proper procedures are not followed or may discourage or defer a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of us.

Special meetings of stockholders. Special meetings of the stockholders may be called only by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors. Stockholders are not permitted to call a special meeting or to require our board of directors to call a special meeting.

No stockholder action by written consent. Our restated certificate of incorporation and restated bylaws do not permit our stockholders to act by written consent. As a result, any action to be effected by our stockholders must be effected at a duly called annual or special meeting of the stockholders.

Super-majority stockholder vote required for certain actions. The Delaware General Corporation Law, or DGCL, provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless the corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our restated certificate of incorporation requires the affirmative vote of the holders of at least 80% of our outstanding voting stock to amend or repeal certain provisions of our restated certificate of incorporation. This 80% stockholder vote would be in addition to any separate class vote that might in the future be required pursuant to the terms of any preferred stock that might then be outstanding. In addition, an 80% vote is also required for any amendment to, or repeal of, our restated bylaws by the stockholders. Our restated bylaws may be amended or repealed by a vote of a majority of the total number of authorized directors.

Provisions of Delaware Law Governing Business Combinations

We are subject to the "business combination" provisions of Section 203 of the DGCL. In general, such provisions prohibit a publicly held Delaware corporation from engaging in any "business combination" transactions with any "interested stockholder" for a period of three years after the date on which the person became an "interested stockholder," unless:

- prior to such date, the board of directors approved either the "business combination" or the transaction which resulted in the "interested stockholder" obtaining such status; or
- upon consummation of the transaction which resulted in the stockholder becoming an "interested stockholder," the "interested stockholder" owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the "interested stockholder") those shares owned by (a) persons who are directors and also officers and (b) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to such time the "business combination" is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 $\frac{2}{3}$ % of the outstanding voting stock which is not owned by the "interested stockholder."

A "business combination" is defined to include mergers, asset sales and other transactions resulting in financial benefit to a stockholder. In general, an "interested stockholder" is a person who, together with affiliates and

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associates, owns 15% or more of a corporation's voting stock or within three years did own 15% or more of a corporation's voting stock. The statute could prohibit or delay mergers or other takeover or change in control attempts with respect to us and, accordingly, may discourage attempts to acquire us.

DESCRIPTION OF SECURITIES TO BE OFFERED

We may offer shares of our common stock, preferred stock, warrants to purchase common stock or preferred stock, debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt, or units consisting of any combination of the other types of securities offered from time to time in one or more offerings under this prospectus at prices and on terms to be determined at the time of any offering. This prospectus provides you with a general description of the securities we and/or any selling stockholder may offer. Each time we and/or any selling stockholder offer a type or series of securities under this prospectus, we will provide a prospectus supplement and/or free writing prospectus that will describe the specific amounts, prices and other important terms of the securities.

Common Stock. We and/or any selling stockholder may issue and/or sell, as applicable, shares of our common stock from time to time. Holders of shares of our common stock are entitled to one vote for each share held of record on all matters to be voted on by stockholders and do not have cumulative voting rights. Subject to the preferences that may be applicable to any then outstanding shares of preferred stock, the holders of our outstanding shares of common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of funds legally available for dividend payments. The holders of our common stock have no preferences or rights of conversion, exchange, pre-emption or other subscription rights. There are no redemption or sinking fund provisions applicable to our common stock. In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the rights, preferences and privileges of the shares of each wholly unissued series, and any qualifications, limitations or restrictions thereon, including dividend rights, voting rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for other securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the rights, preferences and privileges of the preferred stock of such series, as well as any qualifications, limitations or restrictions thereon, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. We will describe the specific terms of a particular series of preferred stock in the prospectus supplement related to that series. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you, as well as the complete certificate of designation, for complete information on any applicable series of preferred stock.

Warrants. We may issue warrants for the purchase of common stock and/or preferred stock in one or more series. We may issue warrants independently or together with common stock and/or preferred stock, and the warrants may be attached to or separate from these securities. We will describe the specific terms of any warrants we may offer in the prospectus supplement related to such warrants. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you, as well as the complete warrant agreements and warrant certificates, for complete information on the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address

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of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

Debt Securities. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in this instrument governing the debt, to all of our senior indebtedness. Convertible or exchangeable debt securities will be convertible into or exchangeable into our common stock or preferred stock. In this prospectus, we have summarized certain general features of the debt securities. The applicable prospectus supplement will describe the specific debt securities being offered, the price at which they will be offered and other key terms including, as applicable, maturity dates, interest rates, denominations, redemption, conversion, exchange, covenants and events of default. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you, as well as the complete indenture that contains the terms of the debt securities, for complete information on the series of debt securities being offered. We will file as exhibits to the registration statement of which this prospectus is a part, the form of indenture and any supplemental agreements that describe the terms of the series of debt securities we are offering before the issuance of the related series of debt securities.

We may evidence each series of debt securities we will issue by an indenture that we enter into with a trustee. We will indicate the name and address of the trustee, if applicable, in the prospectus supplement relating to the particular series of debt securities being offered.

Units. We may issue, in one or more series, units consisting of any combination of the securities described in this prospectus. We will describe the terms of the units we may offer in the prospectus supplement related to such units. The applicable prospectus supplement may describe the price or prices at which we will issue the units; the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately; any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and whether the units will be issued in fully registered or global form. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you, as well as the complete unit agreement that contains the terms of the units. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

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

USE OF PROCEEDS

Except as described in any prospectus supplement or in any related free writing prospectus that we may authorize to be provided to you, we intend to use the net proceeds received by us from the sale of the securities described in this prospectus for general corporate purposes. Unless otherwise set forth in a prospectus supplement, we will not receive any proceeds from the sale of securities by any selling stockholder.

SELLING STOCKHOLDERS

Selling stockholders are persons or entities that, directly or indirectly, have acquired or will from time to time acquire, our securities. Such selling stockholders may be parties to registration rights agreements with us, or we otherwise may have agreed or will agree to register their securities for resale. The initial purchasers of our

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securities, as well as their transferees, pledges, donees or successors, all of whom we refer to as “selling stockholders,” may from time to time offer and sell our securities pursuant to this prospectus and any applicable prospectus supplement. The applicable prospectus supplement will set forth the name of each of the selling stockholders and the number of securities beneficially owned by such selling stockholder that are covered by such prospectus supplement. The applicable prospectus supplement will also disclose whether any of the selling stockholders has held any position or office with, has been employed by or otherwise has had a material relationship with us during the three years prior to the date of the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We and/or any selling stockholder may sell our securities from time to time in one or more transactions. We and/or any selling stockholder may sell our securities to or through agents, underwriters, dealers, remarketing firms or other third parties or directly to one or more purchasers or through a combination of any of these methods of sale. In some cases, we and/or any selling stockholder or dealer acting with us and/or any selling stockholder or on behalf of us and/or any selling stockholder may also purchase our securities and reoffer them to the public. We and/or any selling stockholder may also offer and sell, or agree to deliver, our securities pursuant to, or in connection with, any option agreement or other contractual arrangement.

Agents whom we designate may solicit offers to purchase our securities.

We and/or any selling stockholder will name any agent involved in offering or selling our securities, and disclose any commissions that we will pay to the agent, in the applicable prospectus supplement.

Unless we and/or any selling stockholder indicate otherwise in the applicable prospectus supplement, agents will act on a best efforts basis for the period of their appointment. Agents may be deemed to be underwriters under the Securities Act, of any of our securities that they offer or sell.

We and/or any selling stockholder may use an underwriter or underwriters in the offer or sale of our securities.

If we and/or any selling stockholder use an underwriter or underwriters, we will execute an underwriting agreement with the underwriter or underwriters at the time that we reach an agreement for the sale of our securities. We and/or any selling stockholder will include the names of the specific managing underwriter or underwriters, as well as the names of any other underwriters, and the terms of the transactions, including the compensation the underwriters and dealers will receive, in the applicable prospectus supplement. The underwriters will use the applicable prospectus supplement, together with the prospectus, to sell our securities. The underwriters may offer and sell our securities at a fixed price or prices which may be changed, at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices, any of which may represent a discount from the prevailing market price.

We may also, from time to time, authorize a dealer or agents to sell our securities. If we and/or any selling stockholder use a dealer, we will sell our securities to the dealer, as principal. The dealer will then sell our securities to the public at varying prices that the dealer will determine at the time it sells our securities. We and/or any selling stockholder will include the name of the dealer and the terms of the transactions with the dealer in the applicable prospectus supplement.

We and/or any selling stockholder may solicit directly offers to purchase our securities, and we may directly sell our securities to institutional or other investors. We and/or any selling stockholder will describe the terms of direct sales in the applicable prospectus supplement.

We and/or any selling stockholder may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) of the Securities Act.

We and/or any selling stockholder will indemnify agents, underwriters and dealers against certain liabilities, including liabilities under the Securities Act. The terms and conditions of any indemnification will be described in the applicable prospectus supplement. Agents, underwriters and dealers, or their affiliates, may engage in transactions with, or perform services for, us or our affiliates in the ordinary course of business.

We and/or any selling stockholder may authorize agents and underwriters to solicit offers by certain institutions to purchase our securities at the public offering price under delayed delivery contracts. If we and/or any selling stockholder use delayed delivery contracts, we will disclose that we are using them in the prospectus supplement and will tell you when we will demand payment and when delivery of our securities will be made under the

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delayed delivery contracts. These delayed delivery contracts will be subject only to the conditions that we describe in the prospectus supplement. We and/or any selling stockholder will describe in the applicable prospectus supplement the commission that underwriters and agents soliciting purchases of our securities under delayed delivery contracts will be entitled to receive.

Unless otherwise specified in connection with a particular underwritten offering of our securities, the underwriters will not be obligated to purchase offered securities unless specified conditions are satisfied, and if the underwriters do purchase any offered securities, they will purchase all offered securities.

In connection with underwritten offerings of the offered securities and in accordance with applicable law and industry practice, the underwriters in certain circumstances are permitted to engage in certain transactions that stabilize, maintain or otherwise affect the price of our securities, including the entry of stabilizing bids or syndicate covering transactions. If the underwriters create a short position in our securities in connection with the offering (*i.e.*, if they sell more securities than are set forth on the cover page of the applicable prospectus supplement), the underwriters may reduce that short position by purchasing our securities in the open market or as otherwise provided in the applicable prospectus supplement.

The underwriters may also impose a penalty bid, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. In general, purchases of a security for the purpose of stabilization or to reduce a short position could cause the price of the security to be higher than it might be in the absence of such purchases. The imposition of a penalty bid might also affect the price of our securities to the extent that it were to discourage resales of our securities. The underwriters are not required to engage in these activities and may end any of these activities at any time.

Such purchasers in the foregoing scenarios will be subject to the applicable provisions of the Securities Act and the Exchange Act and the rules and regulations thereunder, including Rule 10b-5 and Regulation M. Regulation M may restrict the ability of any person engaged in the distribution of the securities to engage in market-making activities with respect to those securities. In addition, the anti-manipulation rules under the Exchange Act may apply to sales of our securities in the market. This may affect the marketability of our securities and the ability of any person to engage in market-making activities with respect to our securities.

We and/or any selling stockholder may effect sales of securities in connection with forward sale, option or other types of agreements with third parties. Any distribution of securities pursuant to any forward sale agreement may be effected from time to time in one or more transactions that may take place through a stock exchange, including block trades or ordinary broker's transactions, or through broker-dealers acting either as principal or agent, or through privately-negotiated transactions, or through an underwritten public offering, or through a combination of any such methods of sale, at market prices prevailing at the time of sale, prices relating to such prevailing market prices or at negotiated or fixed prices.

The specific terms of the lock-up provisions, if any, in respect of any given offering will be described in the applicable prospectus supplement.

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon by Hogan Lovells US LLP, Washington, DC.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report On Internal Control Over Financial Reporting) incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2023 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's requirement for additional financing to fund future operations as described in Note 3 to the financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

\$300,000,000



Common Stock

PROSPECTUS SUPPLEMENT

TD Cowen

May 7, 2024

Calculation of Filing Fee Tables

424(b)(5)
(Form Type)

Madrigal Pharmaceuticals, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

| | Security Type | Security Class Title | Fee Calculation or Carry Forward Rule | Amount Registered | Proposed Maximum Offering Price Per Unit | Maximum Aggregate Offering Price | Fee Rate | Amount of Registration Fee ⁽¹⁾ | Carry Forward Form Type | Carry Forward File Number | Carry Forward Initial Effective Date | Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward |
|------------------------------------|----------------------------|--|---------------------------------------|-------------------|--|----------------------------------|------------|---|-------------------------|---------------------------|--------------------------------------|---|
| Newly Registered Securities | | | | | | | | | | | | |
| Fees to Be Paid | Equity | Common Stock, \$0.0001 par value per share | Rule 457(o) | \$125,174,107 | N/A | \$125,174,107 | 0.00014760 | \$18,476 | | | | |
| Fees Previously Paid | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | | | | |
| Carry Forward Securities | | | | | | | | | | | | |
| Carry Forward Securities | Equity | Common Stock, \$0.0001 par value per share | 415(a)(6) | \$174,825,893 | | \$174,825,893 | | | 424(b)(5) | 333-566666 | May 9, 2023 | \$19,266 ⁽²⁾ |
| | Total Offering Amounts | | | | | \$300,000,000 | | N/A | | | | |
| | Total Fees Previously Paid | | | | | | | N/A | | | | |
| | Total Fee Offsets | | | | | | | N/A | | | | |
| | Net Fee Due | | | | | | | \$18,476 | | | | |

- (1) In accordance with Rules 456(b) and 457(r) under the Securities Act of 1933, as amended, the registrant initially deferred payment of all of the registration fees for the Registration Statement on Form S-3, filed on May 7, 2024.
- (2) The Registrant is registering shares of common stock having a proposed maximum aggregate offering price of up to \$300,000,000 pursuant to this prospectus supplement. Pursuant to Rule 415(a)(6) under the Securities Act of 1933, as amended (the "Securities Act"), the securities registered pursuant to this prospectus supplement include \$174,825,893 of unsold securities (the "Unsold Securities") of the Registrant that had been previously registered pursuant to the registration statement on Form S-3 (File No. 333-256666) and a prospectus supplement, dated May 9, 2023 (the "Prior Prospectus"). In connection with the registration of the Unsold Securities on the Prior Prospectus, the Registrant paid a registration fee of \$19,266 which was carried forward to the Registrant's registration statement on Form S-3 filed on May 7, 2024 (the "2024 Automatic Shelf") to which this prospectus supplement relates. Pursuant to Rule 415(a)(6), the offering of the Unsold Securities registered under the Prior Prospectus was deemed terminated as of the date of effectiveness of the 2024 Automatic Shelf.