

PROSPECTUS SUPPLEMENT
(To Prospectus dated June 1, 2021)



3,914,910 Shares of Common Stock

This prospectus supplement relates to the possible resale, from time to time, by the selling stockholder named in this prospectus supplement of up to an aggregate of 3,914,910 shares of our common stock, which includes 1,969,797 shares of common stock issuable upon the conversion of our Series A Convertible Preferred Stock and 400,000 shares of common stock issuable upon the conversion of our Series B Convertible Preferred Stock.

We are not selling any shares of common stock under this prospectus supplement and will not receive any proceeds from the sale of shares by the selling stockholder.

Sales of shares of common stock by the selling stockholder may occur at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices. We provide more information about how the selling stockholder may sell its shares of common stock in the section entitled "Plan of Distribution" on page S-13. The selling stockholder may sell shares to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from the selling stockholder, the purchasers of the shares, or both.

We are paying the cost of registering the shares of common stock covered by this prospectus supplement as well as various related expenses. The selling stockholder is responsible for all selling commissions, transfer taxes and other costs related to the offer and sale of its shares.

Our common stock is traded on The Nasdaq Global Select Market under the trading symbol "MDGL." On August 7, 2023, the last reported sale price of our common stock on The Nasdaq Global Select Market was \$179.49 per share.

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-8 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.

The date of this prospectus is August 8, 2023

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ABOUT THIS PROSPECTUS SUPPLEMENT

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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.

Throughout this prospectus supplement, when we refer to the selling stockholder, we are referring to the selling stockholder identified in this prospectus supplement and, as applicable, its permitted transferees or other successors-in-interest that may be identified in a prospectus supplement or, if required, post-effective amendment to the registration statement of which this prospectus supplement is a part. The selling stockholder is offering to sell, and seeking offers to buy, the shares of common stock only in jurisdictions where offers and sales thereof are permitted.

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 the selling stockholder have authorized anyone to provide you with any different information. We and the selling stockholder 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.

Unless otherwise indicated, information contained in or incorporated by reference into this prospectus supplement and the accompanying 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 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

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numerous known and unknown risks and uncertainties. Some of these risks and uncertainties are described under the heading “Risk Factors” beginning on page S-8 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:

- anticipated or estimated future results, including the risks and uncertainties associated with our future operating performance and financial position;
- our possible or assumed future results of operations and expenses, business strategies and plans (including ex-U.S. launch/partnering plans), 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;
- our ability to delay certain research activities and related clinical expenses as necessary;
- our projected resources and sufficiency of capital to fund our operating expenses through the projected commercial launch of resmetirom, assuming Food and Drug Administration ("FDA") approval is obtained;
- 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 our lead product candidate, resmetirom (formerly known as MGL-3196), including projected market size, sector leadership, and patient treatment estimates for non-alcoholic steatohepatitis ("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;
- resmetirom's potential to be a cost-effective specialty therapy for NASH patients with significant liver fibrosis;
- plans, objectives and timing for making a Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) submission to the FDA;
- projections or objectives for obtaining accelerated or full approval for resmetirom for NASH patients with significant fibrosis (or non-cirrhotic NASH patients) and NASH patients with compensated cirrhosis;
- 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;

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- 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 and/or first-to-market treatment option for patients with NASH and liver fibrosis;
- anticipated or estimated future results of operations and expenses as we expand our resmetirom clinical development program and our commercial development program;
- ex-U.S. launch/partnering plans;
- 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 liver fibrosis reduction with resmetirom or improvement using non-invasive tests, including the use of ELF, FibroScan, MRE and/or MRI-PDFE;
- 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;
- our continued reliance on third-party contract manufacturers for the manufacture of our 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.

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.

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Forward-looking statements are subject to a number of risks and uncertainties including, but not limited to: our clinical and commercial development of resmetirom; enrollment and trial outlook uncertainties, generally, based on blinded, locked or limited trial data and in relation to COVID-19 related measures and individual precautionary measures that may be implemented or continued for an uncertain period of time; 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, if at all; 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; 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. 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, 2022, filed with the SEC on February 23, 2023, as amended by our Form 10-K/A filed with the SEC on March 3, 2023, and as updated by the risk factors discussed in our other filings with the SEC. 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 or the rules of the Nasdaq Stock Market 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. Because it is only a summary, it 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 fiscal year ended December 31, 2022 filed with the SEC on February 23, 2023, as amended by our Form 10-K/A filed with the SEC on March 3, 2023, as well as in our other filings with the SEC.

Overview

We are a clinical-stage biopharmaceutical company pursuing novel therapeutics for nonalcoholic steatohepatitis (NASH), a liver disease with high unmet medical need. Our lead product candidate, resmetirom, is a proprietary, liver-directed, selective thyroid hormone receptor- β , or THR- β , agonist being developed as a once-daily oral pill for the potential treatment of patients with NASH with fibrosis and NASH with compensated cirrhosis. NASH is a serious inflammatory form of nonalcoholic fatty liver disease, or NAFLD. NAFLD has become the most common liver disease in the United States and other developed countries and is characterized by an accumulation of fat in the liver with no other apparent causes.

NASH can progress to cirrhosis or liver failure, require liver transplantation and can also result in liver cancer. Progression of NASH to end stage liver disease will soon surpass all other causes of liver failure requiring liver transplantation. Importantly, beyond these critical conditions, NASH and NAFLD patients additionally suffer heightened cardiovascular risk and, in fact, die more frequently from cardiovascular events than from liver disease.

NASH and NAFLD have grown as a consequence of rising worldwide obesity-related disorders. In the United States, NAFLD is estimated to affect approximately 25% of the population, and approximately 25% of those will progress from NAFLD to NASH. Current estimates place NASH prevalence at approximately 22 million people in the United States by 2024, with similar prevalence in Europe and Asia. The prevalence of NASH is also increasing in developing regions due to the adoption of a more sedentary lifestyle and a diet consisting of processed foods with high fat and fructose content.

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

Common stock offered by the selling stockholder	3,914,910 shares of our common stock (which includes 1,969,797 shares of common stock issuable upon the conversion of our Series A Convertible Preferred Stock and 400,000 shares of common stock issuable upon the conversion of our Series B Convertible Preferred Stock held by the selling stockholder).
Terms of the offering	The selling stockholder will determine when and how it will sell the common stock offered in this prospectus supplement, as described in “Plan of Distribution.
Use of Proceeds	We will not receive any proceeds from the sale of the shares of our common stock covered by the selling stockholder
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.

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 Related to This Offering

The selling stockholder named in this prospectus supplement holds a significant portion of our total common stock (including shares of our common stock issuable upon conversion of shares of our Series A Convertible Preferred Stock and Series B Convertible Preferred Stock), and any sale of such shares into the market in the future, or the perception that these sales might occur, could cause the market price of our common stock to drop significantly.

The selling stockholder named in this prospectus supplement may offer and sell up to 3,914,910 shares of our common stock (which includes 1,969,797 shares of common stock issuable upon the conversion of our Series A Convertible Preferred Stock and 400,000 shares of common stock issuable upon the conversion of our Series B Convertible Preferred Stock, each of which are common stock equivalents with no voting rights, that are convertible into shares of common stock on a 1-for-1 basis only to the extent that after giving effect to such conversion the holders thereof and their affiliates and any persons who are members of a Section 13(d) group with the holders or their affiliates would beneficially own (in the aggregate, for purposes of Rule 13d-3 under the Securities Exchange Act of 1934, as amended (the “Exchange Act”)) no more than 4.99% of the outstanding common stock, which may be increased or decreased up to 19.99% at the holder’s election on 61 days’ notice and certain limitations) that they current hold, which represents approximately 18.8% of our total outstanding shares of common stock as of July 31, 2023 on a fully as-converted to common stock basis. Sales of a substantial number of shares of our common stock in the public market by the selling stockholder named in this prospectus supplement, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales by the selling stockholder may have on the prevailing market price of our common stock.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale or other disposition of shares of our common stock (including shares of our common stock issuable upon conversion of shares of our Series A Convertible Preferred Stock or Series B Convertible Preferred Stock) by the selling stockholder pursuant to this prospectus supplement.

We will bear the out-of-pocket costs, expenses and fees incurred in connection with the registration of shares of our common stock pursuant to this prospectus supplement. Other than registration expenses and up to \$50,000 of reasonable legal expenses of one special counsel for the selling stockholder, or Registration Expenses, the selling stockholder will bear underwriting discounts, commissions, placement agent fees or other similar expenses payable with respect to sales of shares of our common stock.

SELLING STOCKHOLDER

We are registering the resale of 3,914,910 shares of our common stock (which includes 1,969,797 shares of common stock issuable upon the conversion of our Series A Convertible Preferred Stock and 400,000 shares of common stock issuable upon the conversion of our Series B Convertible Preferred Stock) held by the selling stockholder identified below to permit it (or its donees, pledgees, transferees or other successors-in-interest selling shares of common stock or interests in shares of common stock received after the date of this prospectus supplement from the selling stockholder as a gift, pledge, partnership distribution or other transfer) to resell or otherwise dispose of these shares in the manner contemplated under the section entitled “Plan of Distribution” in this prospectus supplement (as may be supplemented and amended). As described below, the Company is obligated under a Registration Rights Agreement with the selling stockholder to register additional shares of common stock acquired by the selling stockholder, so the Company may be required to file additional prospectus supplements in the future to increase the number of shares that are registered for resale by the selling stockholder.

The selling stockholder may sell some, all or none of its shares of our common stock. We do not know how long the selling stockholder will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholder regarding the sale or other disposition of any of the shares. The shares covered hereby may be offered from time to time by the selling stockholder. As a result, we cannot estimate the number of shares of common stock the selling stockholder will beneficially own after completing sales, or completing sales from time to time, under this prospectus supplement. In addition, after the date of this prospectus supplement, the selling stockholder may have sold, transferred or otherwise disposed of all or a portion of its shares of common stock since the date on which they provided information for this table and as of the date of this prospectus supplement.

The Series A Convertible Preferred Stock is a common stock equivalent with no voting rights and is convertible into shares of common stock on a 1-for-1 basis. However, the shares of Series A Convertible Preferred Stock are only convertible to the extent that after giving effect to such conversion the holders thereof, together with their affiliates and any persons who are members of a Section 13(d) group with the holders and/or their affiliates would beneficially own in the aggregate, for purposes of Rule 13d-3 under the Exchange Act, no more than 4.99% of the outstanding common stock of the Company (the “Series A Beneficial Ownership Limitation”). As a result of the Series A Beneficial Ownership Limitation, the number of shares of common stock that may be issued upon conversion of the shares of Series A Convertible Preferred Stock by the selling stockholder may change depending upon changes in the outstanding shares of common stock. By notice to the Company, the selling stockholder may increase or decrease the Series A Beneficial Ownership Limitation to any other percentage; provided that any such increase or decrease will not be effective until the 61st day after such notice is delivered to the Company. Due to the fact that the Series A Beneficial Ownership Limitation is in effect as of the date of this prospectus supplement, the selling stockholder is presently unable, as of the date of this prospectus supplement, to convert any shares of Series A Convertible Preferred Stock.

The Series B Convertible Preferred Stock is a common stock equivalent with no voting rights and is convertible into shares of common stock on a 1-for-1 basis. However, the shares of Series B Convertible Preferred Stock are only convertible to the extent that immediately prior to or after giving effect to such conversion the holders thereof, together with their affiliates and any persons who are members of a Section 13(d) group with the holders and/or their affiliates would beneficially own in the aggregate, for purposes of Rule 13d-3 under the Exchange Act, no more than 4.99% of the outstanding common stock of the Company (“Series B Beneficial Ownership Limitation”). As a result of the Series B Beneficial Ownership Limitation, the number of shares of Common Stock that may be issued upon conversion of the shares of Series B Convertible Preferred Stock by the selling stockholder may change depending upon changes in the outstanding shares of Common Stock. By notice to the Company, the selling stockholder may increase or decrease the Series B Beneficial Ownership Limitation to any other percentage not in excess of 19.99%; provided that any such increase will not be effective until the 61st day after such notice is delivered to the Company. Due to the fact that the Series B Beneficial Ownership Limitation

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is in effect as of the date of this prospectus supplement, the selling stockholder is presently unable, as of the date of this prospectus supplement, to convert any shares of Series B Convertible Preferred Stock.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to our capital stock. Generally, a person “beneficially owns” shares of our capital stock if the person has or shares with others the right to vote those shares or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days. The information in the table below and the footnotes thereto regarding shares of common stock to be beneficially owned after the offering assumes the sale of all shares being offered by the selling stockholder under this prospectus supplement. The percentage of shares owned prior to and after the offering is based on the following outstanding share counts as of July 31, 2023: 18,471,233 shares of common stock, 1,969,797 shares of Series A Convertible Preferred Stock and 400,000 shares of Series B Convertible Preferred Stock. The information under the heading “13(d) Beneficial ownership” in the table below presents the beneficial ownership of the selling stockholders reflecting the Series A Beneficial Ownership Limitation and the Series B Beneficial Ownership Limitation. Solely for purposes of the table below, the information under the headings “Beneficial ownership before the offering, on a fully-converted and as-converted basis” and “Beneficial ownership after the offering” disregards the Series A Beneficial Ownership Limitation and the Series B Beneficial Ownership Limitation. All share ownership information below is provided from information derived from the Schedule 13D filed by entities affiliated with Baker Bros. Advisors LP on June 20, 2023 and information provided by Baker Bros. Advisors LP to the Company after June 20, 2023 and prior to the date of this prospectus supplement.

<i>Selling Stockholder</i>	13(d) Beneficial ownership (1)		Beneficial ownership before the offering, on a fully-converted and as-converted basis (2)		Number of shares being offered by the selling stockholders	Beneficial ownership after the offering (2)(3)	
	Number of shares	%	Number of shares	%		Number of shares	%
Entities affiliated with Baker Bros. Advisors LP (4)	1,545,113	8.4%	3,914,910	18.8%	3,914,910	—	—

- (1) Reflects the 4.99% Series A Beneficial Ownership Limitation and Series B Beneficial Ownership Limitation described above.
- (2) Solely for purposes of this table, disregards the 4.99% Series A Beneficial Ownership Limitation and Series B Beneficial Ownership Limitation described above, and presumes full conversion of both of the Series A Convertible Preferred Stock and Series B Convertible Preferred Stock.
- (3) Assumes that all shares being registered in this prospectus are resold to third parties and that the selling stockholder sells all shares of common stock registered under this prospectus supplement held by them.
- (4) Based on information provided by the selling stockholder. The selling stockholder owns via (i) 667, L.P., 148,821 shares of common stock, up to 200,378 shares of common stock issuable upon conversion of the Series A Convertible Preferred Stock and up to 39,250 shares of common stock issuable upon conversion of the Series B Convertible Preferred Stock; and (ii) Baker Brothers Life Sciences, L.P., 1,396,292 shares of common stock, up to 1,769,419 shares of common stock issuable upon conversion of the Series A Convertible Preferred Stock and up to 360,750 shares of common stock issuable upon conversion of the Series B Convertible Preferred Stock. Baker Bros. Advisors LP (the “Adviser”) is the investment adviser to 667, L.P. and Baker Brothers Life Sciences, L.P. (collectively the “Funds”) and has the sole voting and investment power with respect to the securities held by the Funds and thus may be deemed to beneficially own such securities. Baker Bros. Advisors (GP) LLC (the “Adviser GP”) is the sole general partner of the Adviser and thus may be deemed to beneficially own the securities held by the Funds. The managing members of the Adviser GP are Julian C. Baker and Felix J. Baker, who may be deemed to beneficially own the securities held by the Funds. Julian C. Baker, Felix J. Baker, the Adviser and the Adviser GP disclaim beneficial ownership of all shares held by the Funds, except to the extent of their indirect pecuniary interest

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therein. The business address of the Adviser, the Adviser GP, Julian C. Baker and Felix J. Baker is 860 Washington Street, 3rd Floor, New York, NY 10014.

Madrigal Relationship and Agreements with the Selling Stockholder

On June 15, 2023, Julian Baker and Raymond Cheong, Ph.D./MD were appointed to the Company Board as Class III directors and will serve terms lasting until the Company's Annual Meeting of Stockholders to be held in 2025, and until their respective successors have been elected and qualified. The same day the Board determined that it was appropriate for the Company to institute changes to its Board governance structure and implement a separation of the Chairman and Chief Executive Officer functions. Effective June 15, 2023, Julian Baker was appointed to serve as the independent Chairman of the Board of Directors and Paul A. Friedman, M.D. continued service as the Company's Chief Executive Officer and as a Class I director on the Board until the Company's Annual Meeting of Stockholders to be held in 2026, and until his successor has been elected and qualified. Mr. Baker and Dr. Cheong participate in the compensation arrangements applicable to the Company's non-employee directors and Board committee members.

Mr. Baker and Dr. Cheong are affiliated with Baker Bros. Advisors LP and its related funds (collectively, "Baker Bros."), which are significant owners of the Company's capital stock, as disclosed in SEC filings. Mr. Baker is a managing member of the general partner of Baker Bros. Advisors LP, and Dr. Cheong is a Managing Director at Baker Brothers Investments. In connection with the appointment of Mr. Baker and Dr. Cheong to the Board, the BBA Investors (defined below) waived rights under that certain Securities Purchase Agreement, dated June 20, 2017 (the "2017 SPA"), as amended by Amendments No. 1 and 2 (collectively, the "SPA"), to designate a director to the Board while Mr. Baker or Dr. Cheong are on the Board or to appoint a Board observer subject the SPA, while Mr. Baker or Dr. Cheong are on the Board or serving as a Board observer. For a description of such rights and obligations under the SPA, see "– 2017 Securities Purchase Agreement, as Amended" below.

Registration Rights Agreement

Pursuant to the terms of the 2017 SPA, the Company agreed with certain fund affiliates of Baker Bros. (the "Baker Bros. Funds" or "BBA Investors") that if the BBA Investors determined, based on the totality of the circumstances, that they may be deemed to be "affiliates" of the Company within the meaning of Rule 144 of the Securities Act of 1933, as amended (the "Securities Act"), whether through the exercise of their board designation rights under the SPA or otherwise, the Company would enter into the registration rights agreement with the BBA Investors in the form attached to the 2017 SPA (the "Registration Rights Agreement"). The BBA Investors informed the Company prior to the filing of this prospectus supplement that they may be deemed to be "affiliates" of the Company and thereafter the Company and the BBA Investors entered into the Registration Rights Agreement with the Company on August 7, 2023 covering certain resale registration rights with respect to shares of the Company's common stock (including shares of common stock issuable upon the conversion of any securities of the Company) that are now held or are hereafter acquired by the BBA Investors (the "Registrable Securities"). Under the Registration Rights Agreement, and following request by the BBA Investors, the Company filed this prospectus supplement.

The Company is obligated under the Registration Rights Agreement to register additional Registrable Securities acquired by the BBA Investors, so the Company may be required to file additional prospectus supplements in the future to increase the number of Registrable Securities that are registered for resale by the BBA Investors. The Company is obligated to use its reasonable best efforts to keep the related registration statement associated with this prospectus supplement (or other appropriate successor forms) effective until the earlier of such time that (i) all Registrable Securities have been sold or may be sold freely without limitations or restrictions as to volume or manner of sale pursuant to Rule 144 of the Securities Act, or (ii) all Registrable Securities otherwise cease to be considered Registrable Securities pursuant to the terms of the Registration Rights Agreement. Under the Registration Rights Agreement, the Baker Bros. Funds have the right to one underwritten public offering per calendar year, but no more than three underwritten public offerings in total, to effect the sale or distribution of

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their Registrable Securities, subject to specified exceptions, conditions and limitations. The rights of the Baker Bros. Funds concerning Registrable Securities under the Registration Rights Agreement will continue in effect for up to ten years following the date of the Registration Rights Agreement.

The foregoing description of the Registration Rights Agreement does not purport to be complete and is qualified in its entirety by reference to the full text of the Registration Rights Agreement, which is incorporated by reference as an exhibit to our Quarterly Report on Form 10-Q filed with the SEC on August 8, 2023.

2017 Securities Purchase Agreement, as Amended

Pursuant to the 2017 SPA, at any time that Richard S. Levy, M.D., ceases to be a member of the Company Board, the BBA Investors have the right to designate one member of the Company Board (the “Board Designation Right”) for so long as the BBA Investors : (i) collectively hold at least 984,899 shares of the Company’s Series A Convertible Preferred Stock (including the Company’s common stock issued upon conversion thereof), and (ii) collectively hold the Company’s common stock and Common Stock Equivalents (as defined in the 2017 SPA) (for purposes of this clause (ii) only, on an as-converted basis) representing at least 9.5% of the outstanding shares of common stock. In addition, pursuant to the 2017 SPA, the BBA Investors have a right to designate one Board observer until such time as the Board Designation Right is exercised. As described in the second paragraph under “ – Madrigal Relationship and Agreements with the Selling Stockholder,” in connection with the appointment of Mr. Baker and Dr. Cheong to the Company Board, the BBA Investors waived the foregoing rights to designate a director to the Board while Mr. Baker or Dr. Cheong are on the Board or to appoint a Board observer subject the SPA, while Mr. Baker or Dr. Cheong are on the Board or serving as a Board observer.

2022 Securities Purchase Agreement

On December 21, 2022, the Company entered into a Securities Purchase Agreement (the “2022 Securities Purchase Agreement”) with the BBA Investors and Avoro Life Sciences Fund LLC (“Avoro”). Pursuant to the 2022 Securities Purchase Agreement, we issued and sold to (1) the BBA Investors 400,000 shares of the Company’s Series B Convertible Preferred Stock at a price of \$225.00 per share, for aggregate consideration of \$90 million and (2) Avoro 44,444 shares of the Company’s common stock at a price of \$225.00 per share.

PLAN OF DISTRIBUTION

We are registering the shares of common stock held by the selling stockholder to permit the resale of these shares of common stock by the selling stockholder from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling stockholder of the shares of our common stock. We will bear all fees and expenses, including Registration Expenses, incident to our obligation to register the shares of common stock.

The selling stockholder may sell all or a portion of the shares of common stock beneficially owned by it and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of common stock are sold through underwriters or broker-dealers, the selling stockholder will be responsible for underwriting discounts or commissions or agent's commissions. The shares of common stock may be sold on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, in the over-the-counter market or in transactions otherwise than on these exchanges or systems or in the over-the-counter market and in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions. The selling stockholder may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- "at the market" or through market makers or into an existing market for the shares;
- settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;
- broker-dealers may agree with the selling stockholder to sell a specified number of such shares at a stipulated price per share;
- the distribution of the shares to the selling stockholder's partners, members or shareholders;
- through the writing or settlement of options or other hedging transactions, whether such options are listed on an options exchange or otherwise;
- through one or more underwritten offerings on a firm commitment or best efforts basis;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling stockholder also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, as permitted by that rule, or Section 4(1) under the Securities Act, if available, rather than under this prospectus supplement, provided that they meet the criteria and conform to the requirements of those provisions.

Broker-dealers engaged by the selling stockholder may arrange for other broker-dealers to participate in sales. If the selling stockholder effects such transactions by selling shares of common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholder or commissions from purchasers of the

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shares of common stock for whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to be negotiated, but, except as set forth in an applicable prospectus supplement, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with FINRA Rule 5110.

In connection with sales of the shares of common stock or otherwise, the selling stockholder may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the shares of common stock in the course of hedging in positions they assume. The selling stockholder may also sell shares of common stock short and the selling stockholder may deliver shares of common stock covered by this prospectus supplement to close out short positions and to return borrowed shares in connection with such short sales. The selling stockholder may also loan or pledge shares of common stock to broker-dealers that in turn may sell such shares, to the extent permitted by applicable law. The selling stockholder may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus supplement, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus supplement (as supplemented or amended to reflect such transaction).

The selling stockholder may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if a selling stockholder defaults in the performance of its secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time pursuant to this prospectus supplement or any amendment or prospectus supplement under Rule 424(b)(3) or other applicable provision of the Securities Act, amending, if necessary, the list of selling stockholder to include the pledgee, transferee or other successors-in-interest as a selling stockholder under this prospectus. The selling stockholder also may transfer and donate the shares of common stock in other circumstances in which case the transferees, donees, pledgees or other successors-in-interest will be the selling beneficial owners for purposes of this prospectus.

The selling stockholder and any broker-dealer or agents participating in the distribution of the shares of common stock may be deemed to be “underwriters” within the meaning of Section 2(11) of the Securities Act in connection with such sales. In such event, any commissions paid, or any discounts or concessions allowed to, any such broker-dealer or agent and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. If a selling stockholder is deemed to be an “underwriters” within the meaning of Section 2(11) of the Securities Act, it will be subject to the prospectus delivery requirements of the Securities Act and may be subject to certain statutory liabilities of, including but not limited to, Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Exchange Act.

The selling stockholder has informed us that it is not a registered broker-dealer and does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the common stock. Upon us being notified in writing by the selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of common stock through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, prospectus supplement will be filed, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the name of the selling stockholder and of the participating broker-dealer(s), (ii) the number of shares involved, (iii) the price at which such the shares of common stock were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus, and (vi) other facts material to the transaction.

Under the securities laws of some states, the shares of common stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with. There can be no assurance that the selling stockholder will sell any or all of the shares of common stock registered pursuant to the registration statement, of which this prospectus forms a part.

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The selling stockholder and any other person participating in such distribution will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including, without limitation, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of common stock by the selling stockholder and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock to engage in market-making activities with respect to the shares of common stock. All of the foregoing may affect the marketability of the shares of common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock.

We will pay all expenses of the registration of the shares of common stock pursuant to the Registration Rights Agreement, including, without limitation, SEC filing fees and expenses of compliance with state securities or “blue sky” laws; provided, however, that the selling stockholder will pay all underwriting discounts and selling commissions, if any, and except as included in Registration Expenses, any legal expenses incurred by it. We will indemnify the selling stockholder against certain liabilities, including some liabilities under the Securities Act, in accordance with the Registration Rights Agreement, or the selling stockholder will be entitled to contribution. We may be indemnified by the selling stockholder against civil liabilities, including liabilities under the Securities Act, that may arise from any written information furnished to us by the selling stockholder specifically for use in this prospectus supplement, in accordance with the related Registration Rights Agreement, or we may be entitled to contribution.

LEGAL MATTERS

The validity of the securities offered by this prospectus supplement will be passed upon for us by Hogan Lovells US LLP, Washington, D.C.

EXPERTS

The financial statements incorporated in this Prospectus by reference to Madrigal Pharmaceuticals, Inc.'s Amendment No. 1 to the Annual Report on Form 10-K dated March 3, 2023 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 of Madrigal Pharmaceuticals, Inc. for the year ended December 31, 2022 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 June 1, 2021 (File No. 333-256666). 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, 2022, as filed with the SEC on [February 23, 2023](#), as amended by Amendment No. 1 to our Annual Report on Form 10-K/A, as filed with the SEC on [March 3, 2023](#) (including the portions of our Definitive Proxy Statement on Schedule 14A filed on [May 1, 2023](#) that are expressly incorporated by reference therein);
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2023 and June 30, 2023, as filed with the SEC on [May 9, 2023](#) and [August 8, 2023](#);
- our Current Reports on Form 8-K, as filed with the SEC on [January 10, 2023](#), [February 9, 2023](#), [May 9, 2023](#) (Item 1.01), [June 20, 2023](#), [June 20, 2023](#), [June 30, 2023](#) and [July 17, 2023](#); and
- 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:

Alex Howarth
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 4 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 June 1, 2021.

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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 ™ 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, 2020, as filed with the SEC on February 25, 2021](#), including the information specifically incorporated therein by reference from our [Definitive Proxy Statement on Schedule 14A, as filed with the SEC on April 30, 2021](#);
- our [Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2021, as filed with the SEC on May 6, 2021](#);
- our [Current Report on Form 8-K, as filed with the SEC on May 18, 2021](#); and
- the description of our common stock contained in our Registration Statement on [Form 8-A](#) filed with the SEC on January 26, 2007, including any amendment thereto or report filed for the purpose of updating such descriptions, including but not limited to the description of our common stock contained in [Exhibit 4.1](#) hereto and incorporated into this registration statement.

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:

Alex G. Howarth
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 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 "allow," "anticipates," "be," "believes," "continue," "could," "demonstrates," "design," "estimates," "expects," "forecasts," "future," "hopeful," "goal," "intends," "may," "might," "plans," "potential," "predicts," "predictive," "projects," "seeks," "should," "will," "will achieve," "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:

- anticipated or estimated future results, including the risks and uncertainties associated with our future operating performance and financial position;
- our possible or assumed future results of operations and expenses, business strategies and plans, capital needs and financing plans, market trends, competitive position, industry environment and potential growth opportunities;
- our clinical trials, research and development activities, and the timing and results associated with the future development of our lead product candidate, MGL-3196 (resmetirom);
- our primary and secondary study endpoints for resmetirom, the potential for achieving such endpoints and projections, including those regarding potential future non-alcoholic steatohepatitis ("NASH") resolution, safety, fibrosis treatment, cardiovascular effects and lipid treatment with resmetirom;
- optimal dosing levels for resmetirom and projections regarding potential NASH or nonalcoholic fatty liver disease ("NAFLD") patient benefits with resmetirom;
- market demand for and acceptance of our products;
- research, development and commercialization of new products;
- obtaining and maintaining regulatory approvals, including, but not limited to, potential regulatory delays or rejections;

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- risks associated with meeting the objectives of clinical studies, including, but not limited to our ability to achieve enrollment objectives concerning patient number (including an adequate safety database) and/or timing 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 than our past trials;
- risks related to our ability to accomplish our 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 clinical-stage biopharmaceutical company pursuing novel therapeutics that target a specific thyroid hormone receptor pathway in the liver, which is a key regulatory mechanism common to a spectrum of cardio-metabolic and fatty liver diseases with high unmet medical need. Our lead candidate, resmetirom, is a first-in-class, orally administered, small-molecule, liver-directed, thyroid hormone receptor (THR)- β selective agonist that is currently in two Phase 3 clinical studies, MAESTRO-NASH and MAESTRO-NAFLD-1, designed to demonstrate multiple benefits across a broad spectrum of NASH and NAFLD patients.

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 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

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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 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

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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 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.

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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.

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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 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.

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In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8.0% of the aggregate amount of the securities offered by this prospectus.

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, 2020 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

Calculation of Filing Fee Tables

424(b)(3)
(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 (1)(2)	Proposed Maximum Offering Price Per Unit (3)	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee (4)
Newly Registered Securities								
Fees to Be Paid	Equity	Common Stock, \$0.0001 par value per share	Rule 457(c)	3,914,910	\$186.80	\$731,305,188	0.00011020	\$80,590
Carry Forward Securities								
Carry Forward Securities	N/A	N/A	N/A	N/A		N/A		
Total Offering Amounts						\$731,305,188		\$80,590
Total Fees Previously Paid								—
Total Fee Offsets								—
Net Fee Due								\$80,590

- (1) The shares of Common Stock, par value \$0.0001 per share (“Common Stock”), of the registrant will be offered for resale by the selling stockholder. Pursuant to Rule 416 under the Securities Act, this registration statement also covers any additional number of shares of Common Stock issuable upon stock splits, stock dividends, or other distribution, recapitalization or similar events with respect to the shares of Common Stock being registered pursuant to this registration statement.
- (2) Consists of an aggregate of 3,914,910 shares of the Common Stock, including an aggregate of 1,969,797 shares of Common Stock issuable upon the conversion of Series A Convertible Preferred Stock and 400,000 shares of common stock issuable upon the conversion of Series B Convertible Preferred Stock of the registrant.
- (3) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(c) of the Securities Act of 1933, as amended (the “Securities Act”). The proposed maximum offering price per share and maximum aggregate offering price are calculated using the average of the high and low prices of the Common Stock as reported on the Nasdaq Global Market on August 7, 2023, which date is within five business days prior to the filing of this prospectus supplement.
- (4) 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 (Registration No. 333-256666), filed on June 1, 2021.