

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

LYRA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

84-1700838
(I.R.S. Employer
Identification Number)

480 Arsenal Way
Watertown, MA 02472
(617) 393-4600

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Maria Palasis, Ph.D.
President and Chief Executive Officer
480 Arsenal Way
Watertown, MA 02472
(617) 393-4600

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:
Peter N. Handrinos
Wesley C. Holmes
Latham & Watkins LLP
200 Clarendon Street, 27th Floor
Boston, MA 02116
(617) 948-6000

APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC: From time to time after the effective date of this registration statement.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. [ ]

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. [x]

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. [ ]

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. [ ]

If this form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. [ ]

If this form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. [ ]

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer [ ] Accelerated filer [ ]
Non-accelerated filer [x] Smaller reporting company [x]
Emerging growth company [x]

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. [ ]

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, dated June 28, 2023.

PROSPECTUS



## LYRA THERAPEUTICS, INC.

21,967,353 Shares

Common Stock

Offered by the Selling Securityholders

The selling securityholders may offer and sell up to 21,967,353 shares in the aggregate of common stock identified above, of which 12,236,714 shares are presently issued and outstanding and 9,730,639 shares are issuable upon exercise of presently issued and outstanding warrants to purchase common stock, from time to time in one or more offerings. This prospectus provides you with a general description of the securities. See the section of this prospectus entitled “Description of Securities—Warrants” for more information. We will receive the proceeds from any exercise of the warrants for cash, if any. We will not receive any proceeds from the sale of our common stock by the selling securityholders.

Each time any of the selling securityholders offers and sells securities, such selling securityholders may provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

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

**INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE “[RISK FACTORS](#)” ON PAGE 6 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.**

Our common stock is listed on the Nasdaq Global Market under the symbol “LYRA.” On June 27, 2023, the last reported sale price of our common stock on the Nasdaq Global Market was \$4.11 per share.

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

The date of this prospectus is \_\_\_\_\_, 2023.

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, using a “shelf” registration process. By using a shelf registration statement, the selling securityholders may, from time to time, sell up to 21,967,353 shares of common stock in one or more offerings as described in this prospectus. In connection with the offer and sale of securities by the selling securityholders, the selling securityholders may provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. Any such prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and any applicable prospectus supplement or free writing prospectuses, together with the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.”

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

When we refer to “Lyra,” “we,” “our,” “us” and the “Company” in this prospectus, we mean Lyra Therapeutics, Inc. and its consolidated subsidiaries, unless otherwise specified. When we refer to “you,” we mean the potential holders of the applicable series of securities.

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

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

### Available Information

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

Our web site address is <https://lyratherapeutics.com>. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus.

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

### Incorporation by Reference

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

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

- Our Annual Report on [Form 10-K](#) for the year ended December 31, 2022, filed with the SEC on March 29, 2023.
- Our [Definitive Proxy Statement](#) on Schedule 14A, filed with the SEC on April 25, 2023.
- Our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2023, filed with the SEC on May 12, 2023.
- Our Current Reports on Form 8-K filed with the SEC on [March 29, 2023](#), [May 12, 2023](#), [May 31, 2023](#) and [June 15, 2023](#).
- The description of our common stock contained in our Registration Statement on [Form 8-A](#), filed with the SEC on April 27, 2020, pursuant to Section 12(b) of the Securities Act, as updated by "Description of Securities" filed as [Exhibit 4.5](#) to our Annual Report on Form 10-K for the year ended December 31, 2022, and any other amendment or report filed with the SEC for the purpose of updating such description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

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You may request a free copy of any of the documents incorporated by reference in this prospectus by writing or telephoning us at the following address:

**Lyra Therapeutics, Inc.**  
**480 Arsenal Way**  
**Watertown, MA 02472**  
**(617) 393-4600**

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

## THE COMPANY

We are a clinical-stage biotechnology company focused on the development and commercialization of therapies for the localized treatment of patients with chronic rhinosinusitis, or CRS. Our proprietary technology is designed to consistently deliver medicines directly to the affected tissue for sustained periods with a single administration. Our product candidates, LYR-210 and LYR-220, are bioresorbable nasal implants designed to be administered in a brief, non-invasive, in-office procedure and intended to deliver up to six months of continuous anti-inflammatory drug therapy to the sinonasal passages for the treatment of CRS. The drug embedded within LYR-210 and LYR-220 is mometasone furoate, or MF, which is the active ingredient in various U.S. Food and Drug Administration, or FDA, approved drugs and has a well-established efficacy and safety profile. CRS is an inflammatory disease of the paranasal sinuses which leads to debilitating symptoms and significant morbidities and affects approximately 14 million people in the United States.

LYR-210 is designed to treat CRS patients both with and without nasal polyps who have failed previous medical management and have not undergone endoscopic sinus surgery. A pivotal Phase 3 program of LYR-210, called the ENLIGHTEN program, consists of two pivotal trials, ENLIGHTEN I and ENLIGHTEN II, and is currently ongoing. ENLIGHTEN I is a 52-week, multi-center, randomized, blinded, sham-controlled trial designed to evaluate the efficacy and safety of LYR-210 in approximately 180 surgically naïve CRS who have failed prior medical management. The trial consists of three stages – a 2- to 4-week screening and run-in stage, a 24-week treatment stage followed by a 28-week safety extension stage. In the treatment stage, patients are randomized 2:1 to receive LYR-210 (7,500 µg) or sham-procedure. At the end of the treatment stage, patients in the control group receive crossover LYR-210 treatment while patients in the LYR-210 group are re-randomized 1:1 to either receive a crossover sham-procedure or a repeat treatment with LYR-210 (7,500 µg). The ENLIGHTEN I trial was initiated in February 2022.

ENLIGHTEN II is a 24-week, multi-center, randomized, blinded, sham-controlled trial designed to evaluate the efficacy and safety of LYR-210 in approximately 180 surgically naïve CRS patients who have failed prior medical management. The trial consists of two stages – a 2- to 4-week screening and run-in stage and a 24-week treatment stage. Patients are randomized 2:1 to receive LYR-210 (7,500 µg) or sham-procedure. ENLIGHTEN II was initiated in September 2022.

The primary endpoint of both ENLIGHTEN I and ENLIGHTEN II is change from baseline (CFBL) at week 24 in the composite score of 3 cardinal symptoms, or 3CS, score. The 3CS are nasal blockage/obstruction/congestion, anterior/posterior nasal discharge, and facial pain/pressure. Secondary endpoints include CFBL in individual cardinal symptoms at week 24, CFBL in CT sinus opacification score at week 24, CFBL in SNOT-22 at week 24, rescue treatment use through week 24.

We have advanced LYR-210 through our Phase 2 randomized, controlled, patient blinded LANTERN clinical trial, designed to evaluate the safety and efficacy in CRS patients both with and without nasal polyps who have failed previous medical management but have not undergone endoscopic sinus surgery. The trial was designed to enroll 99 evaluable patients with the option to expand to up to 150 patients at sites in the United States, Australia, Austria, Czech Republic, New Zealand, and Poland. Due to COVID-19, we discontinued enrollment at 67 patients and did not open any sites in the United States. In December 2020, we reported positive topline results from our Phase 2 LANTERN clinical trial, including that the 7,500 µg dose of LYR-210 achieved statistically significant improvement in the composite four cardinal symptoms score, or 4CSS, in favor of the treatment arm as measured by the change from baseline at weeks 16, 20, and 24. The 4CSS are nasal blockage/obstruction/congestion, anterior/posterior nasal discharge, facial pain/pressure, and olfactory loss. However, although a strong treatment effect was observed at week 4, LYR-210 did not achieve the primary endpoint of change from baseline in 4CSS at week 4 at either the 7,500 µg dose or 2,500 µg dose relative to the control group. We believe this was due primarily to the discontinuation of enrollment related to the COVID-19 pandemic. As a result of the decrease in the number of patients enrolled from planned (99 evaluable) to actually enrolled (67), a greater magnitude of change from baseline in 4CSS at week 4 and/or a smaller standard deviation

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associated with the change from baseline was required in order to achieve statistical significance for the primary endpoint at week 4. LYR-210 was observed to be safe and well-tolerated at all doses in the trial, and no treatment-related serious adverse events were reported.

In addition, we conducted a separate characterization study in the United States to collect certain pharmacokinetic, or PK, data. The PK study was a 56-day open label, multi-center, U.S. study of the PK and safety of LYR-210 in adult subjects with chronic rhinosinusitis. The primary objective of the study was to establish the PK profile of LYR-210. The study enrolled 24 patients, half of whom received LYR-210 2,500 µg and the other half received LYR-210 7,500 µg. The study indicated that both doses were safe and well tolerated, with the mean maximum plasma concentration, or C<sub>max</sub>, observed with the 7,500 µg dose well below the C<sub>max</sub> established for FDA-approved formulations of mometasone furoate, or MF. MF blood plasma levels observed during the PK study support LYR-210's ability to deliver consistent and steady dosing over the entire treatment period.

In our Phase 1 clinical trial, LYR-210 met its primary safety endpoint, and we observed that patients generally experienced significant, rapid, clinically meaningful, and durable improvement in SNOT-22 scores, an established patient symptom severity scale, through week 25, which was the end of the trial.

LYR-220, our second pipeline product candidate, is in Phase 2 development for CRS patients who have undergone a prior sinus surgery but continue to have persistent disease. LYR-220 is also designed to utilize MF, and employs a larger matrix designed for patients whose nasal cavity is enlarged due to sinus surgery. In November 2021, we initiated the Phase 2 BEACON clinical trial for LYR-220 which is a controlled, randomized, parallel-group study to evaluate safety, tolerability, pharmacokinetics, and efficacy comparing two designs of LYR-220 to control over a 24-week period in approximately 40 symptomatic adult CRS subjects who have had a prior bilateral sinus surgery. The trial consists of two parts – Part 1 is designed to assess the feasibility of placement and procedural refinements in up to 10 patients who will receive one of two designs of LYR-220; in Part 2, approximately 40 patients will be randomized 1:1 to receive either one of two designs of LYR-220 or sham procedure. The primary endpoint of the trial is incidence of product-related unexpected serious adverse events. Other safety endpoints include incidence of serious and non-serious adverse events, new or worsening of abnormal clinically significant findings in lab values, ophthalmology exams, and nasal endoscopies. Efficacy endpoints include change from baseline in 3CS, SNOT-22 and other CRS symptoms, CFBL in ethmoid opacification by CT, and use of rescue treatments.

In September 2022, we announced positive initial data from the Part 1, non-randomized portion of the BEACON trial, demonstrating the feasibility and tolerability of LYR-220 placement bilaterally in this patient population. All six patients were treated for at least six weeks and no serious or unexpected product related adverse events have been reported. Enrollment is complete in the Part 2, randomized stage of the BEACON trial.

We were incorporated under the laws of the state of Delaware in November 2005 under the name WMR Biomedical, Inc. In July 2018, we changed our name to Lyra Therapeutics, Inc. Our principal executive offices are located at 480 Arsenal Way, Watertown, MA 02472 and our telephone number is (617) 393-4600. Our website address is [www.lyratherapeutics.com](http://www.lyratherapeutics.com). The information contained in, or accessible through, our website does not constitute a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference. Our common stock is listed on the Nasdaq Global Market under the symbol "LYRA".



## **RISK FACTORS**

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

## **USE OF PROCEEDS**

We are registering the resale of shares of our common stock that may be issued upon exercise of warrants. We will receive the proceeds from any exercise of warrants for cash. We intend to use the proceeds from the exercise of warrants for cash for general corporate and working capital purposes.

We will not receive any of the proceeds from the sale of common stock being offered by any of the selling securityholders.

## DESCRIPTION OF SECURITIES

As of June 1, 2023, we had one class of securities registered under Section 12 of the Exchange Act.

The following description of our securities and certain provisions of our restated certificate of incorporation, which we refer to as our certificate of incorporation, and our amended and restated bylaws, which we refer to as our bylaws, are summaries and are qualified in their entirety by reference to the full text of our certificate of incorporation, our bylaws and the applicable securities, each of which has been publicly filed with the SEC, and the applicable provisions of the General Corporation Law of the State of Delaware, or the DGCL. See “Where You Can Find More Information; Incorporation by Reference.” Our authorized capital stock consists of:

- 200,000,000 shares of common stock, par value \$0.001 per share; and
- 10,000,000 shares of preferred stock, par value \$0.001 per share.

### Common Stock

Our common stock is listed on the Nasdaq Global Market under the symbol “LYRA.”

*Voting Rights.* Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Our certificate of incorporation and bylaws also provide that our directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon. In addition, the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon is required to amend or repeal, or to adopt any provision inconsistent with, several of the provisions of our certificate of incorporation. See below under “–Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws–Amendment of Charter Provisions.”

*Rights Upon Liquidation.* In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

### Transfer Agent

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

### Dividend

Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock. On March 20, 2012, we declared and paid a special cash dividend of \$0.2630467 per share of our common stock, or the Special Dividend, which totaled approximately \$42,115 in the aggregate. Other than the Special Dividend, we have never declared or paid any cash dividends on our common stock. We do not intend to pay cash dividends for the foreseeable future. We currently expect to retain all future earnings, if any, for use in the development, operation and expansion of our business. Any determination to pay cash dividends in the future will depend upon, among

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other things, our results of operations, plans for expansion, tax considerations, available net profits and reserves, limitations under law, financial condition, capital requirements and other factors that our board of directors considers to be relevant.

### **Preferred Stock**

Under the terms of our certificate of incorporation, our board of directors is authorized to direct us to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. There are no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

### **Options**

As of June 1, 2023, options to purchase an aggregate of 124,440 shares of our common stock were outstanding under our 2005 Equity Incentive Plan, or our 2005 Plan (all of which were vested and exercisable as of such date), options to purchase 478,235 shares of common stock were outstanding under our 2016 Equity Incentive Plan, or our 2016 Plan (of which 445,520 shares were vested and exercisable as of such date), options to purchase 2,837,100 shares of common stock were outstanding under our 2020 Incentive Award Plan, or our 2020 Plan (of which 879,757 shares were vested and exercisable as of such date), restricted stock units covering 243,703 shares of common stock were outstanding under our 2020 Plan and options to purchase 2,243,002 shares of common stock were outstanding under our 2022 Employment Inducement Plan (none of which were vested or exercisable as of such date).

### **Warrants**

#### *2022 Pre-Funded Warrants*

On April 7, 2022, we entered into a securities purchase agreement with certain purchasers named therein, pursuant to which we agreed to sell securities to such purchasers in a private placement. In the private placement, the purchasers had the option to purchase either shares of our common stock or, in lieu thereof, pre-funded warrants, or the 2022 Pre-Funded Warrants, to purchase shares of our common stock, each with an exercise price of \$0.001 per share. Accordingly, we issued 2022 Pre-Funded Warrants to purchase 5,000,000 shares of our common stock upon the closing of the private placement.

As of June 1, 2023, 2022 Pre-Funded Warrants to purchase an aggregate of 5,000,000 shares of our common stock were outstanding.

The 2022 Pre-Funded Warrants are exercisable until 5:00 p.m., New York time, on April 12, 2027. The exercise price and number of shares of common stock issuable upon exercise of the 2022 Pre-Funded Warrants may be adjusted in certain circumstances, including in the event of a stock dividend, a forward or reverse split of our shares of common stock, and certain other events. However, the 2022 Pre-Funded Warrants will not be adjusted for issuances of common stock at prices below their respective exercise prices.

We issued the 2022 Pre-Funded Warrants in certificated form. A holder of a 2022 Pre-Funded Warrant certificate may exercise such 2022 Pre-Funded Warrant upon surrender of the applicable warrant certificate on or

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prior to the applicable expiration date at our principal office, with the exercise form on the reverse side of the warrant certificate completed and executed as indicated, accompanied by full payment of the exercise price for the number of warrants being exercised.

Subject to limited exceptions, a holder of 2022 Pre-Funded Warrants will not have the right to exercise any portion of its 2022 Pre-Funded Warrants if the holder (together with such holder's affiliates, and any persons acting as a group together with such holder or any of such holder's affiliates) would beneficially own a number of shares of our common stock in excess of 9.99% of the shares of our common stock then outstanding after giving effect to such exercise, or the 2022 Pre-Funded Warrant Beneficial Ownership Limitation; provided, however, that upon notice to us, the holder may increase or decrease the 2022 Pre-Funded Warrant Beneficial Ownership Limitation, provided that in no event shall the 2022 Pre-Funded Warrant Beneficial Ownership Limitation exceed 19.99% and any increase in the 2022 Pre-Funded Warrant Beneficial Ownership Limitation will not be effective until 61 days following notice of such increase from the holder to us.

The holders of the 2022 Pre-Funded Warrants must pay the exercise price in cash upon exercise of the 2022 Pre-Funded Warrants, unless such holders are utilizing the cashless exercise provision of the 2022 Pre-Funded Warrants. The 2022 Pre-Funded Warrants may be exercised (in the sole discretion of the holder), in whole or in part, at such time by means of a "cashless exercise" in which the holder of such 2022 Pre-Funded Warrants shall be entitled to receive that number of warrant shares determined according to the following formula:

$$\frac{[(A-B)*(X)]}{(A)}$$

Where:

A = the VWAP (as defined below) on the trading day immediately preceding the date of such election;

B = the exercise price then in effect; and

X = the number of shares of our common stock for which the 2022 Pre-Funded Warrant is being exercised (which shall include both the number of shares of our common stock issued to the holder thereof and the number of shares of our common stock subject to the portion of the warrant being cancelled in payment of the exercise price).

As used above, the "VWAP" means, for any date, the price determined by the first of the following clauses that applies: (i) if our common stock is then listed on The Nasdaq Global Select Market, The Nasdaq Global Market, The Nasdaq Capital Market or the New York Stock Exchange, any such market being referred to as the Trading Market, the daily volume-weighted average price of the Common Stock for such date (or the nearest preceding date) on the Trading Market as reported by Bloomberg Financial L.P. (based on a "Trading Day" from 9:30 a.m. Eastern Time to 4:02 p.m. Eastern Time); (ii) the volume-weighted average price of our common stock for such date (or the nearest preceding date) on the OTC Bulletin Board; (iii) if our common stock is not then listed on a Trading Market or quoted on the OTC Bulletin Board and if prices for our common stock are then reported in the "Pink Sheets" published by the Pink Sheets, LLC (or a similar organization or agency succeeding to its functions of reporting prices), the most recent bid price per share of our common stock so reported; or (iv) in all other cases, the fair market value of a share of our common stock as determined by a good faith determination of our Board of Directors.

We do not intend to apply for listing of the 2022 Pre-Funded Warrants on any securities exchange or other trading system.

### *2023 Pre-Funded Warrants*

On May 25, 2023, we entered into a securities purchase agreement with certain purchasers named therein, pursuant to which we agreed to sell securities to such purchasers in a private placement. In the private placement, the purchasers had the option to purchase either shares of our common stock or, in lieu thereof, pre-funded

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warrants, or the 2023 Pre-Funded Warrants, to purchase shares of our common stock, each with an exercise price of \$0.001 per share. Accordingly, we issued 2023 Pre-Funded Warrants to purchase 2,408,188 shares of our common stock upon the closing of the private placement.

As of June 1, 2023, 2023 Pre-Funded Warrants to purchase an aggregate of 2,408,188 shares of our common stock were outstanding.

The 2023 Pre-Funded Warrants are exercisable until 5:00 p.m., New York time, on May 31, 2028. The exercise price and number of shares of common stock issuable upon exercise of the 2023 Pre-Funded Warrants may be adjusted in certain circumstances, including in the event of a stock dividend, a forward or reverse split of our shares of common stock, and certain other events. However, the 2023 Pre-Funded Warrants will not be adjusted for issuances of common stock at prices below their respective exercise prices.

We issued the 2023 Pre-Funded Warrants in certificated form. A holder of a 2023 Pre-Funded Warrant certificate may exercise such 2023 Pre-Funded Warrant upon surrender of the applicable warrant certificate on or prior to the applicable expiration date at our principal office, with the exercise form on the reverse side of the warrant certificate completed and executed as indicated, accompanied by full payment of the exercise price for the number of warrants being exercised.

Subject to limited exceptions, a holder of 2023 Pre-Funded Warrants will not have the right to exercise any portion of its 2023 Pre-Funded Warrants if the holder (together with such holder's affiliates, and any persons acting as a group together with such holder or any of such holder's affiliates) would beneficially own a number of shares of our common stock in excess of 9.99% of the shares of our common stock then outstanding after giving effect to such exercise, or the 2023 Pre-Funded Warrant Beneficial Ownership Limitation; provided, however, that upon notice to us, the holder may increase or decrease the 2023 Pre-Funded Warrant Beneficial Ownership Limitation, provided that in no event shall the 2023 Pre-Funded Warrant Beneficial Ownership Limitation exceed 19.99% and any increase in the 2023 Pre-Funded Warrant Beneficial Ownership Limitation will not be effective until 61 days following notice of such increase from the holder to us.

The holders of the 2023 Pre-Funded Warrants must pay the exercise price in cash upon exercise of the 2023 Pre-Funded Warrants, unless such holders are utilizing the cashless exercise provision of the 2023 Pre-Funded Warrants. The 2023 Pre-Funded Warrants may be exercised (in the sole discretion of the holder), in whole or in part, at such time by means of a "cashless exercise" in which the holder of such 2023 Pre-Funded Warrants shall be entitled to receive that number of warrant shares determined according to the following formula:

$$\frac{[(A-B)*(X)]}{(A)}$$

Where:

A = the VWAP (as defined below) on the trading day immediately preceding the date of such election;

B = the exercise price then in effect; and

X = the number of shares of our common stock for which the 2023 Pre-Funded Warrant is being exercised (which shall include both the number of shares of our common stock issued to the holder thereof and the number of shares of our common stock subject to the portion of the warrant being cancelled in payment of the exercise price).

As used above, the "VWAP" means, for any date, the price determined by the first of the following clauses that applies: (i) if our common stock is then listed on The Nasdaq Global Select Market, The Nasdaq Global Market, The Nasdaq Capital Market or the New York Stock Exchange, or collectively, the Trading Market, the daily volume-weighted average price of the Common Stock for such date (or the nearest preceding date) on the Trading Market as reported by Bloomberg Financial L.P. (based on a "Trading Day" from 9:30 a.m. Eastern

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Time to 4:02 p.m. Eastern Time); (ii) the volume-weighted average price of our common stock for such date (or the nearest preceding date) on the OTC Bulletin Board; (iii) if our common stock is not then listed on a Trading Market or quoted on the OTC Bulletin Board and if prices for our common stock are then reported in the “Pink Sheets” published by the Pink Sheets, LLC (or a similar organization or agency succeeding to its functions of reporting prices), the most recent bid price per share of our common stock so reported; or (iv) in all other cases, the fair market value of a share of our common stock as determined by a good faith determination of our Board of Directors.

We do not intend to apply for listing of the 2023 Pre-Funded Warrants on any securities exchange or other trading system.

### *2023 Purchase Warrants*

On May 25, 2023, we entered into a securities purchase agreement with certain purchasers named therein, pursuant to which we agreed to sell securities to such purchasers in a private placement. In the private placement, the purchasers received common stock purchase warrants, or the 2023 Purchase Warrants, to purchase that number of shares of our common stock equal to one half of the aggregate number of shares of our common stock and shares underlying our 2023 Pre-Funded Warrants stock purchased in the private placement, each with an exercise price equal to \$2.673 per share (subject to standard adjustments for stock splits, stock dividend, rights offerings, pro rata distributions and certain anti-dilution adjustment rights). Accordingly, we issued 2023 Purchase Warrants to purchase 10,030,575 shares of our common stock upon the closing of the private placement.

As of June 1, 2023, 2023 Purchase Warrants to purchase an aggregate of 10,030,575 shares of our common stock were outstanding.

The 2023 Purchase Warrants have an exercise price of \$2.673 per share and are exercisable on or after November 30, 2023. The 2023 Purchase Warrants are exercisable until 5:00 p.m., New York time, on November 30, 2028. The exercise price and number of shares of common stock issuable upon exercise of the 2023 Purchase Warrants may be adjusted in certain circumstances, including in the event of a stock dividend, a forward or reverse split of our shares of common stock, and certain other events. However, the 2023 Purchase Warrants will not be adjusted for issuances of common stock at prices below their respective exercise prices.

We issued the 2023 Purchase Warrants in certificated form. A holder of a 2023 Purchase Warrant certificate may exercise such 2023 Purchase Warrant upon surrender of the applicable warrant certificate on or after the applicable exercisability date and on or prior to the applicable expiration date at our principal office, with the exercise form on the reverse side of the warrant certificate completed and executed as indicated, accompanied by full payment of the exercise price for the number of warrants being exercised.

Subject to limited exceptions, a holder of 2023 Purchase Warrants will not have the right to exercise any portion of its 2023 Purchase Warrants if the holder (together with such holder’s affiliates, and any persons acting as a group together with such holder or any of such holder’s affiliates) would beneficially own a number of shares of our common stock in excess of 4.99% or 9.99%, as elected by each such holder, of the shares of our common stock then outstanding after giving effect to such exercise, or the 2023 Purchase Warrant Beneficial Ownership Limitation; provided, however, that upon notice to us, the holder may increase or decrease the 2023 Purchase Warrant Beneficial Ownership Limitation, provided that in no event shall the 2023 Purchase Warrant Beneficial Ownership Limitation exceed 19.99% and any increase in the 2023 Purchase Warrant Beneficial Ownership Limitation will not be effective until 61 days following notice of such increase from the holder to us.

The holders of the 2023 Purchase Warrants must pay the exercise price in cash upon exercise of the 2023 Purchase Warrants, unless such holders are utilizing the cashless exercise provision of the 2023 Purchase Warrants. The 2023 Purchase Warrants may be exercised (in the sole discretion of the holder), in whole or in part, to the extent the resale of the shares of common stock underlying any such 2023 Purchase Warrant is not

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registered under the Securities Act, at such time by means of a “cashless exercise” in which the holder of such 2023 Purchase Warrants shall be entitled to receive that number of warrant shares determined according to the following formula:

$$\frac{[(A-B)*(X)]}{(A)}$$

Where:

A = the VWAP (as defined below) on the trading day immediately preceding the date of such election;

B = the exercise price then in effect; and

X = the number of shares of our common stock for which the 2023 Purchase Warrant is being exercised (which shall include both the number of shares of our common stock issued to the holder thereof and the number of shares of our common stock subject to the portion of the warrant being cancelled in payment of the exercise price).

As used above, the “VWAP” means, for any date, the price determined by the first of the following clauses that applies: (i) if our common stock is then listed on The Nasdaq Global Select Market, The Nasdaq Global Market, The Nasdaq Capital Market or the New York Stock Exchange, any such market being referred to as the Trading Market, the daily volume-weighted average price of the Common Stock for such date (or the nearest preceding date) on the Trading Market as reported by Bloomberg Financial L.P. (based on a “Trading Day” from 9:30 a.m. Eastern Time to 4:02 p.m. Eastern Time); (ii) the volume-weighted average price of our common stock for such date (or the nearest preceding date) on the OTC Bulletin Board; (iii) if our common stock is not then listed on a Trading Market or quoted on the OTC Bulletin Board and if prices for our common stock are then reported in the “Pink Sheets” published by the Pink Sheets, LLC (or a similar organization or agency succeeding to its functions of reporting prices), the most recent bid price per share of our common stock so reported; or (iv) in all other cases, the fair market value of a share of our common stock as determined by a good faith determination of our Board of Directors.

The Purchase Warrants also include certain rights upon the occurrence of a “fundamental transaction” (as described in the 2023 Purchase Warrants) that is either (1) an all cash transaction, (2) a “Rule 13e-3 transaction” as defined in Rule 13e-3 under the Securities Exchange Act of 1934, as amended, or (3) a fundamental transaction in which the successor or acquiring corporation has no equity securities traded on a national securities exchange, including, but not limited to, the NYSE MKT, the Nasdaq Global Select Market, the Nasdaq Global Market, or the Nasdaq Capital Market, at the time of such fundamental transaction, including the right of the holders thereof to receive from the Company or a successor entity the same type or form of consideration (and in the same proportion) that is being offered and paid to the holders of our common stock in such fundamental transaction in the amount of the Black Scholes value (as described in the 2023 Purchase Warrants) of the unexercised portion of the 2023 Purchase Warrants, exercisable at any time concurrently with, or within 30 days after, the consummation of such fundamental transaction.

We do not intend to apply for listing of the 2023 Purchase Warrants on any securities exchange or other trading system.

### **Registration Rights**

Certain holders of shares of our common stock are entitled to certain rights with respect to the registration of such shares for public resale under the Securities Act, pursuant to our ninth amended and restated investors’ rights agreement, as amended, or the investor rights agreement, until the rights otherwise terminate pursuant to the terms of the investor rights agreement. The registration of shares of common stock as a result of the following rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.



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### ***Form S-1 Registration Rights***

If at any time the holders of at least 30% of the registrable securities then outstanding request in writing that we effect a registration with respect to all or part of such registrable securities then outstanding having an anticipated aggregate offering price that would exceed \$5,000,000, we may be required to register their shares. We are obligated to effect at most (i) three registrations initiated by Perceptive Life Sciences Master Fund Ltd and Perceptive LS (A), LLC, collectively referred to as Perceptive, and (ii) three registrations covering registrable securities held by investors other than Perceptive, in each case, in response to these demand registration rights. If the holders requesting registration intend to distribute their shares by means of an underwriting, the managing underwriter of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

### ***Piggyback Registration Rights***

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

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

If, at any time after we become entitled under the Securities Act to register our shares on a registration statement on Form S-3, the holders of the registrable securities then outstanding request in writing that we effect a registration with respect to all or part of such registrable securities having an anticipated aggregate offering price to the public in the offering of at least \$2,000,000, we will be required to effect such registration; provided, however, that we will not be required to effect such a registration if, within any twelve month period, we have already effected two registrations on Form S-3 for the holders of registrable securities.

### ***Termination of Registration Rights***

The registration rights terminate upon the earlier of the date on which no stockholder holds any registrable securities, the closing of a company sale, as defined in the investor rights agreement, at such time as SEC Rule 144 or another similar exemption under the Securities Act is available for the sale of all of a stockholder's shares without limitation during a three-month period without registration, at such time a stockholder is not an affiliate (as defined under the Securities Act) of the Company or May 5, 2028.

### ***Private Placement Registration Rights***

We agreed to prepare and file with the SEC a registration statement by no later than May 12, 2022 covering the public resale pursuant to the Securities Act of certain shares of our common stock issued, and certain shares of our common stock issuable upon exercise of the 2022 Pre-Funded Warrants issued, in each case, pursuant to a securities purchase agreement dated April 7, 2022, and have further agreed to use commercially reasonable efforts to have such registration statement declared effective as soon as reasonably practicable after the filing thereof, but in no event later than June 11, 2022, or July 11, 2022 if the SEC reviews the registration statement. A registration statement on Form S-3 was filed with the SEC on May 11, 2022 in accordance with the aforementioned obligations.

We have also agreed to prepare and file with the SEC a registration statement by no later than June 30, 2023 covering the public resale pursuant to the Securities Act of certain shares of our common stock issued, and certain shares of our common stock issuable upon exercise of the 2023 Pre-Funded Warrants and the 2023 Purchase Warrants, in each case, pursuant to a securities purchase agreement dated May 25, 2023, and have further agreed to use commercially reasonable efforts to have such registration statement declared effective as soon as reasonably practicable after the filing thereof, but in no event later than July 30, 2023, or August 29,

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2023 if the SEC reviews the registration statement. This registration statement on Form S-3 is being filed with the SEC in accordance with the aforementioned obligations.

### **Expenses and Indemnification**

Ordinarily, other than underwriting discounts (it being understood that the selling securityholders shall not be deemed to be underwriters solely as a result of their participation in this offering) and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling securityholders and blue sky fees and expenses. Additionally, we have agreed to indemnify selling securityholders for damages, and any legal or other expenses reasonably incurred, arising from or based upon any untrue statement of a material fact contained in any registration statement, an omission or alleged omission to state a material fact in any registration statement or necessary to make the statements therein not misleading, or any violation or alleged violation by the indemnifying party of securities laws, subject to certain exceptions.

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

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

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

*Undesignated Preferred Stock.* The ability of our board of directors, without action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

*Stockholder Meetings.* Our bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president (in the absence of a chief executive officer), or by a resolution adopted by a majority of our board of directors.

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

*Elimination of Stockholder Action by Written Consent.* Our certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

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

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*Removal of Directors.* Our certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of the holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote in the election of directors.

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

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

*Choice of Forum.* Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or stockholders to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws; or (4) any action asserting a claim governed by the internal affairs doctrine. Under our certificate of incorporation, this exclusive forum provision will not apply to claims which are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. For instance, the provision would not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Securities Act, Exchange Act, or the rules and regulations thereunder. Our certificate of incorporation further provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Our certificate of incorporation also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to these choice of forum provisions. It is possible that a court of law could rule that either or both of the choice of forum provisions contained in our certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

*Amendment of Charter Provisions.* The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock and the provision prohibiting cumulative voting, would require approval by holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote thereon.

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

## SELLING SECURITYHOLDERS

This prospectus relates to the possible resale by certain of the selling securityholders from time to time of up to an aggregate of 21,967,353 shares of common stock of the Company, \$0.001 par value per share, or Common Stock. The term “selling securityholders” includes donees, pledgees, transferees or other successors in interest selling securities received after the date of this prospectus from a selling securityholder as a gift, pledge, partnership distribution or other transfer.

On May 25, 2023, we entered into a Securities Purchase Agreement, or the Purchase Agreement, with the selling securityholders, pursuant to which we sold in a private placement an aggregate of (i) 17,652,962 shares of Common Stock, or the Shares; (ii) pre-funded warrants, or the Pre-Funded Warrants, to purchase an aggregate of 2,408,188 shares of Common Stock, or the Pre-Funded Warrant Shares, and (iii) warrants, or the Purchase Warrants, to purchase an aggregate of 10,030,575 shares of Common Stock, or the Warrant Shares, for an aggregate purchase price of \$50,000,008.25. Each of the Pre-Funded Warrants is exercisable immediately, until 5:00 p.m., New York time, on May 31, 2028, and has an exercise price of \$0.001 per underlying Pre-Funded Warrant Share, with an aggregate exercise price for all such Pre-Funded Warrants of \$2,408.19. Each of the Purchase Warrants is exercisable on or after November 30, 2023, until 5:00 p.m., New York time, on November 30, 2028, and has an exercise price of \$2.673 per underlying Warrant Share, with an aggregate exercise price for all such Purchase Warrants of \$26,811,726.98. This prospectus relates to the possible resale by certain of the purchasers under the Purchase Agreement of (i) 12,236,714 of the Shares sold under the Purchase Agreement, (ii) 2,408,188 of the Pre-Funded Warrant Shares underlying the Pre-Funded Warrants sold under the Purchase Agreement and (iii) 7,322,451 of the Warrant Shares underlying the Purchase Warrants sold under the Purchase Agreement.

The following table sets forth information concerning the shares of Common Stock that may be offered from time to time by each selling securityholder. The number of shares beneficially owned by each selling securityholder is determined under rules issued by the SEC. Under these rules, beneficial ownership includes any shares as to which the selling securityholder has sole or shared voting power or investment power. Percentage ownership is based on 49,489,777 shares of Common Stock outstanding as of June 1, 2023. In computing the number of shares beneficially owned by a selling securityholder and their percentage ownership, shares of Common Stock subject to options, warrants or other rights held by such selling securityholder that are currently exercisable or will become exercisable within 60 days of June 1, 2023 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other selling securityholder. For purposes of this table, we have assumed that the selling securityholders will have sold all of the securities covered by this prospectus upon the completion of the offering. Each of the selling securityholders listed has sole voting and investment power with respect to the shares beneficially owned by the selling securityholder unless noted otherwise.

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The information in the following table has been provided to us by or on behalf of the selling securityholders and the selling securityholders may have sold, transferred or otherwise disposed of all or a portion of their securities after the date on which they provided us with information regarding their securities. A selling securityholder may sell all, some or none of its securities in this offering. See “Plan of Distribution.”

Selling Securityholder	Common Stock Beneficially Owned Before this Offering		Maximum Number of Shares of Common Stock to be Sold Pursuant to this Prospectus	Common Stock Beneficially Owned Upon Completion of this Offering	
	Number	Percentage		Number	Percentage
Armistice Capital Master Fund Ltd. <sup>(1)</sup>	4,012,036	8.11%	6,018,054 <sup>(2)</sup>	—	—
Citadel CEMF Investments Ltd. <sup>(3)</sup>	2,848,544	5.76%	4,272,816 <sup>(4)</sup>	—	—
Entities affiliated with Venrock Healthcare Capital Partners <sup>(5)</sup>	6,992,903 <sup>(6)</sup>	14.13%	3,612,282 <sup>(7)</sup>	4,584,715	9.26%
Nantahala Capital Partners Limited Partnership <sup>(8)</sup>	336,538	*	183,126 <sup>(9)</sup>	214,454	*
NCP RFM LP <sup>(8)</sup>	546,934	1.11%	369,375 <sup>(10)</sup>	300,684	*
Blackwell Partners LLC – Series A <sup>(8)</sup>	1,735,256	3.51%	1,266,570 <sup>(11)</sup>	890,876	1.80%
Corbin Hedged Equity Fund, L.P. <sup>(8)</sup>	88,137	*	65,148 <sup>(12)</sup>	44,705	*
Pinehurst Partners, L.P. <sup>(8)</sup>	287,792	*	222,099 <sup>(13)</sup>	139,726	*
Samsara BioCapital, L.P. <sup>(14)</sup>	2,780,261	5.62%	1,504,515 <sup>(15)</sup>	1,777,251	3.59%
Woodline Master Fund LP. <sup>(16)</sup>	641,926	1.30%	962,889 <sup>(17)</sup>	—	—
Parkman HP Master Fund LP <sup>(18)</sup>	163,512	*	245,268 <sup>(19)</sup>	—	—
Schonfeld EXT Master Fund LP <sup>(20)</sup>	436,488	*	654,732 <sup>(21)</sup>	—	—
Alyeska Master Fund, L.P. <sup>(22)</sup>	481,446	*	722,169 <sup>(23)</sup>	—	—
Rosalind Master Fund L.P. <sup>(24)</sup>	1,166,615	2.36%	724,878 <sup>(25)</sup>	683,363	1.38%
Pura Vida X Fund LP <sup>(26)</sup>	504,884 <sup>(27)</sup>	1.02%	214,938 <sup>(28)</sup>	361,592	*
Lockheed Martin Corporation Master Retirement Trust <sup>(26)</sup>	908,358 <sup>(29)</sup>	1.84%	386,868 <sup>(30)</sup>	650,446	1.31%
Entities affiliated with DAFNA Capital Management LLC <sup>(31)</sup>	361,084	*	541,626 <sup>(32)</sup>	—	—

\* Less than 1%.

- (1) The securities are directly held by Armistice Capital Master Fund Ltd., a Cayman Islands exempted company (“Master Fund”). The securities may be deemed to be beneficially owned by (i) Armistice Capital, LLC (“Armistice Capital”), as the investment manager of the Master Fund; and (ii) Steven Boyd, as the Managing Member of Armistice Capital. The address of the Master Fund is c/o Armistice Capital, LLC, 510 Madison Ave, 7th Floor, New York, NY 10022.
- (2) Consists of 4,012,036 shares of Common Stock and 2,006,018 shares of Common Stock underlying warrants directly held by Master Fund. The warrants are subject to a beneficial ownership limitation of 4.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and its affiliates owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (3) The securities are directly held by Citadel CEMF Investments Ltd. Citadel Advisors LLC is the portfolio manager of Citadel CEMF Investments Ltd. Citadel Advisors Holdings LP is the sole member of Citadel Advisors LLC. Citadel GP LLC is the General Partner of Citadel Advisors Holdings LP. Kenneth Griffin owns a controlling interest in Citadel GP LLC. Mr. Griffin, as the owner of a controlling interest in Citadel GP LLC, may be deemed to have shared power to vote and/or shared power to dispose of the securities held by Citadel CEMF Investments Ltd. This disclosure shall not be construed as an admission that Mr. Griffin or any of the Citadel related entities listed above is the beneficial owner of any securities of the Company other than the securities actually owned by such person (if any). The business address of Citadel CEMF Investments Ltd. is Southeast Financial Center, 200 S. Biscayne Blvd., Suite 3300, Miami, Florida 33131.
- (4) Consists of 2,848,544 shares of Common Stock and 1,424,272 shares of Common Stock underlying the Purchase Warrant held by Citadel CEMF Investments Ltd. The Purchase Warrant is subject to a beneficial ownership limitation of 9.99% of the outstanding shares of Common Stock, which such limitation restricts

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the Selling Securityholder from exercising that portion of the Purchase Warrant that would result in the Selling Securityholder, together with any of its affiliates or any person acting as a group therewith, beneficially owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation.

- (5) The securities are directly held by (i) Venrock Healthcare Capital Partners EG, L.P. (“VHCP EG”), (ii) VHCP Co-Investment Holdings III, LLC (“VHCP III Co”) and or (iii) Venrock Healthcare Capital Partners III, L.P. (“VHCP III” and, together with VHCP EG and VHCP III Co, the “Entities Affiliated with Venrock”). VHCP Management III, LLC (“VHCPM III”) is the sole general partner of VHCP III and the sole manager of VHCP III Co. VHCP Management EG, LLC (“VHCPM EG”) is the sole general partner of VHCP EG. Dr. Bong Koh and Nimish Shah are the voting members of VHCPM III and VHCPM EG. The address for the Entities Affiliated with Venrock is 7 Bryant Park, 23<sup>rd</sup> Floor, New York, NY 10018.
- (6) Consists of (i) 361,628 shares of Common Stock and 3,668,238 shares of Common Stock underlying pre-funded warrants directly held by VHCP EG; (ii) 32,161 shares of Common Stock and 237,336 shares of Common Stock underlying pre-funded warrants directly held by VHCP III Co.; and (iii) 321,426 shares of Common Stock and 2,372,114 shares of Common Stock underlying pre-funded warrants directly held by VHCP III. Under the terms of the pre-funded warrants held by the Entities Affiliated with Venrock, the Company may not effect the exercise of any such warrant, and a holder will not be entitled to exercise any portion of such warrant, if, upon giving effect to such exercise, the aggregate number of shares of Common Stock beneficially owned by the holder (together with its affiliates and other attribution parties) would exceed 9.99% of the number of shares of Common Stock outstanding immediately after giving effect to the exercise.
- (7) Consists of (i) 1,711,738 shares of Common Stock underlying pre-funded warrants and 855,869 shares of Common Stock underlying warrants directly held by VHCP EG; (ii) 633,114 shares of Common Stock underlying pre-funded warrants and 316,557 shares of Common Stock underlying warrants directly held by VHCP III; and (iii) 63,336 shares of Common Stock underlying pre-funded warrants and 31,668 shares of Common Stock underlying warrants directly held by VHCP III Co.
- (8) The securities are held by Nantahala Capital Partners Limited Partnership, NCP RFM LP (“RFM”), Blackwell Partners LLC – Series A, Corbin Hedged Equity Fund, L.P. and Pinehurst Partners, L.P. Nantahala Capital Management, LLC is a registered investment adviser and has been delegated the legal power to vote and/or direct the disposition of the shares held by each of the above entities as General Partner, Investment Manager, or Sub-Advisor and would be considered the beneficial owner of such securities. The above shall not be deemed to be an admission by the record owners that they are themselves beneficial owners of these securities for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or any other purpose, nor shall the above be deemed an admission that the record owners are “affiliates” within the meaning of that term used under the Securities Act of 1933. Wilmot Harkey and Daniel Mack are managing members of Nantahala Capital Management, LLC and may be deemed to have voting and dispositive power over the shares held by the above entities. The amounts and percentages in the table do not give effect to the beneficial ownership limitations. The address of Nantahala Capital Partners Limited Partnership and RFM is 130 Main Street, 2<sup>nd</sup> Floor, New Canaan, CT 06840. The address of Blackwell Partners LLC – Series A is 280 South Mangum Street, Suite 210, Durham, NC 27701. The address of Corbin Hedged Equity Fund, L.P. and Pinehurst Partners, L.P. is c/o Corporation Trust Center, 1209 Orange Street, Wilmington, DE 19801.
- (9) Consists of 122,084 shares of Common Stock and 61,042 shares of Common Stock underlying warrants directly held by Nantahala Capital Partners Limited Partnership. The warrants are subject to a beneficial ownership limitation of 9.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and certain other persons owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (10) Consists of 246,250 shares of Common Stock and 123,125 shares of Common Stock underlying warrants directly held by RFM. The warrants are subject to a beneficial ownership limitation of 9.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and certain other persons owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.

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- (11) Consists of 844,380 shares of Common Stock and 422,190 Common Stock underlying warrants directly held by Blackwell Partners LLC – Series A. The warrants are subject to a beneficial ownership limitation of 9.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and certain other persons owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (12) Consists of 43,432 shares of Common Stock and 21,716 shares of Common Stock underlying warrants directly held by Corbin Hedged Equity Fund, L.P. The warrants are subject to a beneficial ownership limitation of 9.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and certain other persons owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (13) Consists of 148,066 shares of Common Stock and 74,033 shares of Common Stock underlying warrants directly held by Pinehurst Partners, L.P. The warrants are subject to a beneficial ownership limitation of 9.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and certain other persons owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (14) The securities are directly held by Samsara BioCapital, LP (“Samsara LP”). Samsara BioCapital GP, LLC (“Samsara LLC”) is the general partner of Samsara LP. Samsara LLC may be deemed to beneficially own the shares held by Samsara LP. Srinivas Akkaraju, M.D., Ph.D. is the Managing Member of Samsara LLC and has voting and investment power over the shares held by Samsara LP and, accordingly, may be deemed to beneficially own the shares held by Samsara LP. Each of Samsara LLC and Dr. Akkaraju disclaims beneficial ownership in these shares except to the extent of his or its respective pecuniary interest therein. The address of Samsara is 628 Middlefield Road, Palo Alto, CA 94301.
- (15) Consists of 1,003,010 shares of Common Stock and 501,505 shares of Common Stock underlying warrants directly held by Samsara LP. The warrants are subject to a beneficial ownership limitation of 9.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and its affiliates owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (16) These securities are directly held by Woodline Master Fund LP (“Woodline”). Woodline Partners LP serves as the investment manager of Woodline and may be deemed to be the beneficial owner of the shares of Common Stock held by Woodline. Woodline Partners LP disclaims any beneficial ownership of these shares. The address of Woodline is 4 Embarcadero Center, Suite 3450, San Francisco, CA 94111.
- (17) Consists of 641,926 shares of Common Stock and 320,963 shares of Common Stock underlying warrants directly held by Woodline. The warrants are subject to a beneficial ownership limitation of 4.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and its affiliates owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (18) These securities are directly held by Parkman HP Master Fund LP (“Parkman”). Gregory Martinez is the Managing Member, of Parkman HP Master Fund GP. The address of Parkman is 700 Canal Street, 2<sup>nd</sup> floor, Stamford, CT 06902.
- (19) Consists of 163,512 shares of Common Stock and 81,756 shares of Common Stock underlying warrants directly held by Parkman. The warrants are subject to a beneficial ownership limitation of 4.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and its affiliates owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (20) These securities are directly held by Schonfeld EXT Master Fund LP (“Schonfeld EXT Master”). Schonfeld Strategic Advisors LLC is a Registered Investment Adviser and has been delegated the legal power to vote

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and/or direct the disposition of such securities on behalf of Schonfeld EXT Master as a general partner or investment manager and would be considered the beneficial owner of such securities. The above shall not be deemed to be an admission by the record owners or Schonfeld EXT Master that they are themselves beneficial owners of these securities for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended, or any other purpose. The address of Schonfeld EXT Master is 590 Madison Ave, Floor 23, New York, NY 10022.

- (21) Consists of 436,488 shares of Common Stock and 218,244 shares of Common Stock underlying warrants. The warrants are subject to a beneficial ownership limitation of 4.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and its affiliates owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (22) These securities are directly held by Alyeska Master Fund, L.P. (“Alyeska”). Alyeska Investment Group, L.P., the investment manager of Alyeska, has voting and investment control of the shares held by the Alyeska. Anand Parekh is the Chief Executive Officer of Alyeska Investment Group, L.P. and may be deemed to be the beneficial owner of such shares. Mr. Parekh, however, disclaims any beneficial ownership of the shares held by Alyeska. The registered address of Alyeska is at c/o Maples Corporate Services Limited, P.O. Box 309, Uglund House, South Church Street George Town, Grand Cayman, KY1-1104, Cayman Islands. Alyeska Investment Group, L.P. is located at 77 W. Wacker, Suite 700, Chicago IL 60601.
- (23) Consists of 481,446 shares of Common Stock and 240,723 shares of Common Stock underlying warrants held by Alyeska. The warrants are subject to a beneficial ownership limitation of 9.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and its affiliates owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (24) These securities are directly held by Rosalind Master Fund L.P. (“Rosalind”). Rosalind Advisors, Inc. is the investment advisor to Rosalind and may be deemed the beneficial owner of shares held by Rosalind. Steven Salamon is the portfolio manager of Rosalind Advisors, Inc. and may be deemed to beneficially own the securities held by Rosalind. The address of Rosalind is 15 Wellesley Street West, Suite 326, Toronto, ON, Canada M4Y 0G7.
- (25) Includes 483,252 shares of Common Stock and 241,626 shares of Common Stock underlying warrants directly held by Rosalind. The warrants are subject to a beneficial ownership limitation of 4.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and its affiliates owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (26) These securities are directly held by Pura Vida X Fund LP (the “Pura Vida Fund”) and Lockheed Martin Corporation Master Retirement Trust (“Lockheed”). Pura Vida Investments, LLC (“PVI”) serves as the investment manager to the Pura Vida Fund and Lockheed. Efreem Kamen serves as the managing member of PVI. By virtue of these relationships, PVI and Efreem Kamen may be deemed to have shared voting and dispositive power with respect to the securities held by the Pura Vida Fund and Lockheed. This filing shall not be deemed an admission that PVI and/or Efreem Kamen are beneficial owners of the securities for purposes of Sections 13 and 16 of the Securities Exchange Act of 1934, as amended, or for any other purpose. Each of PVI and Efreem Kamen disclaims beneficial ownership of the securities reported herein except to the extent of each PVI’s and Efreem Kamen’s respective pecuniary interest, if any, therein. The address of PVI is 512 West 22<sup>nd</sup> Street, 7<sup>th</sup> Floor, NY, NY 10011.
- (27) Consists of 361,592 shares of Common Stock and 143,292 shares of Common Stock purchased under the Purchase Agreement directly held by Pura Vida.
- (28) Consists of 143,292 shares of Common Stock purchased under the Purchase Agreement and 71,646 shares of Common Stock underlying warrants directly held by Pura Vida. The warrants are subject to a beneficial ownership limitation of 9.99%, which such limitation restricts the Selling Securityholder from exercising



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that portion of the warrants that would result in the Selling Securityholder and its affiliates owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation.

- (29) Consists of 650,446 shares of Common Stock and 257,912 shares of Common Stock purchased under the Purchase Agreement directly held by Lockheed.
- (30) Consists of 257,912 shares of Common Stock purchased under the Purchase Agreement and 128,956 shares of Common Stock underlying warrants directly held by Lockheed. The warrants are subject to a beneficial ownership limitation of 9.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and its affiliates owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.
- (31) These securities are directly held by DAFNA Lifescience, L.P. (“DAFNA”) and DAFNA Lifescience Select L.P. (“DAFNA Select”). DAFNA Capital Management LLC is the sole general partner of DAFNA and DAFNA Select. The Chief Executive Officer and Chief Investment Officer of DAFNA Capital Management LLC are Dr. Nathan Fischel and Dr. Fariba Ghodsian, respectively. These individuals may be deemed to have shared voting and investment power of the shares held by DAFNA and DAFNA Select. Each of Dr. Fischel and Dr. Ghodsian disclaim beneficial ownership of such shares, except to the extent of his or her pecuniary interest therein. The address of DAFNA and DAFNA Select is 10990 Wilshire Blvd., Suite 1400, Los Angeles, CA 90024.
- (32) Consists of (i) 270,814 shares of Common Stock and 135,407 shares of Common Stock underlying warrants directly held by DAFNA and (ii) 90,270 shares of Common Stock and 45,135 shares of Common Stock underlying warrants directly held by DAFNA Select. The warrants are subject to a beneficial ownership limitation of 4.99%, which such limitation restricts the Selling Securityholder from exercising that portion of the warrants that would result in the Selling Securityholder and its affiliates owning, after exercise, a number of shares of Common Stock in excess of the beneficial ownership limitation. The amounts and percentages in the table do not give effect to the beneficial ownership limitations.

## PLAN OF DISTRIBUTION

The selling securityholders and any of their pledgees, donees, transferees, assignees or other successors-in-interest may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices. The selling securityholders may use one or more of the following methods when disposing of the shares or interests therein:

- 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;
- through brokers, dealers or underwriters that may act solely as agents;
- 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;
- through the writing or settlement of options or other hedging transactions entered into after the effective date of the registration statement of which this prospectus is a part, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling securityholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of disposition; and
- any other method permitted pursuant to applicable law.

The selling securityholders may also sell shares under Rule 144 or Rule 904 under the Securities Act of 1933, as amended, or Securities Act, if available, or Section 4(a)(1) under the Securities Act, rather than under this prospectus.

Broker-dealers engaged by the selling securityholders may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling securityholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling securityholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved.

The selling securityholders 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 they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell shares of common stock from time to time under this prospectus, or under a supplement or amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling securityholders to include the pledgee, transferee or other successors in interest as selling securityholders under this prospectus.

Upon being notified in writing by a selling securityholder 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, we will file a supplement to this prospectus, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the name of each such selling securityholder and of the participating broker-dealer(s), (ii) the number of shares involved, (iii) the price at which such shares of common stock were sold, (iv) the commissions paid or discounts or concessions allowed

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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. In addition, upon being notified in writing by a selling securityholder that a donee or pledgee intends to sell more than 500 shares of common stock, we will file a supplement to this prospectus if then required in accordance with applicable securities law.

The selling securityholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of the shares of common stock or interests in shares of common stock, the selling securityholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling securityholders may also sell shares of common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling securityholders 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, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The selling securityholders and any broker-dealers or agents that are involved in selling the shares may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any profits realized by such selling securityholders or compensation received by such broker-dealers or agents may be deemed to be underwriting commissions or discounts under the Securities Act. The maximum commission or discount to be received by any member of the Financial Industry Regulatory Authority (FINRA) or independent broker-dealer will not be greater than 8% of the initial gross proceeds from the sale of any security being sold.

We have advised the selling securityholders that they are required to comply with Regulation M promulgated under the Securities Exchange Act of 1934, as amended, during such time as they may be engaged in a distribution of the shares. The foregoing may affect the marketability of the common stock.

The aggregate proceeds to the selling securityholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling securityholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

We are required to pay all fees and expenses incident to the registration of the shares. We have agreed to indemnify the selling securityholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act or otherwise.

We have agreed with the selling securityholders to keep the registration statement of which this prospectus constitutes a part effective until the earlier of (a) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with the registration statement and (b) such time as none of the shares covered by this prospectus constitute “registrable securities”, as such term is defined in the registration rights agreement by and among us and the selling securityholders.

**LEGAL MATTERS**

The validity of the common stock being offered by this prospectus has been passed upon for us by Latham & Watkins LLP.

**EXPERTS**

The consolidated financial statements as of December 31, 2022 and 2021 and for each of the two years in the period ended December 31, 2022 incorporated by reference in this Prospectus and in the Registration Statement have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

**PART II**  
**INFORMATION NOT REQUIRED IN PROSPECTUS**

**Item 14. Other Expenses of Issuance and Distribution**

The following is an estimate of the expenses (all of which are to be paid by the registrant) that we may incur in connection with the securities being registered hereby.

SEC registration fee	\$ 9,926
Printing expenses	10,000
Legal fees and expenses	75,000
Accounting fees and expenses	30,000
Miscellaneous	3,050
Total	<u>\$ 127,976</u>

**Item 15. Indemnification of Directors and Officers**

Subsection (a) of Section 145 of the General Corporation Law of the State of Delaware, or the DGCL, empowers a corporation to indemnify any person who was or is a party or who is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe the person's conduct was unlawful.

Subsection (b) of Section 145 empowers a corporation to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that the person acted in any of the capacities set forth above, against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Section 145 further provides that to the extent a director or officer of a corporation has been successful on the merits or otherwise in the defense of any action, suit or proceeding referred to in subsections (a) and (b) of Section 145, or in defense of any claim, issue or matter therein, such person shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by such person in connection therewith; that indemnification provided for by Section 145 shall not be deemed exclusive of any other rights to which the indemnified party may be entitled; and the indemnification provided for by Section 145 shall, unless otherwise provided when authorized or ratified, continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of such person's heirs, executors and administrators. Section 145 also empowers the corporation to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director,

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officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his status as such, whether or not the corporation would have the power to indemnify such person against such liabilities under Section 145.

Section 102(b)(7) of the DGCL provides that a corporation's certificate of incorporation may contain a provision eliminating or limiting the personal liability of a director to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, provided that such provision shall not eliminate or limit the liability of a director (i) for any breach of the director's duty of loyalty to the corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL, or (iv) for any transaction from which the director derived an improper personal benefit.

Any underwriting agreement or distribution agreement that the registrant enters into with any underwriters or agents involved in the offering or sale of any securities registered hereby may require such underwriters or dealers to indemnify the registrant, some or all of its directors and officers and its controlling persons, if any, for specified liabilities, which may include liabilities under the Securities Act of 1933, as amended.

Our bylaws provide that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, a director or officer or is or was serving, or has agreed to serve, at our request, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including, without limitation, attorneys' fees), liabilities, losses, judgments, fines (including, without limitation, excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974), and amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that Indemnitee did not act in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of us, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful. Our bylaws provide that we will indemnify any Indemnitee who was or is a party to or threatened to be made a party to any threatened, pending or completed action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that Indemnitee is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including, without limitation, any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including, without limitation, attorneys' fees) actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which Indemnitee shall have been adjudged to be liable to us, unless, and only to the extent, that the Court of Chancery of Delaware or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of such liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnity for such expenses (including, without limitation, attorneys' fees) which the Court of Chancery of Delaware or such other court shall deem proper.

We have entered into indemnification agreements with each of our directors and officers. These indemnification agreements may require us, among other things, to indemnify our directors and officers for some

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expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of his or her service as one of our directors or officers, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request.

The indemnification rights set forth above shall not be exclusive of any other right which an indemnified person may have or hereafter acquire under any statute, our certificate of incorporation, our bylaws, any agreement, any vote of stockholders or disinterested directors or otherwise.

We maintain a general liability insurance policy that covers certain liabilities of directors and officers of our corporation arising out of claims based on acts or omissions in their capacities as directors or officers.

### **Item 16. Exhibits**

<b>Exhibit Number</b>	<b>Description</b>
3.1	<a href="#"><u>Restated Certificate of Incorporation of Lyra Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed with the SEC on May 5, 2020).</u></a>
3.2	<a href="#"><u>Amended and Restated Bylaws of Lyra Therapeutics, Inc. (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed with the SEC on May 5, 2020).</u></a>
4.1	<a href="#"><u>Ninth Amended and Restated Investor Rights Agreement, dated as of April 7, 2022, by and among Lyra Therapeutics, Inc. and the Investors named therein (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K, filed with the SEC on April 13, 2022), as amended by that certain Amendment No. 1 to Ninth Amended and Restated Investor Rights Agreement, dated as of May 25, 2023, by and among Lyra Therapeutics, Inc. and the Investors named therein (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K, filed with the SEC on May 31, 2023).</u></a>
4.2	<a href="#"><u>Specimen Stock Certificate evidencing the shares of common stock of Lyra Therapeutics, Inc. (incorporated by reference to Exhibit 4.2 to the Amendment to the Company's Registration Statement on Form S-1, filed with the SEC on April 27, 2020).</u></a>
4.3	<a href="#"><u>Form of Common Stock Purchase Warrant, together with a schedule of Warrants, each dated April 12, 2022, issued by the Company to the Investors set forth on such schedule (incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K, filed with the SEC on April 13, 2022).</u></a>
4.4	<a href="#"><u>Form of Pre-Funded Warrant, together with a schedule of Pre-Funded Warrants, each dated as of May 31, 2023, issued by Lyra Therapeutics, Inc. to the Investors set forth on such schedule (incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K, filed with the SEC on May 31, 2023).</u></a>
4.5	<a href="#"><u>Form of Purchase Warrant, together with a schedule of Purchase Warrants, each dated as of May 31, 2023, issued by Lyra Therapeutics, Inc. to the Investors set forth on such schedule (incorporated by reference to Exhibit 4.3 to the Company's Current Report on Form 8-K, filed with the SEC on May 31, 2023).</u></a>
4.6	<a href="#"><u>Description of Securities (incorporated by reference to Exhibit 4.5 to the Company's Annual Report on Form 10-K, filed with the SEC on March 29, 2023).</u></a>
10.1	<a href="#"><u>Securities Purchase Agreement, dated as of May 25, 2023, by and among Lyra Therapeutics, Inc. and the Investors named therein (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, filed with the SEC on May 31, 2023).</u></a>
10.2	<a href="#"><u>Registration Rights Agreement, dated as of May 25, 2023, by and among Lyra Therapeutics, Inc. and the Investors named therein (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K, filed with the SEC on May 31, 2023).</u></a>

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5.1 [Opinion of Latham & Watkins LLP.](#)

23.1 [Consent of Latham & Watkins LLP \(included in Exhibit 5.1\).](#)

23.2 [Consent of BDO USA, LLP.](#)

24.1 [Powers of Attorney \(included on signature page hereto\).](#)

107 [Filing Fee Table.](#)



**Item 17. Undertakings**

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

*provided, however*, that paragraphs (a)(1)(i), (a)(1)(ii), and (a)(1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is a part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(5) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

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(6) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities:

The undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communications that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(h) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Watertown, Commonwealth of Massachusetts, on June 28, 2023.

LYRA THERAPEUTICS, INC.

By: /s/ Maria Palasis

Maria Palasis, Ph.D.  
President and Chief Executive Officer

## POWER OF ATTORNEY

Each of the undersigned officers and directors of the registrant hereby severally constitutes and appoints Maria Palasis, Ph.D. and Jason Cavalier, or either of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, and in any and all capacities, to file and sign any and all amendments, including post-effective amendments, to this registration statement and any other registration statement for the same offering that is to be effective under Rule 462(b) of the Securities Act of 1933, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith and about the premises as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof. This power of attorney shall be governed by and construed with the laws of the State of Delaware and applicable federal securities laws.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed below by the following persons on behalf of the registrant in the capacities and on the dates indicated.

<u>SIGNATURE</u>	<u>TITLE</u>	<u>DATE</u>
<u>/s/ Maria Palasis</u> Maria Palasis, Ph.D.	President, Chief Executive Officer and Director ( <i>principal executive officer</i> )	June 28, 2023
<u>/s/ Jason Cavalier</u> Jason Cavalier	Chief Financial Officer ( <i>principal financial officer and principal accounting officer</i> )	June 28, 2023
<u>/s/ Harlan Waksal</u> Harlan Waksal, M.D.	Executive Chair and Chairperson of the Board	June 28, 2023
<u>/s/ Michael Altman</u> Michael Altman	Director	June 28, 2023
<u>/s/ Edward T. Anderson</u> Edward T. Anderson	Director	June 28, 2023
<u>/s/ C. Ann Merrifield</u> C. Ann Merrifield	Director	June 28, 2023

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<u>SIGNATURE</u>	<u>TITLE</u>	<u>DATE</u>
<hr/> <i>/s/ Konstantin Poukalov</i> Konstantin Poukalov	Director	June 28, 2023
<hr/> <i>/s/ W. Bradford Smith</i> W. Bradford Smith	Director	June 28, 2023
<hr/> <i>/s/ Nancy Snyderman</i> Nancy Snyderman, M.D., FACS	Director	June 28, 2023
<hr/> <i>/s/ James R. Tobin</i> James R. Tobin	Director	June 28, 2023

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 Boston, Massachusetts 02116  
 Tel: +1.617.948.6000 Fax: +1.617.948.6001  
 www.lw.com

**LATHAM & WATKINS** LLP

June 28, 2023

Lyra Therapeutics, Inc.  
 480 Arsenal Way  
 Watertown, MA 02472

FIRM / AFFILIATE OFFICES

Austin	Milan
Beijing	Munich
Boston	New York
Brussels	Orange County
Century City	Paris
Chicago	Riyadh
Dubai	San Diego
Düsseldorf	San Francisco
Frankfurt	Seoul
Hamburg	Shanghai
Hong Kong	Silicon Valley
Houston	Singapore
London	Tel Aviv
Los Angeles	Tokyo
Madrid	Washington, D.C.

Re: Registration Statement on Form S-3; 21,967,353 shares of Common Stock, par value \$0.001 per share

To the addressee set forth above:

We have acted as special counsel to Lyra Therapeutics, Inc., a Delaware corporation (the “**Company**”), in connection with the resale from time to time by the selling securityholders named in the Registration Statement (as defined below) of 21,967,353 shares (the “**Shares**”) of the Company’s common stock, \$0.001 par value per share (“**Common Stock**”). The Shares include (a) 12,236,714 outstanding shares (the “**Issued Shares**”) of Common Stock, (b) 2,408,188 shares (the “**Pre-Funded Warrant Shares**”) of Common Stock issuable upon exercise of outstanding pre-funded warrants to purchase Common Stock (the “**Pre-Funded Warrants**”) and 7,322,451 shares (the “**Purchase Warrant Shares**” and, together with the Pre-Funded Warrant Shares, the “**Warrant Shares**”) of Common Stock issuable upon exercise of outstanding warrants to purchase Common Stock (the “**Purchase Warrants**” and, together with the Pre-Funded Warrants, the “**Warrants**”). The Shares are included in a registration statement on Form S-3 under the Securities Act of 1933, as amended (the “**Act**”), filed with the Securities and Exchange Commission (the “**Commission**”) on June 28, 2023 (the “**Registration Statement**”). This opinion is being furnished in connection with the requirements of Item 601(b)(5) of Regulation S-K under the Act, and no opinion is expressed herein as to any matter pertaining to the contents of the Registration Statement or the related prospectus, other than as expressly stated herein with respect to the issue of the Shares.

As such counsel, we have examined such matters of fact and questions of law as we have considered appropriate for purposes of this letter. With your consent, we have relied upon certificates and other assurances of officers of the Company and others as to factual matters without having independently verified such factual matters. We are opining herein as to the General Corporation Law of the State of Delaware (the “**DGCL**”), and we express no opinion with respect to any other laws.



Subject to the foregoing and the other matters set forth herein, it is our opinion that, as of the date hereof:

1. The Issued Shares have been duly authorized by all necessary corporate action of the Company and are validly issued, fully paid and nonassessable.

2. When the Warrant Shares shall have been duly registered on the books of the transfer agent and registrar therefor in the name or on behalf of the Warrant holders, and have been issued by the Company against payment therefor (not less than par value) in the circumstances contemplated by the Warrants, the issue of the Warrant Shares will have been duly authorized by all necessary corporate action of the Company and the Warrant Shares will be validly issued, fully paid and nonassessable. In rendering the foregoing opinion, we have assumed that: (i) the Company will comply with all applicable notice requirements regarding uncertificated shares provided in the DGCL; (ii) the Warrants have been duly executed and delivered by the Company and, under the internal laws of the State of New York, constitute valid and legally binding obligations of the Company; and (iii) upon the issue of any of the Warrant Shares, the total number of shares of Common Stock then issued and outstanding will not exceed the total number of shares of Common Stock that the Company is then authorized to issue (a) under its Restated Certificate of Incorporation and (b) by the board of directors of the Company in connection with the offering contemplated by the Registration Statement.

This opinion is for your benefit in connection with the Registration Statement and may be relied upon by you and by persons entitled to rely upon it pursuant to the applicable provisions of the Act. We consent to your filing this opinion as an exhibit to the Registration Statement and to the reference to our firm in the prospectus under the heading "Legal Matters." In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission thereunder.

Sincerely,

/s/ LATHAM & WATKINS LLP

Consent of Independent Registered Public Accounting Firm

Lyra Therapeutics, Inc.  
Watertown, Massachusetts

We hereby consent to the incorporation by reference in the Prospectus constituting a part of this Registration Statement of our report dated March 29, 2023 relating to the consolidated financial statements of Lyra Therapeutics, Inc. appearing in the Company's Annual Report on Form 10-K for the year ended December 31, 2022.

We also consent to the reference to us under the caption "Experts" in the Prospectus.

/s/ BDO USA, LLP

Boston, Massachusetts  
June 28, 2023

**Calculation of Filing Fee Table**

**Registration Statement on Form S-3**  
(Form Type)

**LYRA THERAPEUTICS, INC.**  
(Exact Name of Registrant as Specified in its Charter)

**Table 1: Newly Registered and Carry Forward Securities**

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit(2)	Maximum Aggregate Offering Price(2)	Fee Rate	Amount of Registration Fee
Fees to Be Paid	Equity	Common Stock, par value \$0.001 per share	457(c)	21,967,353 <sup>(1)</sup>	\$4.10	\$90,066,147.30	0.00011020	\$9,926
		<b>Total Offering Amounts</b>				\$90,066,147.30		\$9,926
		<b>Total Fees Previously Paid</b>						—
		<b>Total Fee Offsets</b>						—
		<b>Net Fee Due</b>						\$9,926

- (1) Consists of 12,236,714 shares of our common stock issued to the selling securityholders, 2,408,188 shares of our common stock issuable to certain of the selling securityholders upon exercise of pre-funded warrants to purchase our common stock and 7,322,451 shares of our common stock issuable to the selling securityholders upon exercise of warrants to purchase our common stock. Pursuant to Rule 416 under the Securities Act of 1933, as amended, the shares of common stock being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the shares of common stock being registered hereunder as a result of stock splits, stock dividends or similar transactions.
- (2) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(c) of the Securities Act, on the basis of the average of the high and low prices for a share of the registrant's common stock as reported on the Nasdaq Capital Market on June 27, 2023, which date is a date within five business days prior to the filing of this registration statement.