PROSPECTUS

88,738,387 Shares of Common Stock



This prospectus relates to (i) the resale of 4,286,500 shares of common stock, par value \$0.0001 per share (the "Common Stock") issued in connection with the Domestication by certain of the selling securityholders named in this prospectus (each a "selling securityholder" and, collectively, the "selling securityholders"), (ii) the resale of 69,655,827 shares of Common Stock issued in connection with the Business Combination by certain of the selling securityholders, (iii) the resale of 13,093,331 shares of Common Stock issued in a private placement (the "PIPE Financing") by certain of the selling securityholders, and (iv) the resale of 1,702,729 shares of Common Stock reserved for issuance upon the exercise of certain outstanding options to purchase Common Stock. This prospectus also covers any additional securities that may become issuable by reason of stock splits, stock dividends or other similar transactions.

We are registering the resale of these securities to satisfy certain registration rights we have granted. We will not receive any of the proceeds from the sale of the securities by the selling securityholders. We will pay the expenses associated with registering the sales by the selling securityholders, as described in more detail in the section titled "Use of Proceeds" appearing elsewhere in this prospectus.

The selling securityholders may sell the securities described in this prospectus in a number of different ways and at varying prices. We provide more information about how the selling securityholders may sell their securities in the section titled "*Plan of Distribution*" appearing elsewhere in this prospectus.

The selling securityholders may sell any, all or none of the securities and we do not know when or in what amount the selling securityholders may sell their securities hereunder following the effective date of this registration statement.

Our Common Stock is listed on The Nasdaq Global Select Market ("Nasdaq") under the symbol "NAUT." On August 8, 2022, the last quoted sale price for our Common Stock as reported on Nasdaq was \$2.91.

We are an "emerging growth company," as defined under the federal securities laws, and, as such, may elect to comply with certain reduced public company reporting requirements for future filings.

Investing in our securities involves a high degree of risk. Before buying any securities, you should carefully read the discussion of the risks of investing in our securities in the section titled "<u>Risk Factors</u>" beginning on page 7 of this prospectus and under similar headings in any amendments or supplements to this prospectus and the documents incorporated herein by reference.

You should rely only on the information contained in this prospectus or any prospectus supplement or amendment hereto. We have not authorized anyone to provide you with different information.

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

The date of this prospectus is August 8, 2022.

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You should rely only on the information contained in this prospectus, information incorporated by reference into this prospectus or any supplement to this prospectus prepared by us or on our behalf. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making 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 is accurate only as of the date on the front cover of this 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 such dates.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the "SEC") using the "shelf" registration process. Under this shelf registration process, the selling securityholders hereunder may, from time to time, sell the securities offered by them described in this prospectus. We will not receive any proceeds from the sale by such selling securityholders of the securities offered by them described in this prospectus.

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 or incorporated by reference into this prospectus or any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. Neither we nor the selling securityholders take responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. Neither we nor the selling securityholders will make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted.

You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover 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.

We may also provide a prospectus supplement or post-effective amendment to the registration statement to add information to, or update or change information contained in, this prospectus. You should read both this prospectus and any applicable prospectus supplement or post-effective amendment to the registration statement together with the additional information to which we refer you in the section of this prospectus titled "Where You Can Find Additional Information" and "Incorporation by Reference."

MARKET AND INDUSTRY DATA

We obtained the industry and market data used throughout this prospectus and the documents incorporated by reference herein from our own internal estimates and research, as well as from independent market research, industry and general publications and surveys, governmental agencies, publicly available information and research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In some cases, we do not expressly refer to the sources from which this data is derived. In addition, while we believe the industry and market data included in this prospectus is reliable and based on reasonable assumptions, such data involve material risks and other uncertainties and are subject to change based on various factors, including those discussed in the section entitled "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties or by us.

TRADEMARKS

This prospectus and the documents incorporated by reference herein contain references to trademarks and service marks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this

prospectus and the documents incorporated by reference herein may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that the applicable licensor will not assert, to the fullest extent under applicable law, its rights to these trademarks and trade names. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of it by, any other companies.

THE COMPANY

This summary highlights information contained in greater detail elsewhere in this prospectus. This summary is not complete and does not contain all of the information you should consider in making your investment decision. You should read the entire prospectus carefully before making an investment in our Common Stock, including the section entitled "Risk Factors" and the documents we have incorporated by reference in this prospectus, along with our consolidated financial statements and related notes incorporated by reference in this prospectus.

OVERVIEW

We are a development stage life sciences company creating a platform technology for quantifying and unlocking the complexity of the proteome. Our mission is to transform the field of proteomics by democratizing access to the proteome and enabling fundamental advancements across human health and medicine. We were founded on the belief that incremental advancements of existing technologies are inadequate, and that a bold scientific leap would be required to radically reinvent proteomics and revolutionize precision medicine. Our vision is to integrate our breakthrough innovations in computer science, engineering, and biochemistry to develop and commercialize a proteome analysis platform of extreme sensitivity and scale. To accomplish this, we have built a prototype of our proteome analysis system, an instrument to perform massively parallel single protein molecule measurements which will be further developed to deliver the speed, simplicity, accuracy, and versatility that we believe is necessary to establish a new gold standard in the field.

The human proteome, the make-up of all the proteins in a human, is among the most dynamic and valuable sources of biological insight in modern-day science. Unlike the genome, which is largely unchanging throughout an individual's lifetime, the proteome is an ever-changing source of biological information. Our proteins directly control and determine the functions of our cells, yet we lack the ability to measure all of them with the ease, breadth and sensitivity that is used to measure DNA today. We believe that deep characterization of the proteome will have the potential to unveil an entirely new layer of complexity and valuable biological information that may have significant implications across life sciences, healthcare and drug development.

Approximately 95% of FDA-approved drug targets are proteins, and yet today we still lack the ability to routinely read and quantify all of the proteins in our cells, or to fully map the downstream changes and modifications to those proteins which may define their biological function.

By leveraging our novel design coupled with advanced machine learning software, we believe our Nautilus platform, which includes our end-to-end solution comprised of the proteomic analysis system, consumables, and software, has the potential to rapidly and reproducibly identify approximately 95% of proteins in a sample from virtually any organism, and could have the ability to detect and map the diverse landscape of modifications on those proteins. We believe that unlocking proteomics has the potential to create a long-term transformation of basic science, translational research, and healthcare.

CORPORATE INFORMATION

On June 9, 2021 (the "Closing Date"), Nautilus Biotechnology, Inc., a Delaware corporation (f/k/a ARYA Sciences Acquisition Corp III, a Cayman Islands exempted company and our predecessor company ("ARYA")) (the "Company"), consummated the previously announced merger pursuant to that certain Business Combination Agreement, dated as of February 7, 2021 (the "Business Combination Agreement"), by and among ARYA, Mako Merger Sub, Inc., a Delaware corporation and wholly-owned subsidiary of ARYA ("Mako Merger Sub"), and Nautilus Subsidiary, Inc., a Delaware corporation (f/k/a Nautilus Biotechnology, Inc.) ("Legacy Nautilus").

Pursuant to terms of the Business Combination Agreement, on the Closing Date, (i) ARYA changed its jurisdiction of incorporation by deregistering as a Cayman Islands exempted company and continuing and domesticating as a corporation incorporated under the laws of the State of Delaware (the "Domestication"), upon which ARYA changed its name to "Nautilus Biotechnology, Inc." (together with its consolidated subsidiaries, "New Nautilus" or "Nautilus") and (ii) Mako Merger Sub merged with and into Legacy Nautilus (the "Merger" and collectively, with the other transactions described in the Business Combination Agreement, the "Business Combination"), with Legacy Nautilus as the surviving company in the Merger and, after giving effect to such Merger, Legacy Nautilus becoming a wholly-owned subsidiary of New Nautilus. As of the open of trading on June 10, 2021, the Common Stock of the Company, formerly those of ARYA, began trading on The Nasdaq Global Select Market ("Nasdaq") under the symbol "NAUT."

Our principal executive offices are located at 2701 Eastlake Avenue East, Seattle, WA 98102, and our telephone number is (206) 333-2001.

Our website address is http://www.nautilus.bio. The information on, or that can be accessed through, our website is not part of this prospectus, and you should not consider information contained on our website in deciding whether to purchase shares of our Common Stock. We have included our website address in this prospectus solely as an inactive textual reference.

We use the Nautilus logo and other marks as trademarks in the United States and other countries. This prospectus contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without a trademark symbol, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). We will remain an emerging growth company until the earliest to occur of: the last day of the fiscal year in which we have more than \$1.07 billion in annual revenues; the date we qualify as a "large accelerated filer," with at least \$700 million of equity securities held by non-affiliates; the issuance, in any three-year period, by us of more than \$1.0 billion in non-convertible debt securities; and the last day of the fiscal year ending after the fifth anniversary of ARYA's initial public offering.

Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a) (2)(B) of the Securities Act of 1933, as amended (the "Securities Act"), for complying with new or revised accounting standards. In other words, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected not to opt out of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we, as an emerging growth company, can adopt the new or revised standard at the time private companies adopt the new or revised standard. This may make comparison of our financial statements with certain other public companies difficult or impossible because of the potential differences in accounting standards used.

Additionally, we are a "smaller reporting company" as defined in Item 10(f)(1) of Regulation S-K. Smaller reporting companies may take advantage of certain reduced disclosure obligations, including, among other things, providing only two years of audited financial statements. We may continue to remain a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than \$250 million as of June 30 of the prior fiscal year or (ii) our annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million as of June 30 of the prior fiscal year.

Unless expressly indicated or the context requires otherwise, the terms "Nautilus," "New Nautilus," the "Company," the "Registrant," "we," "us" and "our" in this prospectus refer to Nautilus Biotechnology, Inc., the parent entity formerly named ARYA Sciences Acquisition Corp III, after giving effect to the Domestication and the Business Combination, and as renamed Nautilus Biotechnology, Inc., and where appropriate, our wholly-owned subsidiaries (including Legacy Nautilus).

The Offering

An aggregate of 88,738,387 shares of Common Stock consisting of (a) 13,093,331 shares of Common Stock issued in the PIPE Financing, (b) 4,286,500 shares of Common Stock issued in connection with the Domestication, (c) 69,655.827 shares of Common Stock issued in connection with the Business Combination and (d) 1,702,729 shares of Common Stock issuable upon the exercise of certain outstanding options to purchase Common Stock.

All aforementioned shares of Common Stock were initially registered in our Initial Registration Statement, and no new shares are being registered hereunder.

Shares of Common Stock Offered Hereunder

Use of Proceeds

We will not receive any proceeds from the sale of our shares of common stock offered by the selling

securityholders under this prospectus (the "Securities"). See the section titled "Use of Proceeds"

appearing elsewhere in this prospectus for more information.

Common Stock Outstanding 124,562,745 shares of Common Stock as of June 30, 2022.

Risk Factors See the section titled "Risk Factors" and other information included in this prospectus and the documents incorporated by reference for a discussion of factors that you should consider carefully before deciding to

invest in our Common Stock.

Nasdaq symbol "NAUT" for our Common Stock.

The number of shares of Common Stock outstanding is based on 124,562,745 shares of Common Stock as of June 30, 2022 and excludes the following, in each case as of June 30, 2022:

- 6,148,270 shares of our Common Stock issuable upon the exercise of outstanding options under the Nautilus Subsidiary, Inc. 2017 Equity Incentive Plan (the "2017 Plan") as of such date, which were assumed by the Company in connection with the Business Combination, with a weighted average exercise price of \$3.50 per share;
- 5,502,254 shares of our Common Stock issuable upon the exercise of outstanding options under our 2021 Equity Incentive Plan (the "2021 Plan") as of such date, with a weighted average exercise price of \$5.02 per share;
- 17,384,590 shares of our Common Stock reserved for future issuance under our 2021 Plan; and
- 2.439.577 shares of our Common Stock reserved for future issuance under our 2021 Employee Stock Purchase Plan (the "ESPP").

RISK FACTORS SUMMARY

Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information contained in this prospectus, including our consolidated financial statements and related notes, before deciding to invest in our securities. If any of the following risks actually occur, our business, operating results, financial condition and prospectus could be materially and adversely affected. In that event, the market price of our common stock could decline, and you could lose part or all of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that adversely affect our business or results of operations.

Our business is subject to numerous risks and uncertainties that you should consider before investing in our company, as more fully described below. The principal factors and uncertainties that make investing in our company risky include, among others:

Risks Related to Our Business

- We are a development stage company that has incurred net losses in every period to date, has not yet commercialized any products, and expects to continue to incur significant losses as we develop our business.
- Our business is entirely dependent on the successful development and commercialization of our proteomics platform (the "Nautilus platform"), which remains in the development stage and could be subject to delays, technical challenges and market acceptance challenges.
- We may not compete successfully with our initial or future products in the highly competitive life sciences technology market.
- · We are dependent upon third parties for certain aspects of the development and commercialization of the Nautilus platform.
- Our business depends significantly on research and development spending by pharmaceutical companies as well as by academic institutions and other research institutions and any reduction in spending could limit demand for our products.
- We may not be able to launch our Nautilus platform successfully and even if it is successful, we may experience material delays in our
 commercialization program relative to current expectations.
- Our operating results may fluctuate significantly in the future, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.
- We may need to raise additional capital to fund our development and commercialization plans.

Risks Related to Our Intellectual Property

- We may be unable to obtain and maintain sufficient intellectual property protection for our products and technology, or if the scope of our
 intellectual property protection obtained is not sufficiently broad, competitors could develop and commercialize products similar or identical to
 ours.
- We may not be able to protect our intellectual property and proprietary rights throughout the world.

Risks Related to Litigation

- We may become involved in litigation to enforce or defend our intellectual property rights, or to defend ourselves from claims that we infringe the
 intellectual property rights of others.
- We may face liability and/or negative publicity for any unknown defects or errors in our products.

Risks Related to Regulatory and Legal Compliance Matters

- Our products may, in the future, be subject to regulation by the FDA or other regulatory authorities.
- We are currently subject to, and may in the future become subject to additional, U.S. federal and state laws and regulations, as well as the laws and regulations of other countries, relating to how we collect, store and process personal information.
- Future expansion of our development and commercialization activities outside of the United States, may subject us to an increased risk of inadvertently conducting activities in a manner that violates the U.S. Foreign Corrupt Practices Act and similar laws.
- Environmental and health safety laws, including any failure to comply with such laws, may result in liabilities, expenses and restrictions on our operations.
- Our employees, independent contractors, consultants, commercial partners, distributors and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

Risks Related to our Operations

- · We may experience a significant disruption in our information technology systems or breaches of data security.
- We are highly dependent on our key personnel, and if we are unable to recruit and retain key executives and scientists, we may not be able to achieve our goals.
- Our operations and financial results could be adversely impacted by global and national events, such as the COVID-19 pandemic, conflicts in Eastern Europe, and general economic downturns.
- · Global supply chain interruptions may negatively impact the development and commercialization of our products.

Risks Related to Our Common Stock

The price of and market for our Common Stock may be volatile, which could result in substantial losses for investors and/or an inability to readily trade in our Common Stock.

General Risk Factors

- · We will incur significant increased costs and management resources as a result of operating as a public company.
- Reports published by analysts, including projections in those reports that differ from our actual results, could adversely affect the price and trading volume of our common shares.
- Our ability to timely and accurately report our financial results and projections as a public company may be impacted by the effectiveness of our internal controls, and our estimates and judgments relating to critical accounting policies.

RISK FACTORS

An investment in our Common Stock involves a high degree of risk. In addition to the risk and uncertainties described under the section titled "Cautionary Note Regarding Forward-Looking Statements," you should consider carefully the risks and uncertainties incorporated by reference to our most recent Annual Report on Form 10-K, any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained in 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 before acquiring any of such securities. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that adversely affect our business or results of operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements in this prospectus and the documents incorporated by reference herein may constitute "forward-looking statements" for purposes of the federal securities laws. Our forward-looking statements include, but are not limited to, statements regarding our or our management team's expectations, hopes, beliefs, intentions or strategies regarding the future, including those relating to the Business Combination and its expected benefits; the success, cost, timing and progress of development of our proteomics platform (the "Nautilus platform"); the potential attributes and benefits of the Nautilus platform; our ability to successfully implement our three phase commercial launch plan; and our ability to obtain funding for our operations. Forward-looking statements include statements relating to our management team's expectations, hopes, beliefs, intentions or strategies regarding the future, including those relating to the Business Combination and related transactions. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. The words "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intends," "may," "might," "plan," "possible," "potential," "predict," "project," "should," "will," "would" and similar expressions may identify forward-looking statements, but the absence of these words does not mean that a statement is not forward-looking.

These forward-looking statements are based on current expectations and beliefs concerning future developments and their potential effects. There can be no assurance that future developments affecting us will be those that we have anticipated. These forward-looking statements involve a number of risks, uncertainties (some of which are beyond our control) or other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements. As a result of a number of known and unknown risks and uncertainties, our actual results or performance may be materially different from those expressed or implied by these forward-looking statements. Some factors that could cause actual results to differ include, but are not limited to, the following:

- our dependence on the success of our Nautilus platform, which remains in the development stage and subject to scientific and technical validation;
- our expectations regarding the timing and progress of the development of the Nautilus platform;
- our estimates of our addressable market, market growth, future revenue, key performance indicators, expenses, capital requirements and needs for additional financing;
- our expectations regarding the rate and degree of market acceptance of the Nautilus platform;
- · the impact of the Nautilus platform on the field of proteomics and the size and growth of the addressable proteomics market;
- · our ability to manage and grow our business and commercialize our Nautilus platform;
- · our ability to successfully implement our three phase commercial launch plan;
- the implementation of our business model and strategic plans for the Nautilus platform;

- our ability to establish and maintain intellectual property protection for our products or avoid or defend claims of infringement;
- our ability to recognize the anticipated benefits of the Business Combination, which may be affected by, among other things, competition, our
 ability to grow and manage future growth effectively, and our ability to retain our key employees;
- our expectations regarding the use of proceeds from the Business Combination;
- the performance of third-party manufacturers and suppliers;
- changes in applicable laws or regulations;
- our ability to raise financing in the future;
- our success in retaining or recruiting, or changes required in, our officers, key employees or directors or other key personnel;
- the volatility of the trading price of our common stock;
- our ability to develop and commercialize new products;
- our expectations about market trends;
- the impact of local, regional, national and international economic conditions and events;
- the effect of COVID-19 on the foregoing; and
- the risks and uncertainties described under the heading "Risk Factors" and in our current and periodic reports, and other filings, filed from time to time with the SEC that are incorporated by reference into this prospectus.

Should one or more of these risks or uncertainties materialize, or should any of our assumptions prove incorrect, actual results may vary in material respects from those projected in these forward-looking statements. Some of these risks and uncertainties may in the future be amplified by the COVID-19 outbreak and there may be additional risks that we consider immaterial or which are unknown. It is not possible to predict or identify all such risks.

The forward-looking statements made in this prospectus relate only to events as of the date on which the statements are made. We undertake no obligation to update any forward-looking statements made in this prospectus to reflect events or circumstances after the date of this prospectus or to reflect new information or the occurrence of unanticipated events, except as required by law. We may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or

incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

USE OF PROCEEDS

All of the Securities offered by the selling securityholders pursuant to this prospectus will be sold by the selling securityholders for their respective accounts. We will not receive any of the proceeds from the sale of the Securities hereunder.

With respect to the registration of shares of our Common Stock offered by the selling securityholders pursuant to this prospectus, the selling securityholders will pay any underwriting discounts and commissions and expenses incurred by them for brokerage, accounting, tax or legal services or any other expenses incurred by them in disposing of the Securities. We will bear all other costs, fees and expenses incurred in effecting the registration of the Securities covered by this prospectus, including, without limitation, all registration and filing fees, Nasdaq listing fees, and fees of our counsel and our independent registered public accountants.

SELLING SECURITYHOLDERS

This prospectus relates to the resale by the selling securityholders from time to time of up to an aggregate of 88,738,387 shares of Common Stock (consisting of up to an aggregate of (a) 13,093,331 shares of our Common Stock that were issued to the PIPE Investors in the PIPE Financing, (b) 4,286,500 shares of Common Stock issued in connection with the Domestication, (c) 69,655,827 shares of Common Stock issued in connection with the Business Combination and (d) 1,702,729 shares of Common Stock issuable upon the exercise of certain outstanding options to purchase Common Stock). The selling securityholders may from time to time offer and sell any or all of the shares of Common Stock set forth below pursuant to this prospectus and any accompanying prospectus supplement. When we refer to the "selling securityholders" in this prospectus, we mean the persons listed in the table below and their permitted transferees who later come to hold any of the selling securityholders' interest in the Common Stock in accordance with the terms of the applicable agreements governing their respective registration rights, other than through a public sale.

The following table sets forth, based on written representations from the selling securityholders as of July 29, 2022 and subsequent filings with the SEC, as applicable, the names of the selling securityholders, the aggregate number of shares of Common Stock beneficially owned by the selling securityholders, the aggregate number of shares of Common Stock that the selling securityholders may offer pursuant to this prospectus and the number of shares of Common Stock that would be beneficially owned by the selling securityholders after the sale of the shares of Common Stock offered hereby assuming that the selling securityholders sell all of the shares of Common Stock covered by this prospectus. The percentage of beneficial ownership after the offered shares of Common Stock are sold is calculated based on 124,663,186 shares of Common Stock outstanding as of July 29, 2022.

We have determined beneficial ownership in accordance with the rules of the SEC and the information is not necessarily indicative of beneficial ownership for any other purpose. Unless otherwise indicated below, to our knowledge, the persons and entities named in the tables have sole voting and sole investment power with respect to the shares of Common Stock set forth below, subject to community property laws where applicable.

We cannot advise you as to whether the selling securityholders will in fact sell any or all of such Common Stock. In addition, the selling securityholders may sell, transfer or otherwise dispose of, at any time and from time to time, the Common Stock in transactions exempt from the registration requirements of the Securities Act after the date of this prospectus. Information about the selling securityholders, including those listed below, may change over time. Since the effectiveness of the initial prospectus, certain securityholders may have sold or otherwise transferred their securities registered thereunder. For purposes of this table, we have assumed that the selling securityholders will have sold all of the shares of Common Stock covered by this prospectus upon the completion of the offering.

Selling securityholder information for each additional selling securityholder, if any, will be set forth by a prospectus supplement to the extent required prior to the time of any offer or sale of such selling securityholder's shares pursuant to this prospectus. Any prospectus supplement may add, update, substitute, or change the information contained in this prospectus, including the identity of each selling securityholder and the number of shares registered on its behalf. A selling securityholder may sell or otherwise transfer all, some or none of such shares in this offering. See "*Plan of Distribution*."

Name of Selling Securityholder AH Bio Fund II, L.P., for itself and as nominee for AH Bio	Common Stock Beneficially Owned Prior to Offering	Number of Shares of Common Stock Being Offered	Common Stock Beneficially Owned After the Offered Shares of Common Stock are Sold	
			Number	Percent
Fund II-B, L.P. ⁽¹⁾	16,298,006	16,298,006	_	_
Alexandria Venture Investments, LLC ⁽²⁾	200,000	200,000	_	_
Ally Bridge MedAlpha Master Fund L.P. ⁽³⁾ Andreessen Horowitz LSV Fund II, L.P., for itself and as	1,080,566	1,080,566	_	-
nominee for Andreessen Horowitz LSV Fund II-B, L.P. and				
Andreessen Horowitz LSV Fund II-Q, L.P.(4)	1,355,911	1,355,911	_	_
ARYA Sciences Holdings III ⁽⁵⁾	4,146,500	4,146,500	_	_
AVMI Investments, Inc. (6)	200,000	200,000		_
Bain Capital Life Sciences Fund II, L.P. ⁽⁷⁾	1,782,858	891,429	891,429	*
BCIP Life Sciences Associates, LP ⁽⁷⁾	217,142	108,571	108,571	*
Blackwell Partners LLC – Series A ⁽⁸⁾	156,793	81,278	75,515	k
Bradley L. Campbell ⁽²⁹⁾	30,000	30,000	_	_
Decheng Capital Global Healthcare Fund (Master), LP ⁽⁹⁾	300,000	300,000	_	_
Farzad Nazem ⁽¹⁰⁾	2,010,893	1,924,426	86,467	k
Funds Managed by RTW Investments, LP ⁽¹¹⁾	1,100,000	600,000	500,000	k
Hand Capital LLC ⁽¹²⁾	1,888,146	1,888,146	_	
Madrona Venture Fund VI-A, LP ⁽¹³⁾	222,376	222,376	_	_
Madrona Venture Fund VI, LP ⁽¹³⁾	5,798,394	5,798,394	_	_
Matthew and Elizabeth Posard Trust ⁽¹⁴⁾	100,000	100,000	_	_
Matthew McIlwain ⁽¹⁵⁾	6,602,592	6,379,155	223,437	a)
Matthew Posard ⁽¹⁶⁾	504,943	368,476	136,467	k
Melissa Epperly ⁽¹⁷⁾	159,028	72,561	86,467	*
Nantahala Capital Partners Limited Partnership ⁽⁸⁾	54,727	29,502	25,225	k
Nantahala Capital Partners SI, LP ⁽⁸⁾	309,321	142,326	166,995	×
Nantahala Capital Partners II Limited Partnership ⁽⁸⁾	97,621	79,459	18,162	×
NCP RFM LP ⁽⁸⁾	80,200	80,200	_	_
Parag Mallick ⁽¹⁸⁾	21,423,911	21,143,911	280,000	*
Perceptive Life Sciences Master Fund, Ltd ⁽¹⁹⁾	9,111,151	8,414,113	697,038	*
PFV I, LLC ⁽²⁰⁾	5,280,476	5,280,476	_	_
Saqib Islam ⁽²⁹⁾	30,000	30,000	_	
Sujal Patel ⁽²¹⁾	18,247,832	17,497,732	750,100	k
Sujal Patel 2020 Children's Trust, u/a/d/ December 3, 2020 ⁽²²⁾	1,814,035	1,814,035	_	_
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10dd wider 7	30,000	30,000	_	_
VCVC V LLC ⁽²³⁾	3,586,492	3,586,492	_	_
Vijay Pande ⁽²⁴⁾	122,747	36,280	86,467	*
VC Capital Holdings Columbia LLC ⁽²³⁾	3,586,493	3,586,493	_	_

WS Investment Company, LLC (21A) ⁽²⁵⁾	35,000	35,000	_	_
The Dream Finder Foundation ⁽²⁶⁾	200,000	200,000	_	_
Jesus A Zavaleta III C/F Janhavi Amrita Singhal UTMA/TX until Age 21 ⁽²⁷⁾	5,000	5,000	_	_
Jesus A Zavaleta III C/F Janhavi Amrita Singhal UTMA/TX until Age $21^{(28)}$	5,000	5,000	_	_
Total Shares	92,870,727	88,738,387	4,132,340	3.3%

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- (1) AH Equity Partners Bio II, L.L.C ("AH EP Bio II") has sole voting and dispositive power with regard to the securities held by AH Bio Fund II, L.P. ("AH Bio Fund II") and AH Bio Fund III-B, L.P. ("AH Bio Fund II") and together with AH Bio Fund II, the "AH Bio Fund II Entities"). The managing members of AH EP Bio II are Marc Andreessen and Ben Horowitz. Marc Andreessen and Ben Horowitz share voting and dispositive power with respect to the shares held by the AH Bio Fund II Entities. Vijay Pande, a member of the board of directors of the Company, is a general partner of entities affiliated with Andreessen Horowitz.
- (2) The selling securityholder is a subsidiary of Alexandria Real Estate Equities, Inc., a publicly held corporation.
- (3) Mr. Fan Yu is the sole shareholder of ABG Management Ltd., which is the sole member of Ally Bridge Group (NY) LLC. Ally Bridge Group (NY) LLC manages Ally Bridge MedAlpha Master Fund L.P.'s ("Ally Bridge") investments. As such, each of the foregoing entities and Mr. Fan Yu may be deemed to share beneficial ownership of the shares held of record by Ally Bridge. Each of them disclaims any such beneficial ownership.
- (4) AH Equity Partners LSV II, L.L.C. ("AH EP LSV II") has sole voting and dispositive power with regard to the securities held by Andreessen Horowitz LSV Fund II, L.P. ("AH LSV Fund II"), Andreessen Horowitz LSV Fund II-B, L.P. ("AH LSV Fund II-B") and Andreessen Horowitz LSV Fund II-Q, L.P. ("AH LSV Fund II-Q," and together with AH LSV Fund II and AH LSV Fund II-B, the "AH LSV Fund II Entities"). The managing members of AH EP LSV II are Marc Andreessen and Ben Horowitz. Marc Andreessen and Ben Horowitz share voting and dispositive power with respect to the shares held by the AH LSV Fund II Entities. Vijay Pande, a member of the board of directors of the Company, is a general partner of entities affiliated with Andreessen Horowitz.
- (5) Adam Stone and Michael Altman are members of the board of directors of the selling securityholder and have voting and investment power over the shares held by the selling securityholder. Each of Mr. Altman and Mr. Stone disclaim beneficial ownership of such securities except to the extent of his pecuniary interest therein. Mr. Altman is a member of the board of directors of the Company.
- (6) Wanda M. Cook and Michael J. McCullough share voting and investment power over the shares held by the selling securityholder.
- (7) Bain Capital Life Sciences Investors, LLC ("BCLSI") is the manager of the general partner of Bain Capital Life Sciences Fund II, L.P. and governs the investment strategy and decision-making process with respect to investments held by BCIP Life Sciences Associates, LP. As a result, BCLSI may be deemed to share voting and dispositive power over the shares held by Bain Capital Life Sciences Fund II, L.P. and BCIP Life Sciences Associates, LP.
- (8) Nantahala Capital Management, LLC may be deemed to beneficially own 86,136 additional shares of Common Stock in the Company on behalf of managed funds and/or accounts not listed above as selling securityholders. Nantahala Capital Management, LLC is a registered investment adviser and has been delegated the legal power to vote and/or direct the disposition of such securities on behalf of the selling securityholder 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 the selling securityholder 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. 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 selling securityholder.
- (9) Xiangmin Cui has voting and investment power over the shares held by the selling securityholder. The selling securityholder is an investment company registered under the Investment Company Act of 1940, as amended.
- (10) Consists of (i) 122,747 shares of Common Stock issuable upon exercise of options held by Mr. Nazem and (ii) 1,888,146 shares of Common Stock held by HAND Capital, LLC. 57,896 options to purchase shares of common stock are exercisable within 60 days of July 29, 2022. The remaining options to purchase shares of Common Stock vest evenly on the 15th day of each month through June 15, 2023, subject to Mr. Nazem's continued status as a service provider through each vesting date. Mr. Nazem is the manager of HAND Capital, LLC and as such has voting and investment power over the shares held by HAND Capital, LLC. Mr. Nazem is a member of the board of directors of the Company.
- (11) Consists of (i) 298,128 shares of Common Stock held by RTW Innovation Master Fund, Ltd. ("RTW Innovation Fund"), (ii) 744,682 shares of Common Stock held by RTW Master Fund, Ltd. ("RTW Master Fund"), and (iii) 57,190 shares of Common Stock held by RTW Venture Fund Limited ("RTW Venture Fund," and together with RTW Master Fund and RTW Innovation Fund, the "RTW Funds"). RTW Investments, LP is the investment manager to the RTW Funds. Roderick Wong, M.D., is the managing partner and chief investment officer

- of RTW Investments, LP. and as such has sole voting and investment control over such shares. Dr. Wong disclaims beneficial ownership of the reported securities held by the RTW Funds, except to the extent of any pecuniary interest therein.
- (12) Farzad Nazem and Noosheen Hashemi have voting and investment power over the shares held by the selling securityholder. Mr. Nazem is a member of the board of directors of the Company.
- (13) Madrona Investment Partners VI, L.P. ("Madrona Partners VI") is the general partner of each of Madrona Venture Fund VI-A, LP ("Madrona Fund VI-A") and Madrona Venture Fund VI, LP ("Madrona Fund VI"), and Madrona VI General Partner, LLC ("Madrona VI LLC") is the general partner of Madrona Partners VI. Matthew McIlwain, together with Tom Alberg, Paul Goodrich, Scott Jacobson, Len Jordon, Tim Porter, and Soma Somasegar, are the managing members of Madrona VI LLC, and each may be deemed to share voting and investment power over the securities held by Madrona Fund VI and Madrona Fund VI-A. Each of such individuals disclaims beneficial ownership over such securities except to the extent of his pecuniary interest therein. Mr. McIlwain is a member of the board of directors of the Company.
- (14) Matthew Posard and Elizabeth Posard share voting and investment power over the shares held by the selling securityholder. Mr. Posard is a member of the board of directors of the Company.
- (15) Consists of (i) 459,075 shares of Common Stock held directly by Mr. McIlwain (322,105 of which are registered for resale pursuant to this prospectus), (ii) 122,747 shares of Common Stock issuable upon exercise of options held by Mr. McIlwain, (iii) 5,798,394 shares of Common Stock held by Madrona Fund VI, and (iv) 222,376 shares of Common Stock held by Madrona Fund VI-A. 57,896 options to purchase shares of common stock are exercisable within 60 days of July 29, 2022. The remaining options to purchase shares of Common Stock vest evenly on the 15th day of each month through June 15, 2023, subject to Mr. McIlwain's continued status as a service provider through each vesting date. Mr. McIlwain is a member of the board of directors of the Company.
- (16) Consists of (i) 354,943 shares of Common Stock issuable upon exercise of options held by Mr. Posard, (ii) 100,000 shares of Common Stock held by the Matthew and Elizabeth Posard Trust (the "Posard Trust") and (iii) 50,000 shares of Common Stock held by Mr. Posard (which are not registered for resale under this prospectus). 257,451 options to purchase shares of Common Stock are exercisable within 60 days of July 29, 2022. Of the remaining options to purchase shares of Common Stock (i) 32,641 shares of Common Stock that are issuable upon the exercise of options vest evenly on the 1st of each month through September 1, 2024, and (ii) 64,851 shares of Common Stock that are issuable upon the exercise of options vest evenly on the 15th of each month through June 15, 2023, subject to Mr. Posard's continued status as a service provider through each vesting date. Mr. Posard is a member of the board of directors of the Company
- (17) Consists of 159,028 shares of Common Stock issuable upon exercise of options held by Ms. Epperly. 59,912 options to purchase shares of common stock are exercisable within 60 days of July 29, 2022. Of the remaining options to purchase shares of Common Stock (i) 34,265 shares of Common Stock that are issuable upon the exercise of options vest evenly on the last day of each month through January 31, 2024 and (ii) 64,851 shares of Common Stock that are issuable upon the exercise of options vest evenly on the 15th of each month through June 15, 2023, subject to Ms. Epperly's continued status as a service provider through each vesting date.
- (18) Consists of (i) 20,479,892 shares of Common Stock directly owned by Dr. Mallick, (ii) 200,000 shares of Common Stock owned by The Dream Finder Foundation, as described in footnote 27 below, and (iii) 744,019 shares of Common Stock issuable upon exercise of options held by Dr. Mallick. 183,670 shares of Common Stock issuable upon exercise of options are exercisable within 60 days of July 29, 2022. Of the remaining options to purchase shares of Common Stock (i) 280,349 shares of Common Stock that are issuable upon the exercise of options vest evenly on the last day of each month through January 31, 2025 and (ii) 280,000 shares of Common Stock that are issuable upon the exercise of options vest as follows: 25% vest on February 25, 2023 and the remaining shares subject to the option vest evenly on the 25th of each month through February 25, 2026, subject to Dr. Mallick's continued status as a service provider through each vesting date. If, during the period beginning three months before a change in control through the one-year anniversary of a change in control, Dr. Mallick's employment with the Company is terminated either (x) by the Company without cause, and excluding by reason of Dr. Mallick's death or disability or (y) by Dr. Mallick for good reason, then 100% of any unvested shares shall immediately vest. Dr. Mallick is the Chief Scientist and a member of the board of directors of the Company.
- (19) Perceptive Advisors LLC ("Perceptive") is the investment advisor to Perceptive Life Sciences Master Fund, Ltd (the "Master Fund"). Joseph Edelman is the managing member of Perceptive. Perceptive and Mr. Edelman may be deemed to beneficially own the shares held by the Master Fund.
- (20) Mr. Patel is the manager of PFV I, LLC ("PFV") and as such has voting and investment control over the shares held by PFV. Mr. Patel is the President, Chief Executive Officer, Secretary and a member of the board of directors of the Company.
- (21) Consists of (i) 9,964,488 shares of Common Stock directly owned by Mr. Patel (9,614,388 of which are registered for resale under this prospectus), (ii) 5,280,476 shares of Common Stock held by PFV, (iii) 1,814,035 shares of Common Stock held by the Patel Trust, and (iv) 1,188,833 shares of Common Stock issuable upon exercise of options held by Mr. Patel. 312,145 of the shares of Common Stock issuable upon exercise of options are exercisable within 60 days of July 29, 2022. Of the remaining options to purchase shares of Common Stock (i) 476,688 shares of Common Stock that are issuable upon the exercise of options vest evenly on the last day of each month through January 31, 2025 and (ii) 400,000 shares of Common Stock that are issuable upon the exercise of options vest as follows: 25% vest on February 25, 2023 and the remaining shares subject to the option vest evenly on the 25th of each month through February 25, 2026, subject to Mr. Patel's continued status as a service provider through each vesting date. If, during the period beginning three months before a change in control through the one-year anniversary of a change in control, Mr. Patel's employment with the Company is terminated either (x) by the Company without cause, and excluding by reason of Mr. Patel's death or disability or (y) by Mr. Patel for good reason, then 100% of any

- unvested shares shall immediately vest. Mr. Patel is the President, Chief Executive Officer, Secretary and a member of the board of directors of the Company.
- (22) Mr. Patel is a trustee of the Sujal Patel 2020 Children's Trust, u/a/d December 3, 2020 (the "Patel Trust") and as such has voting and investment control over the shares held by the Patel Trust. Mr. Patel disclaims, for purposes of Section 16 of the Securities Exchange Act of 1934, beneficial ownership of the securities held by the Patel Trust, except to the extent of any pecuniary interest therein, and this report shall not be deemed an admission that Mr. Patel is the beneficial owner of such securities for purposes of Section 16 or for any other purposes. Mr. Patel is the President, Chief Executive Officer, Secretary and a member of the board of directors of the Company.
- (23) VCVC Management V LLC ("VCVC Management") serves as the Manager of VCVC V LLC ("VCVC") and Cercano Management LLC ("VCHC") and Cercano") serves as the investment manager of VCVC Management. VCHC Management LLC ("VCHC Management") serves as the Manager of VC Capital Holdings Columbia LLC ("VCHC") and Cercano serves as the investment manager of VCHC Management. Cercano has sole voting and dispositive power over the shares held by VCHC and VCVC. Each of VCVC Management, VCHC Management and Cercano disclaims, for purposes of Section 16 of the Securities Exchange Act of 1934, beneficial ownership of such securities, except to the extent of its indirect pecuniary interest therein, and this report shall not be deemed an admission that any of VCVC Management, VCHC Management or Cercano is the beneficial owner of such securities for purposes of Section 16 or for any other purposes. Stuart Nagae, an affiliate of Vulcan Capital, was a member of the board of directors of Legacy Nautilus until June 9, 2021.
- (24) Consists of 122,747 shares of Common Stock issuable upon exercise of options held by Mr. Pande. 57,896 options to purchase shares of Common Stock are exercisable within 60 days of July 29, 2022. Of the remaining options to purchase shares of Common Stock 64,851 shares of Common Stock that are issuable upon the exercise of options vest evenly on the 15th of each month through June 15, 2023, subject to Mr. Pande's continued status as a service provider through each vesting date. Mr. Pande has no voting or investment control over the shares held by entities affiliated with Andreessen Horowitz that are included in footnotes 1 and 5. Mr. Pande is a member of the board of directors of the Company.
- (25) WS Investment Management Company, a California corporation ("WSIMCo.") is the Manager of WS Investment Company, LLC ("WS") and has sole voting and dispositive power with respect to the shares held by WS. The managing members of WSIMCo. are Mario Rosati, Robert Latta, Donald Bradley and James Terranova. By virtue of these relationships, the managing members may be deemed to have voting and investment power over the shares held by WS.
- (26) Dr. Mallick has voting and investment control over the shares held by The Dream Finder Foundation. Dr. Mallick disclaims, for purposes of Section 16 of the Securities Exchange Act of 1934, beneficial ownership of the securities held by The Dream Finder Foundation, except to the extent of any pecuniary interest therein, and this report shall not be deemed an admission that Dr. Mallick is the beneficial owner of such securities for purposes of Section 16 or for any other purposes. Dr. Mallick is the Chief Scientist and a member of the board of directors of the Company.
- (27) Jesus A Zavaleta III, custodian, has the power to vote and dispose of the common shares being registered on behalf of Janhavi Amrita Singhal UTMA/TX.
- (28) Jesus A Zavaleta III, custodian, has the power to vote and dispose of the common shares being registered on behalf of Jaya Nirmala Singhal UTMA/TX.
- (29) The selling securityholder was a member of the board of directors of ARYA Sciences Acquisition Corp III prior to the consummation of the Business Combination.

DESCRIPTION OF SECURITIES

The following summary of certain provisions of our securities does not purport to be complete and is subject to our Certificate of Incorporation, our Bylaws and the provisions of applicable law.

Authorized Capitalization

General

Our authorized capital stock consists of 1,000,000,000 shares of our Common Stock, par value \$0.0001 per share, and 200,000,000 shares of our Preferred Stock, par value \$0.0001 per share. As of June 30, 2022, we have 124,562,745 shares of our Common Stock outstanding.

The following summary describes all material provisions of our capital stock.

Our Common Stock

Voting rights. Each share of our Common Stock is entitled to one vote per share on all matters (including the election of directors) submitted to a vote of stockholders, unless otherwise required by law or our certificate of incorporation. Our Certificate of Incorporation and our Bylaws do not provide for cumulative voting rights. Our directors are elected by plurality vote of the shares of our Common Stock present at an annual meeting and entitled to vote. With respect to matters other than the election of directors, at any meeting of the stockholders at which a quorum is present or represented, the affirmative vote of a majority of the voting power of the shares present in person or represented by proxy at such meeting and entitled to vote on the subject matter shall be the act of the stockholders, except as otherwise required by law. The holders of a majority of the stock issued and outstanding and entitled to vote, present in person or represented by proxy, shall constitute a quorum for the transaction of business at all meetings of the stockholders.

Dividend rights. Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of our Common Stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Rights upon liquidation. Upon a liquidation event, holders of our Common Stock are entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock.

Other rights. Holders of our Common Stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our Common Stock. The rights, preferences and privileges of the holders of our 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 in the future.

Preferred Stock

Our board of directors has the authority, without further action by the stockholders, to issue shares of preferred stock in one or more series and to fix the designations, powers, preferences and rights, and the qualifications, limitations or restrictions thereof. These designations, powers, preferences and rights could include dividend rights, conversion rights, voting rights, redemption rights, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of our Common Stock. The issuance of preferred stock could adversely affect the voting power of holders of our Common Stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. As of June 30, 2022, there are no shares of preferred stock outstanding, and we have no present plan to issue any shares of preferred stock.

Election of Directors and Vacancies; Board of Directors

Subject to the rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, the number of directors of our board of directors shall be fixed solely and exclusively by resolution duly adopted from time to time by our board of directors, but currently consists of nine (9) directors, which are divided into three (3) classes, designated Class I, II and III, with each class consisting of three (3) directors. Under our Bylaws, at all meetings of stockholders called for the election of directors, directors shall be elected by a plurality of the voting power of the shares present in person or represented by proxy at the meeting and entitled to vote on the election of directors. All directors are elected to hold office until the expiration of the term for which they are elected and until their successors have been duly elected and qualified or until their earlier resignation or removal.

Except as the DGCL may otherwise require and subject to the rights, if any, of the holders of any series of our Preferred Stock, newly created directorships resulting from any increase in the number of directors and any vacancies on our board of directors resulting from death, resignation, disqualification, removal or other cause shall be filled only by the affirmative vote of a majority of the remaining directors then in office, although less than a quorum, or by a sole remaining director. A director elected or appointed to fill a vacancy resulting from the death, resignation, disqualification or removal of a director or a newly created directorship will hold office until the next election of the class for which such director shall have been chosen until his or her successor shall have been duly elected and qualified, or until such director's death, resignation or removal.

Subject to the rights, if any, of any series our Preferred Stock, any director or our entire board of directors may be removed from office at any time, but only for cause and only by the affirmative vote of the holders of at least 66 2/3% of the voting power of our issued and outstanding capital stock entitled to vote in the election of directors.

In addition to the powers and authority expressly conferred upon them by statute or by our Certificate of Incorporation or our Bylaws, the directors are empowered to exercise all such powers and do all such acts and things as may be exercised or done by us, subject, nevertheless, to the provisions of the DGCL, our Certificate of Incorporation and our Bylaws adopted and in effect from time to time; provided, however, that no Bylaw adopted,

amended, altered or repealed after the date of our Bylaws will invalidate any prior act of our directors or officers which would have been valid if such Bylaw had not been adopted, amended, altered or repealed.

Quorum

The holders of a majority of the voting power of the capital stock issued and outstanding and entitled to vote thereat, present in person or represented by proxy, will constitute a quorum at all meetings of the stockholders for the transaction of business. Where a separate vote by a class or series or classes or series is required, a majority of the voting power of the outstanding shares of such class or series or classes or series, present in person or represented by proxy, shall constitute a quorum entitled to take action with respect to that vote on that matter, except as otherwise provided by law, our Certificate of Incorporation or our Bylaws, each as amended from time to time. If, however, such quorum will not be present or represented at any meeting of the stockholders, the holders of a majority of the voting power present in person or represented by proxy, will have power to adjourn the meeting from time to time, without notice other than announcement at the meeting, until a quorum will be present or represented. At such adjourned meeting at which a quorum will be present or represented, any business may be transacted which might have been transacted at the meeting as originally noticed. If the adjournment is for more than thirty (30) days, or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting will be given to each stockholder entitled to vote at such adjourned meeting as of the record date fixed for notice of such adjourned meeting.

Anti-takeover Effects of Our Certificate of Incorporation and Our Bylaws

Our Certificate of Incorporation and Bylaws contain provisions that may delay, defer or discourage another party from acquiring control of us. We expect that these provisions, which are summarized below, may discourage coercive takeover practices or 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, which we believe may result in an improvement of the terms of any such acquisition in favor of our stockholders. However, they also give our board of directors the power to discourage acquisitions that some stockholders may favor.

Authorized but Unissued Capital Stock

Delaware law does not require stockholder approval for any issuance of authorized shares. However, the listing requirements of Nasdaq, which would apply if and so long as our Common Stock remains listed on Nasdaq, require stockholder approval of certain issuances equal to or exceeding 20% of the then outstanding voting power or then outstanding number of shares of our Common Stock. Additional shares that may be issued in the future may be used for a variety of corporate purposes, including future public offerings, to raise additional capital or to facilitate acquisitions.

One of the effects of the existence of unissued and unreserved common stock may be to enable our board of directors to issue shares to persons friendly to our management, which issuance could render more difficult or discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise and thereby protect the continuity of our management and possibly deprive stockholders of opportunities to sell their shares of our Common Stock at prices higher than prevailing market prices.

Special Meeting, Action by Written Consent and Advance Notice Requirements for Stockholder Proposals

Unless otherwise required by law, and subject to the rights, if any, of the holders of any series of our Preferred Stock, special meetings of our stockholders may be called only by the Chairperson of our board of directors, our Chief Executive Officer, our President, or our board of directors acting pursuant to a resolution adopted by a majority of our board of directors. Unless otherwise required by law, written notice of a special meeting of stockholders, stating the time, place and purpose or purposes thereof, shall be given to each stockholder entitled to vote at such meeting, not less than ten (10) or more than sixty (60) days before the date fixed for the meeting. Business transacted at any special meeting of stockholders will be limited to the purposes stated in the notice.

Our Bylaws also provide that unless otherwise restricted by our Certificate of Incorporation or our Bylaws, any action required or permitted to be taken at any meeting of our board of directors or of any committee thereof may be taken without a meeting, if all members of our board of directors or of such committee, as the case may be, consent thereto in writing or by electronic transmission.

In addition, our Bylaws require advance notice procedures for stockholder proposals to be brought before an annual meeting of the stockholders, including the nomination of directors. Stockholders at an annual meeting may only consider the proposals specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered a timely written notice in proper form to our secretary, of the stockholder's intention to bring such business before the meeting.

These provisions could have the effect of delaying until the next stockholder meeting any stockholder actions, even if they are favored by the holders of a majority of our outstanding voting securities.

Amendment to Certificate of Incorporation and Bylaws

The DGCL provides generally that the affirmative vote of a majority of the outstanding stock entitled to vote on amendments to a corporation's certificate of incorporation or bylaws is required to approve such amendment, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage.

Our Certificate of Incorporation will provide that the following provisions therein may be amended, altered, repealed or rescinded only by the affirmative vote of the holders of at least 66 2/3% in voting power of all the then outstanding shares of our stock entitled to vote thereon and the affirmative vote of at least 66 2/3% of the then outstanding voting securities of the Company, voting together as a single class:

- the provisions authorizing our board of directors to issues shares of our Preferred Stock, with any rights, preferences or privileges as they may
 designate;
- the provisions dividing our board of directors into three classes, each of which stands for election once every three years;
- the provisions providing that a director may only be removed from our board of directors for cause only by the affirmative vote of the holders of at least 66 2/3% of the voting power of our issued and outstanding capital stock entitled to vote in the election of directors;

- the provisions providing that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- · the provisions prohibiting cumulative voting;
- the provisions requiring that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- the provisions regarding calling special meetings of stockholders;
- the provisions regarding notice of stockholder nominations for the election of directors and of business to be brought by stockholders before any meeting of our stockholders; and
- the provision regarding the approval requirements for such amendments;

Our Bylaws may be amended or repealed (A) by the affirmative vote of a majority of our entire board of directors then in office (subject to any bylaw requiring the affirmative vote of a larger percentage of the members of our board of directors) or (B) by our stockholders, provided that the affirmative vote of the holders of at least 66 2/3% of the total voting power of outstanding voting securities, voting together as a single class, shall be required for our stockholders to alter, amend or repeal, or adopt certain provisions of our Bylaws.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the DGCL. In general, Section 203 of the DGCL prevents a public company incorporated in Delaware from engaging in a "business combination" with any "interested stockholder" for three years following the time that the person became an interested stockholder, unless, among other exceptions, the interested stockholder attained such status with the approval of our board of directors or holders of 66 2/3% of the voting power of the outstanding capital stock held by stockholders unaffiliated with the interested stockholder approve the business combination. A business combination includes, among other things, a merger or consolidation involving the interested stockholder and the sale of more than 10% of the company's assets. In general, an interested stockholder is any stockholder that, together with its affiliates, beneficially owns 15% or more of the company's stock. A public company incorporated in Delaware is automatically subject to Section 203 unless it opts out in its original corporate charter or pursuant to a subsequent charter or bylaw amendment approved by stockholders.

Limitations on Liability and Indemnification of Officers and Directors

Our Certificate of Incorporation limits the liability of our directors to the fullest extent permitted by the DGCL, and our Bylaws provide that we will indemnify them to the fullest extent permitted by such law. We have entered into indemnification agreements with our directors and officers and we expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by our board of directors. Under the terms of such indemnification agreements, we will be required to indemnify each of its directors and officers, to the fullest extent permitted by the laws of the state of Delaware, if the basis of the indemnitee's involvement was by reason of the fact that the indemnitee is or was a director or officer of us or any of our subsidiaries or was serving at our request in an official capacity for another entity. Any claims for indemnification by our directors and officers

may reduce our available funds to satisfy successful third-party claims against it and may reduce the amount of money available to it.

Exclusive Jurisdiction of Certain Actions

Our Bylaws provide that, unless we consent in writing to the selection of an alternative forum (an "Alternative Forum Consent"), the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another state court in Delaware or the federal district court for the District of Delaware) will, to the fullest extent permitted by law, be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, stockholders or other employees to us or our stockholders, (iii) any action arising pursuant to any provision of the Delaware General Corporation Law or our Certificate of Incorporation or our Bylaws (each, as may be amended from time to time), or (iv) any action asserting a claim governed by the internal affairs doctrine of the State of Delaware, except for any claim as to which the court does not have jurisdiction over an indispensable party to that claim. The foregoing shall not apply to any claims under the Exchange Act or the Securities Act of 1933, as amended. In addition, unless we give an Alternative Forum Consent, the federal district courts of the United States shall be the sole and exclusive forum for resolving any action asserting a claim arising under the Securities Act of 1933.

Transfer Agent

The transfer agent for our Common Stock is Continental Stock Transfer & Trust Company.

Exchange Listing

Our Common Stock is listed on Nasdaq under the symbol "NAUT."

PLAN OF DISTRIBUTION

We are registering the Securities covered by this prospectus to permit the selling securityholders to conduct public secondary trading of these Securities from time to time after the date of this prospectus. We will not receive any of the proceeds of the sale of the Securities offered by this prospectus. The aggregate proceeds to the selling securityholders from the sale of the Securities will be the purchase price of the Securities less any discounts and commissions. We will not pay any brokers' or underwriters' discounts and commissions in connection with the registration and sale of the Securities covered by this prospectus. The selling securityholders reserve the right to accept and, together with their respective agents, to reject, any proposed purchases of Securities to be made directly or through agents.

The Securities offered by this prospectus may be sold from time to time to purchasers:

- directly by the selling securityholders;
- through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, commissions or agent's commissions from the selling securityholders or the purchasers of the Securities; or
- through a combination of any of these methods of sale.

Any underwriters, broker-dealers or agents who participate in the sale or distribution of the Securities may be deemed to be "underwriters" within the meaning of the Securities Act. As a result, any discounts, commissions or concessions received by any such broker-dealer or agents who are deemed to be underwriters will be deemed to be underwriting discounts and commissions under the Securities Act. Underwriters are subject to the prospectus delivery requirements of the Securities Act and may be subject to certain statutory liabilities under the Securities Act and the Exchange Act. We will make copies of this prospectus available to the selling securityholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. To our knowledge, there are currently no plans, arrangements or understandings between the selling securityholders and any underwriter, broker-dealer or agent regarding the sale of the Securities by the selling securityholders.

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. The selling securityholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. The Securities may be sold in one or more transactions at:

- fixed prices;
- prevailing market prices at the time of sale;
- prices related to such prevailing market prices;
- · varying prices determined at the time of sale; or
- negotiated prices.

These sales may be effected in one or more transactions:

- on any national securities exchange or quotation service on which the Securities may be listed or quoted at the time of sale, including Nasdaq;
- in the over-the-counter market;
- in transactions otherwise than on such exchanges or services or in the over-the-counter market;
- through trading plans entered into by the selling securityholder pursuant to Rule 10b5-1 under the Exchange Act that are in place at the time of an offering pursuant to this prospectus and any applicable prospectus supplement hereto that provide for periodic sales of their securities on the basis of parameters described in such trading plans;
- through one or more underwritten offerings on a firm commitment or best efforts basis;
- settlement of short sales entered into after the date of this prospectus;
- agreements with broker-dealers to sell a specified number of the securities at a stipulated price per share;
- in "at the market" offerings, as defined in Rule 415 under the Securities Act, at negotiated prices, at prices prevailing at the time of sale or at prices related to such prevailing market prices, including sales made directly on a national securities exchange or sales made through a market maker other than on an exchange or other similar offerings through sales agents
- in privately negotiated transactions;
- in options or other hedging transactions, whether through an options exchange or otherwise;
- in distributions to members, limited partners or stockholders of selling securityholders;
- any other method permitted by applicable law; or
- through any combination of the foregoing.

These transactions may include block transactions or crosses. Crosses are transactions in which the same broker acts as an agent on both sides of the trade.

In connection with distributions of the Securities or otherwise, the selling securityholders may enter into hedging transactions with broker-dealers or other financial institutions. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of the Securities in the course of hedging transactions, broker-dealers or other financial institutions may engage in short sales of the Securities in the course of hedging the positions they assume with selling securityholders. The selling securityholders may also sell the Securities short and redeliver the Securities to close out such short positions. The selling securityholders may also enter into option or other transactions with broker-dealers or other financial institutions which require the delivery to such broker-dealer or other financial institution of the Securities offered by this prospectus, which Securities such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to

reflect such transaction). The selling securityholders may also pledge the Securities to a broker-dealer or other financial institution, and, upon a default, such broker-dealer or other financial institution, may effect sales of the pledged Securities pursuant to this prospectus (as supplemented or amended to reflect such transaction).

A selling securityholder may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell the Securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by any selling securityholder or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from any selling securityholder in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement (or a post-effective amendment). In addition, any selling securityholder may otherwise loan or pledge the Securities to a financial institution or other third party that in turn may sell the Securities short using this prospectus. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

At the time a particular offering of the Securities is made, a prospectus supplement, if required, will be distributed, which will set forth the name of the selling securityholders, the aggregate amount of Securities being offered and the terms of the offering, including, to the extent required, (1) the name or names of any underwriters, broker-dealers or agents, (2) any discounts, commissions and other terms constituting compensation from the selling securityholders and (3) any discounts, commissions or concessions allowed or reallowed to be paid to broker-dealers. We may suspend the sale of Securities by the selling securityholders pursuant to this prospectus for certain periods of time for certain reasons, including if the prospectus is required to be supplemented or amended to include additional material information.

The selling securityholders will act independently of us in making decisions with respect to the timing, manner, and size of each resale or other transfer. There can be no assurance that the selling securityholders will sell any or all of the Securities under this prospectus. Further, we cannot assure you that the selling securityholders will not transfer, distribute, devise or gift the Securities by other means not described in this prospectus. In addition, any Securities covered by this prospectus that qualify for sale under Rule 144 of the Securities Act may be sold under Rule 144 rather than under this prospectus. The Securities may be sold in some states only through registered or licensed brokers or dealers. In addition, in some states the Securities may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification is available and complied with.

The selling securityholders and any other person participating in the sale of the Securities will be subject to the Exchange Act. The Exchange Act rules include, without limitation, Regulation M, which may limit the timing of purchases and sales of any of the Securities by the selling securityholders and any other person. In addition, Regulation M may restrict the ability of any person engaged in the distribution of the Securities to engage in market-making activities with respect to the particular securities being distributed. This may affect the marketability of the Securities and the ability of any person or entity to engage in market-making activities with respect to the Securities.

The selling securityholders may, from time to time, pledge or grant a security interest in some shares of the Securities owned by them and, if a selling securityholder defaults in the performance of its secured obligations, the pledgees or secured parties may offer and sell such shares of the Securities, from time to time, under this prospectus, or under an amendment or supplement to this prospectus amending the list of the selling securityholders to include the pledgee, transferee or other successors in interest as the selling securityholders under this prospectus. The selling securityholders also may transfer shares of the Securities 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.

A selling securityholder that is an entity may elect to make an in-kind distribution of the Securities to its members, partners or shareholders pursuant to the registration statement of which this prospectus is a part by delivering a prospectus. To the extent that such members, partners or shareholders are not affiliates of ours, such members, partners or stockholders would thereby receive freely tradable shares of the Securities pursuant to the distribution through a registration statement.

With respect to those Securities being registered pursuant to the Registration Rights Agreement, we have agreed to indemnify or provide contribution to the selling securityholders and all of their officers, directors and control persons, as applicable, and certain underwriters effecting sales of the Securities against certain liabilities, including certain liabilities under the Securities Act. The selling securityholders have agreed to indemnify us in certain circumstances against certain liabilities, including certain liabilities under the Securities Act. The selling securityholders may indemnify any broker or underwriter that participates in transactions involving the sale of the Securities against certain liabilities, including liabilities arising under the Securities Act.

For additional information regarding expenses of registration, see the section titled "Use of Proceeds" appearing elsewhere in this prospectus.

LEGAL MATTERS

The validity of the Securities offered hereby has been passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Certain members of, and investment partnerships comprised of members of, and persons associated with, Wilson Sonsini Goodrich & Rosati, Professional Corporation, directly or indirectly own less than 0.3% of the outstanding shares of our common stock.

EXPERTS

The financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2021 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND ADDITIONAL 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 website address is www.nautilus.bio. 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 applicable 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. 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, 2021, filed with the SEC on February 24, 2022 (our "Annual Report"), including the information specifically incorporated by reference into our Annual Report from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 28, 2022;
- our Quarterly Reports on Form 10-Q for the quarter ended <u>March 31, 2022</u>, filed with the SEC on <u>May 3, 2022</u> and for the quarter ended <u>June 30, 2022</u>, filed with the SEC on August 2, 2022;
- our Current Reports on Form 8-K filed with the SEC on <u>March 31, 2022</u> and <u>June 16, 2022</u> (excluding any information furnished but not filed in such reports under Item 2.02, Item 7.01, or Item 9.01); and
- the description of securities set forth in the section titled "Form 10 Information—Description of Company's Securities" in our Current Report on Form 8-K filed with the SEC on June 10, 2021, and any 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.

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:

Nautilus Biotechnology, Inc. 2701 Eastlake Avenue East Seattle, Washington 98102 (206) 333-2001

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.