PROSPECTUS SUPPLEMENT (to prospectus dated March 1, 2022)

95,645,056 Shares of Common Stock



This prospectus supplement updates and amends the prospectus dated March 1, 2022 (as supplemented to date, the "Prospectus"), which forms a part of our Registration Statement on Post-Effective Amendment No. 1 to the Form S-1 (Registration Statement No. 333-258100) filed with the Securities and Exchange Commission (the "SEC") on February 24, 2022 and declared effective by the SEC on March 1, 2022.

The Prospectus and this prospectus supplement relate 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 (as defined in the Prospectus) by certain of the selling securityholders named in the 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 (as defined in the Prospectus) by certain of the selling securityholders, (iii) the resale of 20,000,000 shares of common stock issued in the PIPE Financing (as defined in the Prospectus) by certain of the selling securityholders, and (iv) the issuance by us and 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 supplement should be read in conjunction with the Prospectus, which is to be delivered with this prospectus supplement. This prospectus supplement updates, amends and supplements the information included or incorporated by reference in the Prospectus. If there is any inconsistency between the information in the Prospectus and this prospectus supplement, you should rely on the information in this prospectus supplement.

This prospectus supplement is not complete without, and may not be delivered or utilized except in connection with, the Prospectus, including any amendments or supplements to it.

Current Report on Form 8-K

On March 31, 2022 and June 16, 2022, we filed Current Reports on Form 8-K with the SEC. The Current Reports on Form 8-K are attached hereto.

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 "Risk Factors" beginning on page 6 of the Prospectus.

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

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

The date of this prospectus supplement is June 16, 2022.

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the **Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): March 30, 2022

NAUTILUS BIOTECHNOLOGY, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation)

001-39434

(Commission File Number)

98-1541723

(I.R.S. Employer Identification No.)

2701 Eastlake Avenue East Seattle, Washington

(Address of principal executive offices)

98102

(Zip code)

(206) 333-2001

(Registrant's telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12) O
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)) O
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class Trading Symbol(s) Name of each exchange on which registered Common Stock, par value \$0.0001 per share **NAUT**

The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company x

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. O

Item 5.02. Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

On March 30, 2022, the board of directors (the "Board") of Nautilus Biotechnology, Inc. (the "Company"), upon recommendation of the Nominating and Governance Committee of the Board, appointed Karen Akinsanya to the Board, effective immediately. Dr. Akinsanya will serve as a Class III director, with a term expiring at the annual meeting of stockholders to be held in 2024.

Dr. Akinsanya has served as President of R&D, Therapeutics of Schrödinger, Inc. (NASDAQ: SDGR), a life sciences company, since February 2022, and its Executive Vice President and Chief Biomedical Scientist since January 2020 and previously served as its Senior Vice President and Chief Biomedical Scientist from April 2018 to December 2019. Prior to joining Schrödinger, Dr. Akinsanya spent 12 years at Merck & Co., Inc., or Merck, a pharmaceutical company, beginning in 2005, where she held a variety of positions across Merck Research Labs, including Associate Vice President, Early Scientific Assessment Lead, Business Development & Licensing from December 2013 to July 2017, Collaboration Lead and Executive Director, Cardiovascular Research from January 2010 to December 2013, and Associate Director of Clinical Pharmacology from October 2005 to December 2009. Prior to Merck, Dr. Akinsanya held a number of roles in drug discovery at Ferring Pharmaceuticals in the United Kingdom and the United States from 1997 to 2005. In 2007, Dr. Akinsanya founded Envision Science Group LLC, or Envision, a translational science consulting company, where she currently serves as President. Dr. Akinsanya provided consulting services on behalf of Envision to companies in the pharmaceutical industry between July 2017 and April 2018. Dr. Akinsanya is currently a member of the board of directors of the Imperial College Foundation and the Board of Trustees of The Rockefeller University. Dr. Akinsanya received a B.Sc. in Biochemistry from Queen Mary College, University of London, a Ph.D. in Endocrine Physiology from the Imperial College and completed postdoctoral studies at the Ludwig Institute for Cancer Research, University College, London. The Board believes that she is qualified to serve as a director of the Company because of her extensive industry background and experience in the life sciences industry.

Dr. Akinsanya will be compensated in accordance with the Company's outside director compensation policy (the "Policy"). Pursuant to the Policy, Dr. Akinsanya will be entitled to receive \$40,000 per year for service as a member of the Board, paid quarterly in arrears on a pro-rata basis.

In connection with her appointment to the Board as a non-employee director and pursuant to the Company's 2021 Equity Incentive Plan and the Policy, Dr. Akinsanya also automatically received an initial award of stock options to purchase 105,998 shares of Common Stock of the Company (the "Initial Award") with an aggregate grant date fair value (determined in accordance with U.S. GAAP) of \$370,000, which will vest as to one thirty-sixth (1/36th) of the shares subject to the Initial Award on a monthly basis following the Initial Award's grant date on the same day of the month as such grant date (or on the last day of the month, if there is no corresponding day in such month), subject to Dr. Akinsanya continuing to be a service provider of the Company.

Dr. Akinsanya has entered into the Company's standard form of indemnification agreement, a copy of which has been filed as Exhibit 10.24 to the Company's Form S-4/A (File No. 333-254796) filed with the Securities and Exchange Commission on April 26, 2021.

There is no arrangement or understanding between Dr. Akinsanya and any other persons pursuant to which Dr. Akinsanya was elected as a director. In addition, Dr. Akinsanya is not a party to any transaction, or series of transactions, required to be disclosed pursuant to Item 404(a) of Regulation S-K. There are no family relationships between Dr. Akinsanya and any of the Company's directors or executive officers.

Item 7.01. Regulation FD Disclosure.

On March 31, 2022, the Company issued a press release announcing Dr. Akinsanya's appointment as a director. A copy of the press release is furnished herewith as Exhibit 99.1.

The information set forth under this Item 7.01, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, regardless of any general incorporation language in such filing, unless expressly incorporated by specific reference in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

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NumberDescription99.1Press Release dated March 31, 2022.

104 Cover page Interactive Data File (embedded with the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: March 31, 2022

NAUTILUS BIOTECHNOLOGY, INC.

By: /s/ Sujal Patel

Name: Sujal Patel

Title: Chief Executive Officer

Nautilus Biotechnology Appoints Karen Akinsanya, Ph.D., to Board of Directors

Schrödinger President of R&D, Therapeutics brings extensive leadership in commercializing breakthrough biotechnologies to company developing platform for comprehensively quantifying the proteome to enable fundamental advancements in biomedicine

SEATTLE, March 31, 2022 – Nautilus Biotechnology, Inc. (NASDAQ: NAUT; or "Nautilus"), a company pioneering a single-molecule protein analysis platform for quantifying the proteome, today announced the appointment of Karen Akinsanya, Ph.D., to its Board of Directors.

Dr. Akinsanya brings more than 25 years of experience in drug discovery and development, commercialization, partnerships, and licensing from across academia and pharmaceutical research and development (R&D). In her current role as President of R&D, Therapeutics at Schrödinger, she leads the company's therapeutics group that leverages Schrödinger's leading physics-based platform for preclinical drug discovery and is responsible for translational research and early development, in addition to business development and collaborations.

Prior to joining Schrödinger, Dr. Akinsanya held positions of increasing responsibility during more than a decade at Merck Research Laboratories, as Associate Director of Clinical Pharmacology driving first-in-human studies through late-stage label studies; Executive Director and therapeutic area lead in Discovery Preclinical and Early Development; and AVP of Business Development and Licensing where she managed the search and evaluation of preproof of concept therapeutic assets and enabling technologies as well as execution and alliance management of a number of significant licensing and partnering deals. Dr. Akinsanya received her B.Sc. in biochemistry at Queen Mary University of London, and her Ph.D. in endocrine physiology from the Royal Postgraduate Medical School at Imperial College in London.

"Dr. Akinsanya's proven leadership in realizing and strategically executing on the potential of high-impact clinical and translational programs as well as transformative technologies is virtually unrivaled in the biopharmaceutical industry," said Sujal Patel, co-founder and CEO of Nautilus. "We are excited to welcome her as the newest member of our board, expanding the breadth and depth of business and scientific acumen that will bolster our go-to-market and commercialization strategy for widening access to and understanding of the human proteome to improve human health."

Dr. Akinsanya is currently a member of the Board of Directors of the Imperial College Foundation, the Board of Trustees of The Rockefeller University, the Scientific Advisory Boards of Variant Bio and Thermo Fisher Scientific, and was previously a Scientific Advisor at CQDM. While at Merck, she provided leadership to the National Medical Fellowships to increase diversity in medicine and access to quality healthcare in underserved communities, and as Executive Ambassador to Merck For Mothers to improve maternal health in more than 30 countries. She founded My Tech Learning and served as a mentor at The Prince's Trust to connect students to educational opportunities in science and technology.

"I'm thrilled to serve on Nautilus' Board of Directors among renowned business leaders who have brought revolutionary innovations in the fields of genomics, cancer therapeutics, and technology to market and are now guiding an innovative approach that has enormous potential for democratizing access to proteomics for all," said Dr. Akinsanya. "The possibilities that Nautilus' platform for unlocking the proteome will present are significant for the future of healthcare, from powering the discovery of breakthrough science to enabling disease diagnosis and the development of therapeutics for unmet needs with greater precision."

Dr. Akinsanya joins a Board of Directors that includes:

- Matt Posard, Board Chair and Founding Principal at Explore DNA, former Senior Vice President and Head of Sales at Illumina
- Michael Altman, Managing Director at Perceptive Advisors
- Melissa Epperly, Chief Financial Officer at Zentalis Pharmaceuticals

- Parag Mallick, Ph.D., Founder and Chief Scientist, Nautilus Biotechnology
- Matt McIlwain, Managing Director at Madrona Venture Group
- Farzad Nazem, Former EVP Engineering and Chief Technology Officer at Yahoo
- Vijay Pande, Ph.D., General Partner at Andreessen Horowitz
- Sujal Patel, Founder and CEO, Nautilus Biotechnology

About Nautilus Biotechnology, Inc.

With its corporate headquarters in Seattle and its research and development headquarters in the San Francisco Bay Area, Nautilus is a development stage life sciences company creating a platform technology for quantifying and unlocking the complexity of the proteome. Nautilus' mission is to transform the field of proteomics by democratizing access to the proteome and enabling fundamental advancements across human health and medicine. To learn more about Nautilus, visit www.nautilus.bio.

Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of federal securities laws. Forward-looking statements in this press release include, but are not limited to, statements regarding Nautilus' expectations regarding the company's business operations, financial performance and results of operations; expectations with respect to the suitability of the Nautilus product platform to investigate proteins and proteoforms; and expectations with respect to the functionality and performance of Nautilus' product platform, its potential impact on pharmaceutical development and drug discovery; statements regarding the partnership between Nautilus' board of directors and management; and the ability of management and board of directors personnel to contribute to the execution of Nautilus' strategic plans and goals. These statements are based on numerous assumptions concerning the development of Nautilus' products and target markets and involve substantial risks, uncertainties and other factors that may cause actual results to be materially different from the information expressed or implied by these forward-looking statements. Risks and uncertainties that could materially affect the accuracy of Nautilus' assumptions and its ability to achieve the forward-looking statements set forth in this press release include (without limitation) the following: Nautilus' product platform is not yet commercially available and remains subject to significant scientific and technical development, which is inherently challenging and difficult to predict, particularly with respect to highly novel and complex products such as those being developed by Nautilus. Even if our development efforts are successful, our product platform will require substantial validation of its functionality and utility in life science research. In the course of Nautilus' scientific and technical development and associated product validation and commercialization, we may experience material delays as a result of unanticipated events. We cannot provide any guarantee or assurance with respect to the outcome of our development, collaboration, and commercialization initiatives or with respect to their associated timelines. For a more detailed description of additional risks and uncertainties facing Nautilus and its development efforts, investors should refer to the information under the caption "Risk Factors" in the Registration Statement on Form S-1 filed with the SEC as well as in our Annual Report on Form 10-K filed for the year ended December 31, 2021. The forward-looking statements in this press release are as of the date of this press release. Except as otherwise required by applicable law, Nautilus disclaims any duty to update any forward-looking statements. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this press release

Disclosure Information

Nautilus uses filings with the Securities and Exchange Commission, its website (www.nautilus.bio), press releases, public conference calls, public webcasts, and its social media accounts as means of disclosing material non-public information and for complying with Regulation FD. Therefore, Nautilus encourages investors, the media, and others interested in Nautilus to review the information it makes public in these locations, as such information could be deemed to be material information.

Media Contact

Thermal for Nautilus Biotechnology Kaustuva Das press@nautilus.bio

Investor Contact

investor relations@nautilus.bio

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 14, 2022

NAUTILUS BIOTECHNOLOGY, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation)

001-39434 (Commission File Number)

98-1541723 (I.R.S. Employer

Identification No.)

2701 Eastlake Avenue East Seattle. Washington (Address of principal executive offices)

98102 (Zip code)

(206) 333-2001

(Registrant's telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425) 0
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)) 0
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Trading Symbol(s) Title of each class Name of each exchange on which registered

Common Stock, par value \$0.0001 per share

The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company x

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. o

Item 5.07. Submission of Matters to a Vote of Security Holders.

Nautilus Biotechnology, Inc. (the "Company") held its 2022 annual meeting of stockholders on June 14, 2022 (the "Annual Meeting"). Of the 124,456,653 shares of the Company's common stock outstanding as of the record date of April 18, 2022, 81,224,940 shares were represented at the Annual Meeting, either by proxy or by attending the meeting. The matters voted on at the Annual Meeting and the votes cast with respect to each such matter are set forth below:

1. Election of Class I Directors. The following nominees were elected to serve as Class I directors, each to hold office until the Company's 2025 annual meeting of stockholders or until his respective successor has been duly elected and qualified:

Nominee	Votes For	Votes Withheld	Broker Non-Votes
Sujal Patel	68,521,823	862,321	11,840,796
Vijay Pande	68,516,709	867,435	11,840,796
Michael Altman	68,518,666	865,478	11,840,796

2. Ratification of Appointment of Independent Registered Public Accounting Firm. The appointment of Pricewaterhouse Coopers LLP as the Company's independent registered public accounting firm for the fiscal year ending December 31, 2022 was ratified based on the following results of voting:

Votes For	Votes Against	Abstentions	Broker Non-Votes
80,903,155	31,871	289,914	<u>-</u>

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: June 16, 2022

NAUTILUS BIOTECHNOLOGY, INC.

By: /s/ Sujal Patel

Name: Sujal Patel

Title: Chief Executive Officer