

Prospectus Supplement
(to Prospectus dated October 22, 2021)

\$124,601,795



Common Stock

We have entered into an Open Market Sale AgreementSM dated August 17, 2018, as amended on November 19, 2021 (the “Sale Agreement”), with Jefferies LLC (the “Agent”), relating to the sale of shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the Sale Agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$150,000,000 from time to time through the Agent acting as sales agent, at our discretion, pursuant to this prospectus supplement and the accompanying prospectus. In addition, as of the date of this prospectus supplement, we had issued and sold shares of our common stock having an aggregate offering price of \$25,398,204.63 pursuant to the Sale Agreement under Registration Statement No. 333-224867, under a prior prospectus dated June 7, 2018 and a related prospectus supplement dated August 17, 2018.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be “at the market offerings” as defined in Rule 415 promulgated under the Securities Act of 1933, as amended (“the Securities Act”) including sales made directly on or through the Nasdaq Capital Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law. The Agent is not required to sell any specific number or dollar amount of securities but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between the Agent and us. Our common stock to which this prospectus supplement relates will be sold through the Agent on any given day. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to the Agent for sales of common stock sold pursuant to the Sale Agreement will be 3.0% of the gross proceeds from each such sale. In connection with the sale of the common stock on our behalf, the Agent may be deemed to be an “underwriter” within the meaning of the Securities Act, and the Agent’s compensation may be deemed to be underwriting commissions or discounts. See “Plan of Distribution” for additional information regarding compensation to be paid to the Agent. We have also agreed to provide indemnification and contribution to the Agent with respect to certain liabilities, including liabilities under the Securities Act.

Our common stock is listed on the Nasdaq Capital Market under the symbol “ABEO.” On November 15, 2021, the last reported sale price of our common stock on the Nasdaq Capital Market was \$0.91 per share.

Investing in our securities involves significant risks. Please read the information contained in or incorporated by reference under the heading “Risk Factors” beginning on page S-4 of this prospectus supplement, and under similar headings in other documents filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.

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

Jefferies LLC

The date of this prospectus supplement is November 19, 2021

TABLE OF CONTENTS

	<u>Page</u>
About This Prospectus Supplement	S-1
Summary	S-2
The Offering	S-3
Risk Factors	S-4
Cautionary Note Regarding Forward-Looking Statements	S-5
Use of Proceeds	S-6
Dilution	S-7
Plan of Distribution	S-8
Legal Matters	S-8
Experts	S-8
Where You Can Find More Information: Incorporation by Reference	S-9

Prospectus

About This Prospectus	1
Cautionary Note Regarding Forward-Looking Statements	2
The Company	3
Risk Factors	4
Use of Proceeds	5
Plan of Distribution	6
General Description of Securities That We May Sell	8
Description of Our Common Stock	9

Description of Our Preferred Stock	11
Description of Our Warrants	12
Description of Our Debt Securities	14
Where You Can Find More Information; Incorporation by Reference	19
Legal Matters	20
Experts	20

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to the offering of our common stock. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we may authorize for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the section of this prospectus supplement entitled “Where You Can Find More Information; Incorporation by Reference.” These documents contain important information that you should consider when making your investment decision.

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the offering of the common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, including the documents incorporated by reference into the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to the combined document consisting of this prospectus supplement and the accompanying prospectus. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference into the accompanying prospectus that was filed with the Securities and Exchange Commission (“SEC”) before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date, the statement in the document having the later date modifies or supersedes the earlier statement.

We are responsible for the information contained in, or incorporated by reference into, this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we may authorize for use in connection with this offering. We have not, and the Agent has not, authorized any other person to provide you with different information, and neither we nor the Agent takes any responsibility for any other information that others may give you.

We are not, and the Agent is not, making an offer to sell or soliciting an offer to buy our common stock in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation.

You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we may authorize for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

Unless the context otherwise requires or as otherwise expressly stated, references in this prospectus to the terms “the Company,” “Abeona,” “we,” “our” and “us” or other similar terms mean Abeona Therapeutics Inc. and its subsidiaries, unless we state otherwise, or the context indicates otherwise.

SUMMARY

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the “Risk Factors” section contained in this prospectus supplement, our financial statements and the related notes thereto, and the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

Overview

We are a clinical-stage biopharmaceutical company developing gene and cell therapies for life-threatening rare genetic diseases. Our lead clinical programs consist of (i) EB-101, an autologous, gene-corrected cell therapy for recessive dystrophic epidermolysis bullosa (“RDEB”), (ii) ABO-102, an adeno-associated virus (“AAV”)-based gene therapy for Sanfilippo syndrome type A (“MPS IIIA”), and (iii) ABO-101, an AAV-based gene therapy for Sanfilippo syndrome type B (“MPS IIIB”). We continue to develop additional AAV-based gene therapies designed to treat ophthalmic and other diseases, next-generation AAV-based gene therapies using the novel AIM™ capsid platform that we have exclusively licensed from the University of North Carolina at Chapel Hill, and internal AAV vector research programs. A number of our product candidates are eligible for orphan drug designation, breakthrough therapy designation, or other expedited review processes in the U.S., Europe, Japan, or other world markets. Our pipeline includes three programs in clinical development—EB-101, ABO-101 and ABO-102— for which we hold several U.S. and European Union regulatory designations, and a pipeline of additional earlier stage programs.

Company Information

We were incorporated in 1974. On October 24, 2014, we changed our name to PlasmaTech Biopharmaceuticals, Inc., and on June 19, 2015, we changed our name to Abeona Therapeutics Inc. to reflect our broader rare disease commitment. Our principal executive office is located at 1330 Avenue of the Americas, 33rd Floor, New York, NY 10019, and our telephone number is +1 (646) 813-4701. Our website is www.abeonatherapeutics.com. We do not incorporate by reference into this prospectus supplement the information on our website, and you should not consider it as part of this prospectus supplement.

THE OFFERING

Common Stock Offered	Shares of our common stock having an aggregate offering price of up to \$124,601,795.
Manner of Offering	“At the market offering” that may be made from time to time through the Agent, as sales agent. See “Plan of Distribution” on page S-8 of this prospectus supplement for a more complete description of the manner of offering.
Sales Agent	Jefferies LLC

Use of Proceeds

We expect to use the net proceeds of this offering, if any, to fund continued development of pipeline products, as well as for working capital and general corporate purposes. General corporate purposes may include repayment of debt, acquisitions, additions to working capital, capital expenditures, research and development and investments in our subsidiaries. See “Use of Proceeds” on page S-6 of this prospectus supplement for a more complete description of the intended use of proceeds from this offering.

Risk Factors

Investing in our securities involves significant risks. Please read the information contained in or incorporated by reference under the heading “Risk Factors” beginning on page S-4 of this prospectus supplement, and under similar headings in other documents filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.

Nasdaq Capital Market symbol

ABEO

S-3

RISK FACTORS

An investment in our securities involves risks. We urge you to consider carefully the risks described below, and in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision, including those risks identified under “Item IA. Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2020 and in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, which are incorporated by reference in this prospectus supplement and which may be amended, supplemented or superseded from time to time by other reports that we subsequently file with the SEC. Additional risks, including those that relate to any particular securities we offer, may be included in a future prospectus supplement or free writing prospectus that we authorize from time to time, or incorporated by reference into this prospectus supplement or the accompanying prospectus in connection with this offering. If any of these risks actually occur, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below entitled “Cautionary Note Regarding Forward-Looking Statements.”

Risks Related to this Offering

Sales of our common stock in this offering, or the perception that such sales may occur, could cause the market price of our common stock to fall.

The issuance and sale from time to time of shares of common stock, or our ability to issue these new shares of common stock in this offering, could have the effect of depressing the market price of our common stock. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

Our management will have broad discretion over the use of the net proceeds from this offering, you may not agree with how we use the proceeds, and the proceeds may not be invested successfully.

Our management will have broad discretion as to the use of the net proceeds from any offering by us and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for Abeona.

You may experience immediate and substantial dilution in the book value per share of the common stock you purchase in the offering.

The offering price per share in this offering may exceed the pro forma net tangible book value per share of our common stock outstanding prior to this offering. Based on an assumed public offering price of \$0.91 per share, which was the last reported sale price of our common stock on the Nasdaq Capital Market on November 15, 2021, you will experience immediate dilution of \$0.21 per share, representing the difference between our pro forma as adjusted net tangible book value per share as of September 30, 2021, after giving effect to this offering and the assumed offering price. The exercise of outstanding stock options will result in further dilution of your investment. See the section below entitled “Dilution” for a more detailed illustration of the dilution you would incur if you participate in this offering.

We will require additional capital funding, the receipt of which may impair the value of our common stock.

Our future capital requirements depend on many factors, including our research, development, sales, and marketing activities. We will need to raise additional capital through public or private equity or debt offerings or through arrangements with strategic partners or other sources in order to continue to develop our drug candidates. There can be no assurance that additional capital will be available when needed or on terms satisfactory to us, if at all. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution and the new equity securities may have greater rights, preferences, or privileges than our existing common stock.

S-4

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, and the other documents we have filed with the SEC that are incorporated herein by reference contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans, objectives of management or other financial items are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “seek,” “intend,” “may,” “plan,” “predict,” “project,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus supplement, particularly as set forth and incorporated by reference in the “Risk Factors” section above, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations, or investments we may make. You should read this prospectus supplement, the accompanying prospectus, and the documents that we incorporate by reference in this prospectus supplement completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, except as otherwise required by law. We advise you, however, to consult any further disclosures we make on related subjects in our future annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K we file with or furnish to the SEC.

S-5

We intend to use the net proceeds from this offering to fund continued development of pipeline products, as well as for working capital and general corporate purposes. General corporate purposes may include research and development, additions to working capital, capital expenditures, acquisitions and investments in our subsidiaries. The amounts and timing of our use of the net proceeds from the sale of securities in this offering will depend on a number of factors, such as the timing and progress of trials of our clinical and pre-clinical product candidates and our development efforts, the timing and progress of any partnering efforts, technological advances, and the competitive environment for our product candidates.

As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending application of the net proceeds as described above, we may invest the net proceeds of this offering in a variety of capital preservation investments, including but not limited to short-term, interest-bearing investment grade securities, money market accounts, certificates of deposit and direct or guaranteed obligations of the U.S. government.

S-6

DILUTION

If you invest in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share and the as adjusted net tangible book value per share after giving effect to this offering. We calculate net tangible book value per share by dividing the net tangible book value, which is tangible assets less total liabilities, by the number of outstanding shares of our common stock. Dilution represents the difference between the portion of the amount per share paid by purchasers of shares in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering. Our net tangible book value as of September 30, 2021 was approximately \$46.2 million, or \$0.45 per share.

Without taking into account any other changes in net tangible book value after September 30, 2021, after giving effect to the sale of our common stock pursuant to this prospectus supplement and accompanying prospectus in the aggregate amount of \$124,601,795 at an assumed offering price of \$0.91 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on November 15, 2021, and after deducting commissions and estimated aggregate offering expenses payable by us, our net tangible book value as of September 30, 2021 would have been \$166.9 million, or \$0.70 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.25 per share to our existing stockholders and an immediate dilution in net tangible book value of \$0.21 per share to new investors. The following table illustrates this per share dilution:

Assumed offering price per share		\$	0.91
Net tangible book value per share as of September 30, 2021	\$	0.45	
Increase per share attributable to new investors	\$	0.25	
As adjusted net tangible book value per share as of September 30, 2021 after giving effect to this offering	\$	0.70	
Dilution per share to new investors purchasing shares in this offering	\$	0.21	

The number of shares of our common stock to be outstanding after this offering is based on 101,867,539 shares of our common stock outstanding as of September 30, 2021, which amount excludes:

- 7,755,196 shares issuable upon the exercise of stock options outstanding as of September 30, 2021 at a weighted average exercise price of \$1.58 per share; and
- 1,617,138 shares of common stock reserved for future issuance under our equity incentive plans.

S-7

PLAN OF DISTRIBUTION

We have entered into an Open Market Sale AgreementSM, as amended by Amendment No. 1 thereto, dated as of November 19, 2021, with Jefferies LLC (the “Agent”), under which we may issue and sell shares of our common stock from time to time through the Agent acting as sales agent, subject to certain limitations, including the number of shares registered under the registration statement to which the offering relates. As of November 19, 2021, we have issued and sold shares of our common stock having an aggregate offering price of \$25,398,204.63 pursuant to the Sale Agreement under Registration Statement No. 333-224867, under a prior prospectus and related prospectus supplement.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be “at the market offerings” as defined in Rule 415 promulgated under the Securities Act, including sales made directly on or through the Nasdaq Capital Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law. We may instruct the Agent not to sell our common stock if the sales cannot be effected at or above the price designated by us from time to time. We or the Agent may suspend the offering of our common stock upon notice and subject to other conditions. As an agent, the Agent will not engage in any transactions that stabilize the price of our common stock. Our common stock to which this prospectus supplement relates will be sold through only one Agent on any given day.

Each time we wish to issue and sell common stock under the Sale Agreement with the Agent, we will notify the Agent of the number of shares to be issued, the dates on which such sales are anticipated to be made, any minimum price below which sales may not be made and other sales parameters as we deem appropriate. Once we have so instructed the Agent, unless the Agent declines to accept the terms of the notice, the Agent has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The Agent’s obligations under the Sale Agreement to sell our common stock are subject to a number of conditions that we must meet.

We will pay the Agent commissions for its services in acting as agent in the sale of our common stock. The Agent will be entitled to compensation at a commission rate equal to 3.0% of the gross sales price per share sold. Because there is no minimum offering amount required as a condition to closing this offering, the actual total public offering amount, commissions, and proceeds to us, if any, are not determinable at this time. In addition, we have agreed to reimburse the Agent for fees and disbursements paid to its legal counsel, in amounts not to exceed \$50,000 in both cases, in connection with the original Sale Agreement and Amendment No. 1 thereto. In accordance with FINRA Rule 5110, these reimbursed fees and expenses are deemed sales compensation for this offering.

We estimate that the total expenses for the offering, excluding compensation payable to the Agent under the terms of the Sale Agreement and Amendment No. 1 thereto, will be approximately \$100,000.

Settlement for sales of our common stock will occur on the second business day following the date on which any sales are made, or on some other date that is agreed upon by us and the Agent in connection with a particular transaction, in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust, or similar arrangement.

In connection with the sale of the common stock on our behalf, the Agent may, and will with respect to sales effected in an “at the market offering,” be deemed to be

an “underwriter” within the meaning of the Securities Act, and the Agent’s compensation may be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to the Agent against certain civil liabilities, including liabilities under the Securities Act.

The offering pursuant to the Sale Agreement will terminate upon the earlier of (i) the issuance and sale of all shares of our common stock subject to the Sale Agreement, or (ii) the termination of the Sale Agreement as permitted therein.

The Agent and its affiliates may in the future provide various investment banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, the Agent will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by Morgan, Lewis & Bockius LLP, Boston, Massachusetts. Covington & Burling LLP, New York, New York, will act as counsel to the Agent in connection with this offering.

EXPERTS

The consolidated financial statements, incorporated by reference from the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2020, have been audited by Whitley Penn LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

S-8

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

We file annual, quarterly, and current reports, proxy statements and other information with the SEC. The SEC maintains a website at www.sec.gov that contains reports, statements, and other information about issuers, such as us, who file electronically with the SEC. We maintain a website at www.abeonatherapeutics.com. However, the information on our website is not incorporated by reference into this prospectus supplement and the accompanying prospectus and you should not consider it a part of this prospectus supplement or the accompanying prospectus.

The SEC allows us to “incorporate by reference” into this prospectus supplement the information in other documents that we file with it. This means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus supplement, and information in documents that we file later with the SEC will automatically update and supersede information contained in documents filed earlier with the SEC or contained in this prospectus supplement. We incorporate by reference into this prospectus supplement the documents listed below; provided, however, that we are not incorporating, in each case, any documents or information deemed to have been furnished and not filed in accordance with SEC rules:

- Our Annual Report on Form 10-K for the year ended [December 31, 2020](#) (filed on March 24, 2021) (including the information in Part III incorporated by reference from the Company’s Definitive Proxy Statement on Schedule 14A, filed on [April 9, 2021](#));
- Our Quarterly Reports on Form 10-Q for the quarterly periods ended [March 31, 2021](#) (filed on May 17, 2021), [June 30, 2021](#) (filed on July 28, 2021) and [September 30, 2021](#) (filed on November 15, 2021);
- Our Current Reports on Form 8-K filed on [February 1, 2021](#), [March 23, 2021](#), [March 30, 2021](#), [April 19, 2021](#) (as amended on [May 28, 2021](#)), [May 28, 2021](#), [July 16, 2021](#), [August 13, 2021](#), [September 21, 2021](#) and [November 15, 2021](#); and
- The description of our common stock, par value \$0.01 per share contained in our Registration Statement on [Form 8-A](#), dated and filed with the SEC on November 4, 2014, as updated by [Exhibit 4.4](#) to our Form 10-K for the fiscal year ended December 31, 2019, and including any amendments or reports 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 Exchange Act 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, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports and documents.

You may obtain a copy of any or all of the documents referred to above which may have been or may be incorporated by reference into this prospectus supplement, except for exhibits to those documents (unless the exhibits are specifically incorporated by reference into those documents) at no cost to you by writing or telephoning us at the following address: Investor Relations, Abeona Therapeutics Inc., 1330 Avenue of the Americas, 33rd Floor, New York, NY 10019, telephone +1 (646) 813-4701.

S-9

PROSPECTUS

\$250,000,000

ABEONA THERAPEUTICS INC.

Common Stock

Preferred Stock

Warrants

Debt Securities

This prospectus will allow us to issue, from time to time at prices and on terms to be determined at or prior to the time of the offering, up to \$250,000,000 of any combination of the securities described in this prospectus. We may also offer common stock or preferred stock upon conversion of or exchange for the debt securities or common stock, preferred stock or debt securities upon the exercise of warrants.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide you with the specific terms of any offering in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplements and any related free writing prospectus will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus, any prospectus supplement, and any related free writing prospectus, as

well as any documents incorporated by reference into this prospectus or any prospectus supplement, carefully before you invest.

Our securities may be sold directly by us to you, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled “Plan of Distribution” in this prospectus and in the applicable prospectus supplement. If any underwriters or agents are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, commissions or discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common stock is listed on The Nasdaq Capital Market (“Nasdaq”), under the symbol “ABEO.” On June 4, 2021, the last reported sale price of our common stock on Nasdaq was \$1.69 per share.

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 4 of this prospectus under the caption “Risk Factors.” We may include specific risk factors in supplements to this prospectus and any related free writing prospectus under the caption “Risk Factors.” This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement.

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

The date of this prospectus is October 22, 2021.

TABLE OF CONTENTS

	Page
ABOUT THIS PROSPECTUS	1
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS	2
THE COMPANY	3
RISK FACTORS	4
USE OF PROCEEDS	5
PLAN OF DISTRIBUTION	6
GENERAL DESCRIPTION OF SECURITIES THAT WE MAY SELL	8
DESCRIPTION OF OUR COMMON STOCK	9
DESCRIPTION OF OUR PREFERRED STOCK	11
DESCRIPTION OF OUR WARRANTS	12
DESCRIPTION OF OUR DEBT SECURITIES	14
WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE	19
LEGAL MATTERS	20
EXPERTS	20

i

ABOUT THIS PROSPECTUS

This prospectus is part of a “shelf” registration statement. Under this shelf registration process, we may sell, at any time and from time to time, in one or more offerings, any combination of the securities described in this prospectus. The exhibits to our Registration Statement contain the full text of certain contracts and other important documents we have summarized in this prospectus. Since these summaries may not contain all the information that you may find important in deciding whether to purchase the securities we offer, you should review the full text of these documents. The Registration Statement and the exhibits can be obtained from the Securities and Exchange Commission (“SEC”) as indicated under the heading “Where You Can Find More Information; Incorporation By Reference.”

This prospectus only provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that contains specific information about the terms of those securities and the terms of that offering. The prospectus supplement may also add, update, or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with the additional information described below under the heading “Where You Can Find More Information; Incorporation By Reference.”

We have not authorized any dealer, agent, or other person to give any information or to make any representation other than those contained or incorporated by reference into this prospectus and any accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference into this prospectus or an accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement, if any, constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and any accompanying prospectus supplement is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

References in this prospectus to the terms “the Company,” “Abeona,” “we,” “our” and “us” or other similar terms mean Abeona Therapeutics Inc., unless we state otherwise or the context indicates otherwise.

1

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement, and the other documents we have filed with the SEC that are incorporated herein by reference contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans, objectives of management or other financial items are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “seek,” “intend,” “may,” “plan,” “predict,” “project,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make.

We have included important factors in the cautionary statements included in this prospectus, particularly as set forth and incorporated by reference into the “Risk Factors” section below, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations, or investments we may make.

You should read this prospectus, any supplements to this prospectus and the documents that we incorporate by reference into this prospectus completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, except as otherwise required by law. We advise you, however, to consult any further disclosures we make on related subjects in our future annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K we file with or furnish to the SEC.

THE COMPANY

Overview

Abeona Therapeutics Inc. is a clinical-stage biopharmaceutical company developing gene and cell therapies for life-threatening rare genetic diseases. Our lead clinical programs consist of (i) EB-101, an autologous, gene-corrected cell therapy for recessive dystrophic epidermolysis bullosa (“RDEB”), (ii) ABO-102, an adeno-associated virus (“AAV”)-based gene therapy for Sanfilippo syndrome type A (“MPS IIIA”), and (iii) ABO-101, an AAV-based gene therapy for Sanfilippo syndrome type B (“MPS IIIB”). We continue to develop additional AAV-based gene therapies designed to treat ophthalmic and other diseases, next-generation AAV-based gene therapies using our own novel capsids and capsids from the AIM™ capsid library that we have exclusively licensed from the University of North Carolina at Chapel Hill, and internal AAV vector research programs. A number of our product candidates are eligible for orphan drug designation, breakthrough therapy designation, or other expedited review processes in the U.S., Europe, Japan, or other world markets. Our pipeline includes three programs in clinical development—EB-101, ABO-101 and ABO-102—for which we hold several U.S. and European Union (“EU”) regulatory designations, and a pipeline of additional earlier stage programs.

Our Mission and Strategy

Abeona is at the forefront of gene and cell therapy research and development. We are a fully-integrated company featuring therapies in clinical development, in-house manufacturing facilities, a robust pipeline, and scientific and clinical leadership. We see our mission as working to create, develop, manufacture, and deliver gene and cell therapies for people impacted by serious diseases. We partner with leading academic researchers, patient advocacy organizations and caregivers to develop therapies that address the underlying cause of a broad spectrum of rare genetic diseases for which no effective treatment options exist today.

Since our last fiscal year, we have continued to make progress toward fulfilling our goal of harnessing the promise of genetic medicine to transform the lives of people impacted by serious diseases and redefining the standard of care through gene and cell therapies. Our strategy to achieve this goal consists of:

Advancing Our Clinical Gene and Cell Therapy Programs and Research and Development with a Focus on Rare and Orphan Diseases.

We have three programs in clinical development—EB-101, ABO-101 and ABO-102—and a pipeline of additional earlier stage programs. Through our gene and cell therapy research and development expertise, we believe we are positioned to introduce efficacious and safe therapeutics to transform the standard of care in devastating diseases and establish our leadership position in the field.

Applying Novel Next-Generation AIM™ Capsid Technology to Develop New In-Vivo Gene Therapies.

We are researching and developing next-generation AAV-based gene therapy using our own novel capsids and capsids from the AIM™ capsid library. We plan to continue to develop AAV capsids capable of improved tissue targeting for various indications and potentially evading immunity to wildtype AAV vectors.

Establishing Leadership Position in Commercial-Scale Gene and Cell Therapy Manufacturing.

We established current Good Manufacturing Practice (“cGMP”), clinical-scale manufacturing capabilities for gene-corrected cell therapy and AAV-based gene therapies in our state-of-the-art Cleveland facility. We believe that our platform provides us with distinct advantages, including flexibility, scale, reliability, and the potential for reduced development risk, reduced cost, and faster times to market. We have focused on establishing internal Chemistry, Manufacturing and Controls (“CMC”) capabilities that drive value for our organization through process development, assay development and manufacturing. We have also deployed robust quality systems governing all aspects of product lifecycle from preclinical through commercial stage.

Establishing Additional Gene and Cell Therapy Franchises and Adjacencies through In-Licensing and Strategic Partnerships.

We seek to be the partner of choice in gene therapy treatment and have closely collaborated with leading academic institutions, key opinion leaders, patient foundations, and industry partners to generate novel intellectual property, accelerate research and development, and understand the needs of patients and their families.

Maintaining and Growing Our IP Portfolio.

We strive to have a leading intellectual property portfolio. To that end, we seek patent rights for various aspects of our programs, including vector engineering and construct design, our production process, and all features of our clinical products including composition of matter and method of administration and delivery. We expect to continue to expand our intellectual property portfolio by aggressively seeking patent rights for promising aspects of our product engine and product candidates.

Company Information

We were incorporated in 1974. On October 24, 2014, we changed our name to PlasmaTech Biopharmaceuticals, Inc., and on June 19, 2015, we changed our name to Abeona Therapeutics Inc. to reflect our broader rare disease commitment. Our principal executive office is located at 1330 Avenue of the Americas, 33rd Floor, New York, NY 10019 and our telephone number is (646) 813-4701. Our website is www.abeonatherapeutics.com. We do not incorporate by reference into this prospectus the information on our website, and you should not consider it as part of this prospectus supplement.

RISK FACTORS

An investment in our securities involves risks and uncertainties. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus. In particular, you should carefully consider the information under the heading “Risk Factors,” as well as the factors listed under the heading “Forward-Looking Statements,” in each case contained in our Annual Report on Form 10-K for our most recent fiscal year, in any Quarterly Reports on Form 10-Q that have been filed since our most recent Annual Report on Form 10-K, and in any other documents that we file (not furnish) with the SEC under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), each of which is incorporated by reference in this prospectus. Any of the risks described could significantly and negatively affect our business, financial condition, results of operations, cash flows and prospects and the trading price of our securities. You could lose all or part of your

USE OF PROCEEDS

Unless otherwise specified in a prospectus supplement accompanying this prospectus, the net proceeds from the sale of the securities to which this prospectus relates will be used to fund continued clinical development of pipeline products, as well as for working capital and general corporate purposes. General corporate purposes may include repayment of debt, acquisitions, additions to working capital, capital expenditures, research and development and investments in our subsidiaries. Net proceeds may be temporarily invested prior to use.

PLAN OF DISTRIBUTION

We may sell the offered securities in any of the ways described below or in any combination or any other way set forth in an applicable prospectus supplement from time to time:

- to or through underwriters or dealers;
- through one or more agents; or
- directly to purchasers or to a single purchaser.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;
- the public offering price of the securities and the proceeds to us and any discounts, commissions or concessions allowed or reallocated or paid to dealers; and
- any securities exchanges on which the securities may be listed.

Any offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

Only the agents or underwriters named in each prospectus supplement are agents or underwriters in connection with the securities being offered thereby.

We may authorize underwriters, dealers or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in each applicable prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in each applicable prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions, and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will be subject only to those conditions set forth in each applicable prospectus supplement, and each prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Agents, underwriters and other third parties described above may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act of 1933, as amended (the "Securities Act"), or to contribution from us with respect to payments which the agents, underwriters or other third parties may be required to make in respect thereof. Agents, underwriters and such other third parties may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

One or more firms, referred to as "remarketing firms," may also offer or sell the securities, if a prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as our agents. These remarketing firms will offer or sell the securities in accordance with the terms of the securities. Each prospectus supplement will identify and describe any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket. Remarketing firms may be entitled under agreements that may be entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale.

The securities we offer may be new issues of securities and may have no established trading market. The securities may or may not be listed on a securities exchange. Underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the liquidity of, or the existence of trading markets for, any of the securities.

Certain persons participating in an offering may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with rules and regulations under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities

originally sold by the dealer are purchased in a short covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

We also may sell any of the securities through agents designated by us from time to time. We will name any agent involved in the offer or sale of these securities and will list commissions payable by us to these agents in the applicable prospectus supplement. These agents will be acting on a best efforts basis to solicit purchases for the period of its appointment, unless stated otherwise in the applicable prospectuses.

We may sell any of the securities directly to purchasers. In this case, we will not engage underwriters or agents in the offer and sale of these securities.

We may engage in sales deemed to be “at the market offerings” as defined in Rule 415 promulgated under the Securities Act, including sales made directly on or through Nasdaq, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices and/or any other method permitted by law. The terms of such “at the market offerings” will be set forth in the applicable prospectus supplement. We may engage an agent to act as a sales agent in such “at the market offerings” on a best efforts basis using commercially reasonable efforts consistent with normal trading and sales practices, on mutually agreed terms between such agent and us. We will name any agent involved in such “at the market offerings” of securities and will list commissions payable by us to these agents in the applicable prospectus supplement.

In addition, we 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 so indicates, in connection with those derivatives, the third parties may sell 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 us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us 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, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. 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.

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

In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc. (“FINRA”), the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate proceeds of the offering.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

7

GENERAL DESCRIPTION OF SECURITIES THAT WE MAY SELL

We may offer and sell, at any time and from time to time:

- Shares of our common stock;
- Shares of our preferred stock;
- Warrants to purchase shares of our common stock, preferred stock and/or debt securities;
- Debt securities consisting of debentures, notes or other evidences of indebtedness; or
- Any combination of these securities.

The terms of any securities we offer will be determined at the time of sale. We may issue debt securities that are exchangeable for or convertible into common stock or any of the other securities that may be sold under this prospectus. When particular securities are offered, a supplement to this prospectus will be filed with the SEC, which will describe the terms of the offering and sale of the offered securities.

8

DESCRIPTION OF OUR COMMON STOCK

Our authorized capital stock consists of 200,000,000 shares of common stock, \$0.01 par value per share, and 2,000,000 shares of preferred stock, \$0.01 par value per share, which may be issued in one or more series. The following summary of the terms of our common stock is subject to and qualified in its entirety by reference to our restated certificate of incorporation (the “Certificate of Incorporation”) and amended and restated bylaws (the “Bylaws”). Please refer to “Where You Can Find More Information; Incorporation By Reference” below for directions on obtaining these documents.

As of June 4, 2021, we had 99,892,667 shares of common stock outstanding and no shares of preferred stock outstanding.

General

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and have the right to vote cumulatively for the election of directors. This means that in the voting at our annual meeting, each stockholder or his proxy may multiply the number of his shares by the number of directors to be elected, then cast the resulting total number of votes for a single nominee, or distribute such votes on the ballot among the nominees as desired. Holders of our common stock are entitled to receive ratably such dividends, if any, as may be declared by our Board of Directors (the “Board”) out of funds legally available therefor, subject to any preferential dividend rights for our outstanding preferred stock.

Upon our liquidation, dissolution, or winding up, the holders of our common stock are entitled to receive ratably our net assets available after the payment of all debts and other liabilities and subject to the prior rights of any of our outstanding preferred stock. Holders of our common stock have no preemptive, subscription, redemption, or conversion rights. The rights, preferences, and privileges of 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 our preferred stock which we may designate and issue in the future.

Our common stockholders may not receive any assets or funds until our creditors have been paid in full and the preferential or participating rights of our preferred stockholders have been satisfied. If we participate in a corporate merger, consolidation, purchase or acquisition of property or stock, or other reorganization, any payments or shares of stock allocated to our common stockholders will be distributed pro rata to holders of our common stock on a per share basis. If we redeem, repurchase, or otherwise acquire for payment any shares of our common stock, we will treat each share of common stock identically.

We may issue additional shares of our common stock, if authorized by the Board, without the common stockholders' approval, unless required by Delaware law or a stock exchange on which our securities are traded. If we receive the appropriate payment, shares of our common stock that we issue will be fully paid and nonassessable.

Anti-Takeover Provisions

We are subject to the provisions of Section 203 of the General Corporation Law of Delaware ("DGCL"). Section 203 prohibits certain publicly held Delaware corporations from engaging in a "business combination" with an "interested stockholder," for a period of three years after the date of the transaction in which the person became an "interested stockholder," unless the business combination is approved in a prescribed manner. A "business combination" includes mergers, asset sales and other transactions resulting in a financial benefit to the interested stockholder. Subject to certain exceptions, an "interested stockholder" is a person or entity who, together with affiliates and associates, owns (or within the preceding three years, did own) 15% or more of the corporation's voting stock. The statute contains provisions enabling a corporation to avoid the statute's restrictions if the stockholders holding a majority of the corporation's voting stock approve the transaction. Moreover, our Certificate of Incorporation provides that our directors shall be divided into three classes, with the terms of each class to expire in different years.

9

In addition, our Certificate of Incorporation, in order to combat "greenmail," provides in general that any direct or indirect purchase by us of any of our voting stock or rights to acquire voting stock known to be beneficially owned by any person or group which holds more than five percent of a class of our voting stock and which has owned the securities being purchased for less than two years must be approved by the affirmative vote of at least two-thirds of the votes entitled to be cast by the holders of voting stock, subject to certain exceptions. The prohibition of "greenmail" may tend to discourage or foreclose certain acquisitions of our securities which might temporarily increase the price of our securities. Discouraging the acquisition of a large block of our securities by an outside party may also have a potential negative effect on takeovers. Parties seeking control of us through large acquisitions of our securities will not be able to resort to "greenmail" should their bid fail, thus making such a bid less attractive to persons seeking to initiate a takeover effort.

Elimination of Monetary Liability for Officers and Directors

Our Certificate of Incorporation incorporates certain provisions permitted under DGCL relating to the liability of directors. The provisions eliminate a director's liability for monetary damages for a breach of fiduciary duty, including gross negligence, except in circumstances involving certain wrongful acts, such as the breach of director's duty of loyalty or acts or omissions involving intentional misconduct or a knowing violation of law. These provisions do not eliminate a director's duty of care. Moreover, these provisions do not apply to claims against a director for certain violations of law, including knowing violations of federal securities law. Our Certificate of Incorporation also contains provisions to indemnify the directors, officers, employees, or other agents to the fullest extent permitted by DGCL. We believe that these provisions will assist us in attracting and retaining qualified individuals to serve as directors.

Our Certificate of Incorporation also contains provisions to indemnify the directors, officers, employees, or other agents to the fullest extent permitted by DGCL. These provisions may have the practical effect in certain cases of eliminating the ability of stockholders to collect monetary damages from directors. We believe that these provisions will assist us in attracting or retaining qualified individuals to serve as our directors.

The Nasdaq Capital Market

Our common stock is listed on Nasdaq under the symbol "ABEO."

Transfer Agent and Registrar

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

10

DESCRIPTION OF OUR PREFERRED STOCK

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

If we offer a specific class or series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

- the title and stated value;
- the number of shares offered, the liquidation preference per share and the purchase price;
- the dividend rate(s), period(s) and/or payment date(s) or method(s) of calculation for such dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption, if applicable;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price (or how it will be calculated), the conversion period and any other terms of conversion (including any anti-dilution provisions, if any);

- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated), the exchange period and any other terms of exchange (including any anti-dilution provisions, if any);
- voting rights, if any, of the preferred stock;
- a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of the Company;
- any material limitations on issuance of any class or series of preferred stock ranking senior to or on parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the Company; and
- any other affirmative, negative, or other covenants or contractual rights which might be attendant with the specific class or series of preferred stock.

The preferred stock offered by this prospectus, when issued, will not have, or be subject to, any preemptive or similar rights.

Transfer Agent and Registrar

The transfer agent and registrar for any series or class of preferred stock will be set forth in each applicable prospectus supplement.

11

DESCRIPTION OF OUR WARRANTS

This section describes the general terms and provisions of our warrants to acquire our securities that we may issue from time to time. The applicable prospectus supplement will describe the specific terms of the warrants offered through that prospectus supplement.

We may issue warrants for the purchase of our debt securities, common stock or preferred stock or other securities issued by us. We may issue warrants independently or together with other securities, and they may be attached to or separate from the other securities. We will file a copy of the warrant and warrant agreement with the SEC each time we issue a series of warrants, and these warrants and warrant agreements will be incorporated by reference into the Registration Statement of which this prospectus is a part. A holder of our warrants should refer to the provisions of the applicable warrant agreement and prospectus supplement for more specific information.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount, and terms of the securities purchasable upon exercise of the warrants;
- if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise and a description of that class or series of our preferred stock;
- if applicable, the exercise price for our debt securities, the amount of our debt securities to be received upon exercise and a description of that series of debt securities;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if the warrants may not be continuously exercised throughout that period, the specific date or dates on which the warrants may be exercised;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars, or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- if applicable, the date from and after which the warrants and the common stock, preferred stock or debt securities will be separately transferable;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

12

- information with respect to book-entry procedures, if any;
- any redemption or call provisions;
- whether the warrants are to be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

After your warrants expire they will become void. All warrants will be issued in registered form. The prospectus supplement may provide for the adjustment of the exercise price of the warrants.

Warrants may be exercised at the appropriate office of the warrant agent, or any other office indicated in the applicable prospectus supplement. Before the exercise of warrants, holders will not have any of the rights of holders of the securities purchasable upon exercise and will not be entitled to payments made to holders of those securities.

The warrant agreements may be amended or supplemented without the consent of the holders of the warrants to which it applies to effect changes that are not inconsistent with the provisions of the warrants and that do not materially and adversely affect the interests of the holders of the warrants. However, any amendment that materially and adversely alters the rights of the holders of warrants will not be effective unless the holders of at least a majority of the applicable warrants then outstanding approve the amendment. Every holder of an outstanding warrant at the time any amendment becomes effective, by continuing to hold the warrant, will be bound by the applicable warrant agreement as amended. The prospectus supplement applicable to a particular series of warrants may provide that certain provisions of the warrants, including the securities for which they may be exercisable, the exercise price and the expiration date, may not be altered without the consent of the holder of each warrant.

Transfer Agent and Registrar

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

13

DESCRIPTION OF OUR DEBT SECURITIES

This section describes the general terms and provisions of the debt securities that we may offer under this prospectus, any of which may be issued as convertible or exchangeable debt securities. We will set forth the particular terms of the debt securities we offer in a prospectus supplement. The extent, if any, to which the following general provisions apply to particular debt securities will be described in the applicable prospectus supplement. The following description of general terms relating to the debt securities and the indenture under which the debt securities will be issued are summaries only and therefore are not complete. You should read the indenture and the prospectus supplement regarding any particular issuance of debt securities.

We will issue any debt under an indenture to be entered into between us and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as amended (the "Indenture Act"), as in effect on the date of the indenture. We have filed or will file a copy of the form of indenture as an exhibit to the Registration Statement in which this prospectus is included. The indenture will be subject to and governed by the terms of the Indenture Act.

We may offer under this prospectus up to an aggregate principal amount of \$250,000,000 in debt securities, or if debt securities are issued at a discount, or in a foreign currency, foreign currency units or composite currency, the principal amount as may be sold for an initial public offering price of up to \$250,000,000. Unless otherwise specified in the applicable prospectus supplement, the debt securities will represent direct, unsecured obligations of the Company and will rank equally with all of our other unsecured indebtedness.

The following statements relating to the debt securities and the indenture are summaries, qualified in their entirety by reference to the detailed provisions of the indenture and the final form indenture as may be filed with a future prospectus supplement.

General

We may issue the debt securities in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will describe the particular terms of each series of debt securities in a prospectus supplement relating to that series, which we will file with the SEC.

The prospectus supplement will set forth, to the extent required, the following terms of the debt securities in respect of which the prospectus supplement is delivered:

- the title of the series;
- the aggregate principal amount;
- the issue price or prices, expressed as a percentage of the aggregate principal amount of the debt securities;
- any limit on the aggregate principal amount;
- the date or dates on which principal is payable;
- the interest rate or rates (which may be fixed or variable) or, if applicable, the method used to determine such rate or rates;
- the date or dates from which interest, if any, will be payable and any regular record date for the interest payable;
- the place or places where principal and, if applicable, premium and interest, is payable;

14

- the terms and conditions upon which we may, or the holders may require us to, redeem or repurchase the debt securities;
- the denominations in which such debt securities may be issuable, if other than denominations of \$1,000 or any integral multiple of that number;
- whether the debt securities are to be issuable in the form of certificated securities (as described below) or global securities (as described below);
- the portion of principal amount that will be payable upon declaration of acceleration of the maturity date if other than the principal amount of the debt securities;
- the currency of denomination;
- the designation of the currency, currencies, or currency units in which payment of principal and, if applicable, premium and interest, will be made;
- if payments of principal and, if applicable, premium or interest, on the debt securities are to be made in one or more currencies or currency units other than the currency of denomination, the manner in which the exchange rate with respect to such payments will be determined;
- if amounts of principal and, if applicable, premium and interest may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index, then the manner in which such amounts will be determined;
- the provisions, if any, relating to any collateral provided for such debt securities;
- any addition to or change in the covenants and/or the acceleration provisions described in this prospectus or in the indenture;

- any events of default, if not otherwise described below under “Defaults and Notice”;
- the terms and conditions, if any, for conversion into or exchange for shares of our common stock or preferred stock;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents; and
- the terms and conditions, if any, upon which the debt securities shall be subordinated in right of payment to other indebtedness of the Company.

We may issue discount debt securities that provide for an amount less than the stated principal amount to be due and payable upon acceleration of the maturity of such debt securities in accordance with the terms of the indenture. We may also issue debt securities in bearer form, with or without coupons. If we issue discount debt securities or debt securities in bearer form, we will describe material U.S. federal income tax considerations and other material special considerations which apply to these debt securities in the applicable prospectus supplement.

We may issue debt securities denominated in or payable in a foreign currency or currencies or a foreign currency unit or units. If we do, we will describe the restrictions, elections, and general tax considerations relating to the debt securities and the foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Exchange and/or Conversion Rights

We may issue debt securities which can be exchanged for or converted into shares of our common stock or preferred stock. If we do, we will describe the terms of exchange or conversion in the prospectus supplement relating to these debt securities.

Transfer and Exchange

We may issue debt securities that will be represented by either:

- “book-entry securities,” which means that there will be one or more global securities registered in the name of a depositary or a nominee of a depositary; or
- “certificated securities,” which means that they will be represented by a certificate issued in definitive registered form.

We will specify in the prospectus supplement applicable to a particular offering whether the debt securities offered will be book-entry or certificated securities.

Certificated Debt Securities

If you hold certificated debt securities issued under an indenture, you may transfer or exchange such debt securities in accordance with the terms of the indenture. You will not be charged a service charge for any transfer or exchange of certificated debt securities but may be required to pay an amount sufficient to cover any tax or other governmental charge payable in connection with such transfer or exchange.

Global Securities

The debt securities of a series may be issued in the form of one or more global securities that will be deposited with a depositary or its nominees identified in the prospectus supplement relating to the debt securities. In such a case, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal amount of outstanding debt securities of the series to be represented by such global security or securities.

Unless and until it is exchanged in whole or in part for debt securities in definitive registered form, a global security may not be registered for transfer or exchange except as a whole by the depositary for such global security to a nominee of the depositary and except in the circumstances described in the prospectus supplement relating to the debt securities. The specific terms of the depositary arrangement with respect to a series of debt securities will be described in the prospectus supplement relating to such series.

No Protection in the Event of Change of Control

Any indenture that governs our debt securities covered by this prospectus may not have any covenant or other provision providing for a put or increased interest or otherwise that would afford holders of our debt securities additional protection in the event of a recapitalization transaction, a change of control of the Company or a highly leveraged transaction. If we offer any covenants or provisions of this type with respect to any debt securities covered by this prospectus, we will describe them in the applicable prospectus supplement.

Covenants

Unless otherwise indicated in this prospectus or the applicable prospectus supplement, our debt securities may not have the benefit of any covenant that limits or restricts our business or operations, the pledging of our assets or the incurrence by us of indebtedness. We will describe in the applicable prospectus supplement any material covenants in respect of a series of debt securities.

Consolidation, Merger, and Sale of Assets

We may agree in any indenture that governs the debt securities of any series covered by this prospectus that we will not consolidate with or merge into any other person or convey, transfer, sell or lease our properties and assets substantially as an entirety to any person, unless such person and such proposed transaction meets various criteria, which we will describe in detail in the applicable prospectus supplement.

Defaults and Notice

The debt securities of any series will contain events of default to be specified in the applicable prospectus supplement, which may include, without limitation:

- failure to pay the principal of, or premium or make-whole amount, if any, on any debt security of such series when due and payable (whether at maturity, by call for redemption, through any mandatory sinking fund, by redemption at the option of the holder, by declaration or acceleration or otherwise);
- failure to make a payment of any interest on any debt security of such series when due;

- our failure to perform or observe any other covenants or agreements in the indenture with respect to the debt securities of such series;
- certain events relating to our bankruptcy, insolvency, or reorganization; and
- certain cross defaults, if and as applicable.

If an event of default with respect to debt securities of any series shall occur and be continuing, we may agree that the trustee or the holders of at least 25% in aggregate principal amount of the then outstanding debt securities of such series may declare the principal amount (or, if the debt securities of such series are issued at an original issue discount, such portion of the principal amount as may be specified in the terms of the debt securities of such series) of all debt securities of such series or such other amount or amounts as the debt securities or supplemental indenture with respect to such series may provide, to be due and payable immediately. Any provisions pertaining to events of default and any remedies associated therewith will be described in the applicable prospectus supplement.

Any indenture that governs our debt securities covered by this prospectus may require that the trustee under such indenture shall, within 90 days after the occurrence of a default, give to holders of debt securities of any series notice of all uncured defaults with respect to such series known to it. However, in the case of a default that results from the failure to make any payment of the principal of, premium or make-whole amount, if any, or interest on the debt securities of any series, or in the payment of any mandatory sinking fund installment with respect to debt securities of such series, if any, the trustee may withhold such notice if it in good faith determines that the withholding of such notice is in the interest of the holders of debt securities of such series. Any terms and provisions relating to the foregoing types of provisions will be described in further detail in the applicable prospectus supplement.

Any indenture that governs our debt securities covered by this prospectus will contain a provision entitling the trustee to be indemnified by holders of debt securities before proceeding to exercise any trust or power under the indenture at the request of such holders. Any such indenture may provide that the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of any series may direct the time, method, and place of conducting any proceedings for any remedy available to the trustee, or of exercising any trust or power conferred upon the trustee with respect to the debt securities of such series. However, the trustee under any such indenture may decline to follow any such direction if, among other reasons, the trustee determines in good faith that the actions or proceedings as directed may not lawfully be taken, would involve the trustee in personal liability or would be unduly prejudicial to the holders of the debt securities of such series not joining in such direction.

17

Any indenture that governs our debt securities covered by this prospectus may endow the holders of such debt securities to institute a proceeding with respect to such indenture, subject to certain conditions, which will be specified in the applicable prospectus supplement and which may include, that the holders of at least a majority in aggregate principal amount of the debt securities of such series then outstanding make a written request upon the trustee to exercise its power under the indenture, indemnify the trustee and afford the trustee reasonable opportunity to act. Even so, such holders may have an absolute right to receipt of the principal of, premium or make-whole amount, if any, and interest when due, to require conversion or exchange of debt securities if such indenture provides for convertibility or exchangeability at the option of the holder and to institute suit for the enforcement of such rights. Any terms and provisions relating to the foregoing types of provisions will be described in further detail in the applicable prospectus supplement.

Modification of the Indenture

We and the trustee may modify any indenture that governs our debt securities of any series covered by this prospectus with or without the consent of the holders of such debt securities, under certain circumstances to be described in a prospectus supplement.

Defeasance; Satisfaction and Discharge

The prospectus supplement will outline the conditions under which we may elect to have certain of our obligations under the indenture discharged and under which the indenture obligations will be deemed to be satisfied.

Regarding the Trustee

We will identify the trustee and any relationship that we may have with such trustee, with respect to any series of debt securities, in the prospectus supplement relating to the applicable debt securities. You should note that if the trustee becomes a creditor of the Company, the indenture and the Indenture Act limit the rights of the trustee to obtain payment of claims in certain cases, or to realize on certain property received in respect of any such claim, as security or otherwise. The trustee and its affiliates may engage in, and will be permitted to continue to engage in, other transactions with us and our affiliates. If, however, the trustee acquires any “conflicting interest” within the meaning of the Indenture Act, it must eliminate such conflict or resign.

Governing Law

The law governing the indenture and the debt securities will be identified in the prospectus supplement relating to the applicable indenture and debt securities.

18

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website at www.sec.gov that contains reports, statements, and other information about issuers, such as us, who file electronically with the SEC. We maintain a website at www.abonatherapeutics.com. However, the information on our website is not incorporated by reference into this prospectus and any prospectus supplement and you should not consider it a part of this prospectus or any accompanying prospectus supplement.

The SEC allows us to “incorporate by reference” into this prospectus the information in other documents that we file with it. This means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information in documents that we file later with the SEC will automatically update and supersede information contained in documents filed earlier with the SEC or contained in this prospectus. We incorporate by reference into this prospectus the documents listed below; provided, however, that we are not incorporating, in each case, any documents or information deemed to have been furnished and not filed in accordance with SEC rules:

- Our Annual Report on [Form 10-K](#) for the year ended December 31, 2020;
- Our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2021;
- Our Current Reports on Form 8-K or 8-K/A filed on [February 1, 2021](#), [March 23, 2021](#), [March 30, 2021](#), [April 19, 2021](#), [May 28, 2021](#), [May 28, 2021](#) and [November 19, 2021](#); and

- The description of our common stock, par value \$0.01 per share contained in our Registration Statement on [Form 8-A](#), dated and filed with the SEC on November 4, 2014, as updated by [Exhibit 4.4](#) to our Form 10-K for the fiscal year ended December 31, 2019, and including any amendments or reports 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 Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of this initial registration statement and prior to the effectiveness of this registration statement, but excluding any information furnished to and not 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 obtain a copy of any or all of the documents referred to above which may have been or may be incorporated by reference into this prospectus, except for exhibits to those documents (unless the exhibits are specifically incorporated by reference into those documents) at no cost to you by contacting us at the following address and telephone number: Investor Relations, Abeona Therapeutics Inc., 1330 Avenue of the Americas, 33rd Floor, New York, NY 10019, telephone (646) 813-4701.

19

LEGAL MATTERS

Unless otherwise specified in the prospectus supplement accompanying this prospectus, Morgan, Lewis & Bockius LLP will provide opinions regarding certain legal matters. Certain partners and attorneys of Morgan, Lewis & Bockius LLP hold shares of our common stock. Additional legal matters may be passed upon for us or any underwriters, dealers, or agents by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements incorporated by reference from the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020 have been audited by Whitley Penn LLP, an independent registered public accounting firm, as stated in their report, which is incorporated by reference into this prospectus. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

20

\$124,601,795



COMMON STOCK

PROSPECTUS SUPPLEMENT

Jefferies LLC

November 19, 2021
