

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

POST-EFFECTIVE AMENDMENT NO. 2
to
FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Annexon, Inc.

(Exact name of Registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

27-5414423
(I.R.S. Employer
Identification No.)

1400 Sierra Point Parkway, Bldg C, Suite 200
Brisbane, California 94005
(650) 822-5500

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

Douglas Love, Esq.
President and Chief Executive Officer
1400 Sierra Point Parkway, Bldg C, Suite 200
Brisbane, California 94005
(650) 822-5500

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

Copies to:

Jennifer Lew
Chief Financial Officer
Annexon, Inc.
1400 Sierra Point Parkway, Bldg C, Suite 200
Brisbane, California 94005
Telephone: (650) 822-5500

Kathleen M. Wells
Brian J. Cuneo
Richard Kim
Latham & Watkins LLP
140 Scott Drive
Menlo Park, CA 94025
Telephone: (650) 328-4600

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

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

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

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

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

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

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

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

Large accelerated filer	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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

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

EXPLANATORY NOTE

Post-Effective Amendment No. 1 to the Registration Statement on Form S-3 (File No. 333-258863), or Post-Effective Amendment No. 1, of Annexon, Inc., or the Company, was filed because the Company expected that it would no longer be a “well-known seasoned issuer” (as such term is defined in Rule 405 of the Securities Act of 1933, as amended) when it filed its Annual Report on Form 10-K for the fiscal year ended December 31, 2021. Accordingly, the Company filed Post-Effective Amendment No. 1 for the purpose of including disclosure required for a registrant other than a well-known seasoned issuer, identifying the securities being registered, registering a specific amount of securities and paying the associated filing fee.

This Post-Effective Amendment No. 2 to the Registration Statement on Form S-3, or Post-Effective Amendment No. 2, is being filed using EDGAR submission type POS AM in order to convert the Registration Statement to the proper EDGAR submission type for a non-automatic shelf registration statement.

This Post-Effective Amendment No. 2 contains:

- a base prospectus, which covers the offering, issuance and sale by the Company of up to \$300 million of the Company’s common stock, preferred stock, debt securities, warrants and/or units; and
- a sales agreement prospectus supplement, which covers the offering, issuance and sale by the Company of up to a maximum aggregate offering price of \$100 million of the Company’s common stock that may be issued and sold from time to time under a sales agreement with Cowen and Company, LLC.

The base prospectus immediately follows this explanatory note. The sales agreement prospectus supplement immediately follows the base prospectus. The specific terms of any other securities to be offered pursuant to the base prospectus will be specified in one or more additional prospectus supplements to the base prospectus. The \$100 million of common stock that may be offered, issued and sold under the sales agreement prospectus supplement is included in the \$300 million of securities that may be offered, issued and sold by the Company under the base prospectus. Upon termination of the sales agreement with Cowen and Company, LLC, any portion of the \$100 million included in the sales agreement prospectus supplement that is not sold pursuant to the sales agreement will be available for sale in other offerings pursuant to the base prospectus and a corresponding prospectus supplement, and if no shares are sold under the sales agreement, the full \$100 million of securities may be sold in other offerings pursuant to the base prospectus and a corresponding prospectus supplement.

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the U.S. Securities and Exchange Commission declares our registration statement effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state or jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MARCH 1, 2022

PROSPECTUS

ANNEXON

biosciences

ANNEXON, INC.

\$300,000,000

**Common Stock
Preferred Stock
Debt Securities
Warrants
Units**

We may offer and sell up to \$300,000,000 in the aggregate of the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

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

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

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "[RISK FACTORS](#)" ON PAGE 5 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "ANNX." On February 28, 2022, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$4.855 per share.

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

The date of this prospectus is _____, 2022.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC using a “shelf” registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings up to a total dollar amount of \$300,000,000 as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.”

We have not authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. In addition, the market and industry data and forecasts that may be included or incorporated by reference in this prospectus, any prospectus supplement or any applicable free writing prospectus may involve estimates, assumptions and other risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” contained in this prospectus, the applicable prospectus supplement and any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

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

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

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

Our corporate website address is www.annexonbio.com. The information on our website, however, is not, and should not be deemed to be, a part of this prospectus.

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

Incorporation by Reference

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

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

- Our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 1, 2022;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2020 from our [Definitive Proxy Statement](#) on Schedule 14A, filed with the SEC on April 22, 2021;
- Our Current Reports on Form 8-K (other than information furnished rather than filed), filed with the SEC on [January 4, 2022](#), [January 20, 2022](#) (other than Items 7.01 and 9.01), [February 3, 2022](#) and [February 22, 2022](#); and
- The description of our common stock, which is registered under Section 12 of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, in our registration statement on [Form 8-A](#), filed on July 21, 2020 and any amendment or reports filed for the purposes of updating the 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, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

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

Annexon, Inc.
1400 Sierra Point Parkway, Bldg C, Suite 200
Brisbane, California 94005
(650) 822-5500
Attention: Investor Relations

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

THE COMPANY

We are a clinical-stage biopharmaceutical company pioneering a new class of complement medicines designed to stop the classical complement pathway at its start, C1q, in order to bring therapies to patients suffering from serious complement-mediated autoimmune, neurodegenerative and ophthalmic disorders. C1q, the initiating molecule of the classical complement pathway, is a core component to the body's immune system that activates a powerful inflammatory cascade. We believe that by stopping the classical complement pathway at its start, our approach may have the potential to provide more complete protection against complement-mediated disorders of the body, brain and eye.

Our proprietary platform leverages well-researched classical complement-mediated autoimmune and neurodegenerative disease processes, both of which are triggered by aberrant activation of C1q. Evidence suggests that potent and selective inhibition of C1q can prevent tissue damage triggered in antibody-mediated autoimmune disease and preserve loss of functioning synapses associated with cognitive and functional decline in complement-mediated neurodegeneration. By taking an upstream complement approach targeting C1q, our treatments are designed to act as an "on/off switch" to block all downstream components of the classical complement pathway that lead to excess inflammation, tissue damage and patient disability in a host of complement-mediated disorders, while preserving the normal immune function of the lectin and alternative complement pathways involved in the clearance of pathogens and damaged cells.

We were incorporated under the laws of the State of Delaware on March 3, 2011. Our principal executive offices are located at 1400 Sierra Point Parkway, Bldg C, Suite 200, Brisbane, California 94005, and our telephone number is (650) 822-5500. Our corporate website address is www.annexonbio.com. Information contained on, or accessible through, our website shall not be deemed incorporated into and is not a part of this prospectus or the registration statement of which it forms a part. We have included our website in this prospectus solely as an inactive textual reference. Because (i) the aggregate worldwide market value of our voting common stock held by non-affiliates, or public float, exceeded \$700 million on June 30, 2021, (ii) we had been subject to the reporting requirements of Section 13(a) or 15(d) of the Exchange Act for at least twelve calendar months, (iii) we had previously filed an annual report under Section 13(a) or 15(d) of the Exchange Act and (iv) we were not eligible for smaller reporting company status because we exceed the public float and revenue threshold for such status, we qualified as a "large accelerated filer" under Rule 12b-2 of the Exchange Act as of the end of the 2021 fiscal year.

RISK FACTORS

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

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following summary describes our capital stock and the material provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, the amended and restated investors' rights agreement to which we and certain of our stockholders are parties and of the Delaware General Corporation Law. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and amended and restated investors' rights agreement, copies of which have been filed as exhibits to the registration statement of which this prospectus is part.

General

Our authorized capital stock consists of 300,000,000 shares of common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, par value \$0.001 per share.

Common Stock

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. The election of directors by our stockholders shall be determined by a plurality of the votes cast and our stockholders do not have cumulative voting rights in the election of directors. Other matters shall be generally decided by the affirmative vote of the holders of a majority of the votes cast (excluding abstentions and broker non-votes) on such matter. In addition, the affirmative vote of holders of 66 2/3% of the voting power of all of the then outstanding voting stock will be required to take certain actions, including amending certain provisions of our amended and restated certificate of incorporation, including the provisions relating to amending our amended and restated bylaws, the classified board and director liability.

Dividends

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

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are fully paid and nonassessable.

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Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of our common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action.

Registration Rights

Under our amended and restated investors' rights agreement, certain holders of shares of our common stock, or their transferees, have the right to require us to register their shares under the Securities Act so that those shares may be publicly resold, and certain holders of shares of our common stock, or their transferees, have the right to include their shares in any registration statement we file, in each case as described below.

Demand Registration Rights

Certain holders of shares of our common stock are entitled to certain demand registration rights. The holders of at least 60% of such registrable securities may, on not more than two occasions, request that we register all or a portion of their shares, subject to certain specified exceptions.

Piggyback Registration Rights

In the event that we propose to register any of our securities under the Securities Act, either for our own account or for the account of other security holders, certain holders of registrable securities will be entitled to certain "piggyback" registration rights allowing them to include their shares in such registration, subject to specified conditions and limitations.

S-3 Registration Rights

Certain holders of shares of our common stock are entitled to certain Form S-3 registration rights. The holders of at least 30% of such registrable securities may, on not more than two registrations on Form S-3 within any 12-month period, request that we register all or a portion of their shares on Form S-3 if we are qualified to file a registration statement on Form S-3, subject to specified exceptions. Such request for registration on Form S-3 must cover securities with an aggregate offering price which equals or exceeds \$1.0 million, net of selling expenses. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Anti-Takeover Effects of Provisions of Delaware Law and Our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

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

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

Delaware Anti-Takeover Statute

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

Undesignated Preferred Stock

The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to effect a change in control of our company. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

Special Stockholder Meetings

Our amended and restated certificate of incorporation provide that a special meeting of stockholders may be called at any time by our board of directors, but such special meetings may not be called by the stockholders or any other person or persons.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Stockholder Action by Written Consent

Our amended and restated certificate of incorporation precludes stockholder action by written consent without a meeting.

Classified Board; Election and Removal of Directors; Filling Vacancies

Our board of directors is divided into three classes, divided as nearly as equal in number as possible. The directors in each class serve for a three-year term, one class being elected each year by our stockholders, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, our stockholders holding a majority of the shares of

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common stock outstanding will be able to elect all of our directors. Our amended and restated certificate of incorporation provides for the removal of any of our directors only for cause and requires a stockholder vote by the holders of at least a 66 2/3% of the voting power of the then outstanding voting stock. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of the board, may only be filled by a resolution of the board of directors unless the board of directors determines that such vacancies shall be filled by the stockholders. This system of electing and removing directors and filling vacancies may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us because it generally makes it more difficult for stockholders to replace a majority of the directors.

Choice of Forum

Our amended and restated certificate of incorporation and amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: any derivative action or proceeding brought on our behalf; any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers or stockholders to us or to our stockholders; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws (as either may be amended from time to time); or any action asserting a claim against us that is governed by the internal affairs doctrine. As a result, any action brought by any of our stockholders with regard to any of these matters will need to be filed in the Court of Chancery of the State of Delaware and cannot be filed in any other jurisdiction; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation and amended and restated bylaws also provide that the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause of action against us or any of our directors, officers, employees or agents and arising under the Securities Act. Nothing in our amended and restated certificate of incorporation and amended and restated bylaws preclude stockholders that assert claims under the Exchange Act from bringing such claims in state or federal court, subject to applicable law.

If any action the subject matter of which is within the scope described above is filed in a court other than a court located within the State of Delaware, or a Foreign Action, in the name of any stockholder, such stockholder shall be deemed to have consented to the personal jurisdiction of the state and federal courts located within the State of Delaware in connection with any action brought in any such court to enforce the applicable provisions of our amended and restated certificate of incorporation and amended and restated bylaws and having service of process made upon such stockholder in any such action by service upon such stockholder's counsel in the Foreign Action as agent for such stockholder. Although our amended and restated certificate of incorporation and amended and restated bylaws contain the choice of forum provision described above, it is possible that a court could find that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder.

Amendment of Charter Provisions

The amendment of any of the above provisions in our amended and restated certificate of incorporation, except for the provision making it possible for our board of directors to issue undesignated preferred stock, requires approval by a stockholder vote by the holders of at least a 66 2/3% of the voting power of the then outstanding voting stock.

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

Limitation on Liability and Indemnification

Our amended and restated certificate of incorporation and our amended and restated bylaws limit our directors' liability, contain provisions that provide that we may indemnify our directors and officers to the fullest extent permitted under the DGCL. The DGCL provides that directors of a corporation will not be personally liable for monetary damages for breach of their fiduciary duties as directors, except for liability for any:

- transaction from which the director derives an improper personal benefit;
- act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or redemption of shares; or
- breach of a director's duty of loyalty to the corporation or its stockholders.

These limitations of liability do not apply to liabilities arising under federal securities laws and do not affect the availability of equitable remedies such as injunctive relief or recession.

The DGCL and our amended and restated bylaws provide that we will, in certain situations, indemnify our directors and officers and may indemnify other employees and other agents, to the fullest extent permitted by law. Any indemnified person is also entitled, subject to certain limitations, to advancement, direct payment or reimbursement of reasonable expenses (including attorneys' fees and disbursements) in advance of the final disposition of the proceeding.

In addition, we have entered, and intend to continue to enter, into separate indemnification agreements with our directors and officers. These indemnification agreements, among other things, require us to indemnify our directors and officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of their services as a director or officer, or any other company or enterprise to which the person provides services at our request.

We also maintain a directors' and officers' insurance policy pursuant to which our directors and officers are insured against liability for actions taken in their capacities as directors and officers.

We believe that these provisions in our amended and restated certificate of incorporation and amended and restated bylaws and these indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or control persons, in the opinion of the SEC, such indemnification is against public policy, as expressed in the Securities Act and is therefore unenforceable.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare, Inc. The transfer agent and registrar's address is 462 South 4th Street, Louisville, Kentucky 40202.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement or free writing prospectus, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a third party to be identified therein, as trustee. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

As used in this section only, “Annexon,” “we,” “our” or “us” refer to Annexon, Inc. excluding our subsidiary, unless expressly stated or the context otherwise requires.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer’s certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;

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- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;
- if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts 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;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

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We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, or the Depository, or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a “book-entry debt security”), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a “certificated debt security”) as set forth in the applicable prospectus supplement. Except as set forth under the heading “Global Debt Securities and Book-Entry System” below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see “Global Securities.”

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control), which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a “successor person”) unless:

- we are the surviving corporation or the successor person (if other than Annexion) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and

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- immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

“Event of Default” means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or Annexon and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Annexon; or
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus

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supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each Securityholder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading "Consolidation, Merger and Sale of Assets";
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;

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- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depositary;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading “Consolidation, Merger and Sale of Assets” and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (“covenant defeasance”).

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and
- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

No Personal Liability of Directors, Officers, Employees or Securityholders

None of our past, present or future directors, officers, employees or securityholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and

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releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum. (Section 10.10)

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. The following summary of material provisions of the warrants and warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;
- the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;
- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;
- the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;
- the terms of any rights to redeem or call the warrants;
- the date on which the right to exercise the warrants will commence and the date on which the right will expire;
- U.S. federal income tax consequences applicable to the warrants; and
- any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

- to vote, consent or receive dividends;
- receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or
- exercise any rights as stockholders of Annexon.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

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A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain U.S. federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in any applicable prospectus supplement or free writing prospectus, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, as depository, or DTC, and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depository to its nominee or by the nominee to the depository, or by the depository or its nominee to a successor depository or to a nominee of the successor depository.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a “banking organization” within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a “clearing corporation” within the meaning of the New York Uniform Commercial Code; and
- a “clearing agency” registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants’ accounts, thereby eliminating the need for physical movement of securities certificates. “Direct participants” in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC’s records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants’ records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC’s partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC’s records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

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So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depository and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depository or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below and unless if otherwise provided in the description of the applicable securities herein or in the applicable prospectus supplement, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in "street name." Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility, disbursement of payments to direct participants is the responsibility of DTC, and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depository with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depository is not obtained, securities certificates are required to be printed and delivered.

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As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

- DTC notifies us that it is unwilling or unable to continue as a depository for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depository is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;
- we determine, in our sole discretion, not to have such securities represented by one or more global securities; or
- an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depository directs. It is expected that these directions will be based upon directions received by the depository from its participants with respect to ownership of beneficial interests in the global securities.

Euroclear and Clearstream

If so provided in the applicable prospectus supplement, you may hold interests in a global security through Clearstream Banking S.A., which we refer to as "Clearstream," or Euroclear Bank S.A./N.V., as operator of the Euroclear System, which we refer to as "Euroclear," either directly if you are a participant in Clearstream or Euroclear or indirectly through organizations which are participants in Clearstream or Euroclear. Clearstream and Euroclear will hold interests on behalf of their respective participants through customers' securities accounts in the names of Clearstream and Euroclear, respectively, on the books of their respective U.S. depositories, which in turn will hold such interests in customers' securities accounts in such depositories' names on DTC's books.

Clearstream and Euroclear are securities clearance systems in Europe. Clearstream and Euroclear hold securities for their respective participating organizations and facilitate the clearance and settlement of securities transactions between those participants through electronic book-entry changes in their accounts, thereby eliminating the need for physical movement of certificates.

Payments, deliveries, transfers, exchanges, notices and other matters relating to beneficial interests in global securities owned through Euroclear or Clearstream must comply with the rules and procedures of those systems. Transactions between participants in Euroclear or Clearstream, on one hand, and other participants in DTC, on the other hand, are also subject to DTC's rules and procedures.

Investors will be able to make and receive through Euroclear and Clearstream payments, deliveries, transfers and other transactions involving any beneficial interests in global securities held through those systems only on days when those systems are open for business. Those systems may not be open for business on days when banks, brokers and other institutions are open for business in the United States.

Cross-market transfers between participants in DTC, on the one hand, and participants in Euroclear or Clearstream, on the other hand, will be effected through DTC in accordance with the DTC's rules on behalf of Euroclear or Clearstream, as the case may be, by their respective U.S. depositories; however, such cross-market transactions will require delivery of instructions to Euroclear or Clearstream, as the case may be, by the counterparty in such system in accordance with the rules and procedures and within the established deadlines (European time) of such system. Euroclear or Clearstream, as the case may be, will, if the transaction meets its settlement requirements, deliver instructions to its U.S. depository to take action to effect final settlement on its behalf by delivering or receiving interests in the global securities through DTC, and making or receiving payment in accordance with normal procedures for same-day fund settlement. Participants in Euroclear or Clearstream may not deliver instructions directly to their respective U.S. depositories.

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Due to time zone differences, the securities accounts of a participant in Euroclear or Clearstream purchasing an interest in a global security from a direct participant in DTC will be credited, and any such crediting will be reported to the relevant participant in Euroclear or Clearstream, during the securities settlement processing day (which must be a business day for Euroclear or Clearstream) immediately following the settlement date of DTC. Cash received in Euroclear or Clearstream as a result of sales of interests in a global security by or through a participant in Euroclear or Clearstream to a direct participant in DTC will be received with value on the settlement date of DTC but will be available in the relevant Euroclear or Clearstream cash account only as of the business day for Euroclear or Clearstream following DTC's settlement date.

Other

The information in this section of this prospectus concerning DTC, Clearstream, Euroclear and their respective book-entry systems has been obtained from sources that we believe to be reliable, but we do not take responsibility for this information. This information has been provided solely as a matter of convenience. The rules and procedures of DTC, Clearstream and Euroclear are solely within the control of those organizations and could change at any time. Neither we nor the trustee nor any agent of ours or of the trustee has any control over those entities and none of us takes any responsibility for their activities. You are urged to contact DTC, Clearstream and Euroclear or their respective participants directly to discuss those matters. In addition, although we expect that DTC, Clearstream and Euroclear will perform the foregoing procedures, none of them is under any obligation to perform or continue to perform such procedures and such procedures may be discontinued at any time. Neither we nor any agent of ours will have any responsibility for the performance or nonperformance by DTC, Clearstream and Euroclear or their respective participants of these or any other rules or procedures governing their respective operations.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

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

Each time that we sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Any common stock will be listed on the Nasdaq Global Select Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or

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purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. 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.

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.

LEGAL MATTERS

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Annexon, Inc. 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 of Annexon, Inc. as of December 31, 2021 and 2020, and for each of the years in the two-year period ended December 31, 2021, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2021 have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. The audit report covering the December 31, 2021 financial statements refers to a change to the accounting for leases.

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the U.S. Securities and Exchange Commission declares our registration statement effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state or jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MARCH 1, 2022

PROSPECTUS SUPPLEMENT

ANNEXON

biosciences

Up to \$100,000,000

Common Stock

We have entered into a sales agreement with Cowen and Company, LLC, or Cowen, relating to shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock, par value \$0.001 per share, having an aggregate offering price of up to \$100 million from time to time through Cowen, acting as our agent.

Our common stock is listed on the Nasdaq Global Select Market under the symbol “ANNX.” On February 28, 2022, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$4.855 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made by any method deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Cowen is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms set forth in the sales agreement. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Cowen for sales of common stock pursuant to the sales agreement will be an amount up to 3.0% of the gross proceeds of the sales price per share of common stock sold under the sales agreement. See “Plan of Distribution” beginning on page S-13 for additional information regarding the compensation to be paid to Cowen. In connection with the sale of the common stock on our behalf, Cowen will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cowen with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act.

INVESTING IN OUR COMMON STOCK INVOLVES RISKS. SEE THE “[RISK FACTORS](#)” ON PAGE S-7 OF THIS PROSPECTUS SUPPLEMENT AND IN THE DOCUMENTS INCORPORATED BY REFERENCE IN THIS PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR COMMON STOCK.

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

Cowen

The date of this prospectus is _____, 2022.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a registration statement that we have filed with the Securities and Exchange Commission, or the SEC, utilizing a “shelf” registration process. By using a shelf registration statement, we may offer shares of our common stock having an aggregate offering price of up to \$100 million from time to time under this prospectus supplement at prices and on terms to be determined by market conditions at the time of offering.

We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates.

We have not, and Cowen has not, authorized anyone to provide any information other than that contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and Cowen take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not, and Cowen is not, making an offer to sell or soliciting an offer to buy our securities in any jurisdiction where 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, 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. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this 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 sections of this prospectus supplement titled “Where You Can Find More Information” and “Information Incorporated by Reference.”

We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus outside the United States. This prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

When we refer to “Annexon,” “we,” “our,” “us” and the “Company” in this prospectus, we mean Annexon, Inc. and its consolidated subsidiary, unless otherwise specified. When we refer to “you,” we mean the potential holders of our common stock.

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“Annexon,” “Annexon Biosciences,” the Annexon logo and other trade names, trademarks or service marks of Annexon are the property of Annexon, Inc. This prospectus also contains references to our trademarks and to trademarks belonging to other entities. Trade names, trademarks and service marks of other companies appearing in this report are the property of their respective holders. We do not intend our use or display of other companies’ trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. Solely for convenience, the trade names and trademarks may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert their rights thereto.

MARKET, INDUSTRY AND OTHER DATA

This prospectus supplement, including the information incorporated by reference herein, contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

PROSPECTUS SUPPLEMENT SUMMARY

This summary provides a general overview of selected information and does not contain all of the information you should consider before buying our common stock. Therefore, you should read the entire prospectus supplement, accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the information incorporated by reference herein and therein, before deciding to invest in our common stock. Investors should carefully consider the information set forth under “Risk Factors” beginning on page S-7 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement, including our Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q.

Annexon, Inc.

Overview

We are a clinical-stage biopharmaceutical company pioneering a new class of complement medicines designed to stop the classical complement pathway at its start, C1q, in order to bring therapies to patients suffering from serious complement-mediated autoimmune, neurodegenerative and ophthalmic disorders. C1q, the initiating molecule of the classical complement pathway, is a core component to the body’s immune system that activates a powerful inflammatory cascade. We believe that by stopping the classical complement pathway at its start, our approach may have the potential to provide more complete protection against complement-mediated disorders of the body, brain and eye.

Our proprietary platform leverages well-researched classical complement-mediated autoimmune and neurodegenerative disease processes, both of which are triggered by aberrant activation of C1q. Evidence suggests that potent and selective inhibition of C1q can prevent tissue damage triggered in antibody-mediated autoimmune disease and preserve loss of functioning synapses associated with cognitive and functional decline in complement-mediated neurodegeneration. By taking an upstream complement approach targeting C1q, our treatments are designed to act as an “on/off switch” to block all downstream components of the classical complement pathway that lead to excess inflammation, tissue damage and patient disability in a host of complement-mediated disorders, while preserving the normal immune function of the lectin and alternative complement pathways involved in the clearance of pathogens and damaged cells.

We are advancing a broad pipeline of product candidates designed to block the activity of C1q and the entire classical complement pathway for a range of complement-mediated diseases. Our development strategy is focused on areas where C1q and the classical complement pathway is the key driver of disease. Our pipeline includes three clinical-stage assets across three therapeutic franchises:

- **Autoimmune.** We are advancing our lead candidate, ANX005, an investigational, full-length monoclonal antibody formulated for intravenous administration for several autoimmune indications. ANX005 is currently being evaluated in a Phase 2/3 clinical trial for the potential treatment of patients with Guillain-Barré Syndrome (GBS) with data anticipated in 2023 and a Phase 2 trial in patients with warm autoimmune hemolytic anemia (wAIHA) with data anticipated in the second half of 2022. Our ANX009 clinical candidate is a subcutaneous formulation of an antigen-binding fragment, or Fab. ANX009 has been evaluated in a Phase 1 trial and based on the data from this trial, we plan to advance ANX009 into a Phase 1b trial in patients with lupus nephritis (LN) with initial data expected in the second half of 2022.
- **Neurodegeneration.** We are also developing ANX005 for the potential treatment of neurodegenerative indications. ANX005 is currently being evaluated in Phase 2 trials in Huntington’s disease (HD) and amyotrophic lateral sclerosis (ALS). Interim data from the HD trial showed improvements in clinical

measures and that ANX005 had been generally well tolerated. We plan to present the full data from our HD trial in the second quarter of 2022. Data from the Phase 2 trial of ANX005 in patients with ALS is expected to be reported in 2023.

- **Ophthalmology.** Our ANX007 program is a Fab formulated for intravitreal administration for the potential treatment of neurodegenerative diseases of the eye. We are currently conducting a Phase 2 trial in patients with geographic atrophy (GA) with data expected in 2023.

Beyond our clinical-stage assets, our preclinical portfolio of next generation product candidates includes ANX105, an investigational monoclonal antibody targeting neurodegenerative indications, and ANX1502, an investigational oral small molecule in development for the treatment of certain autoimmune indications. Based on learnings from our initial trials and our expertise in the role of C1q and the classical complement pathway, we are evaluating additional orphan and large market indications that are driven by aberrant or excess classical complement activation

Corporate Information

We were incorporated under the laws of the State of Delaware on March 3, 2011. Our principal executive offices are located at 1400 Sierra Point Parkway, Bldg C, Suite 200, Brisbane, California 94005, and our telephone number is (650) 822-5500. Our corporate website address is www.annexonbio.com. Information contained on, or accessible through, our website shall not be deemed incorporated into and is not a part of this prospectus or the registration statement of which it forms a part. We have included our website in this prospectus solely as an inactive textual reference. Because (i) the aggregate worldwide market value of our voting common stock held by non-affiliates, or public float, exceeded \$700 million on June 30, 2021, (ii) we had been subject to the reporting requirements of Section 13(a) or 15(d) of the Exchange Act for at least twelve calendar months, (iii) we had previously filed an annual report under Section 13(a) or 15(d) of the Exchange Act and (iv) we were not eligible for smaller reporting company status because we exceed the public float and revenue threshold for such status, we qualified as a “large accelerated filer” under Rule 12b-2 of the Exchange Act as of the end of the 2021 fiscal year.

THE OFFERING

Common Stock Offered by Us	Shares of our common stock having an aggregate offering price of up to \$100 million.
Common Stock Outstanding After this Offering	Up to 59,158,176 shares, assuming sales at a price of \$4.855 per share, which was the closing price of our common stock on the Nasdaq Global Select Market on February 28, 2022. The actual number of shares issued will vary depending on the sales price under this offering.
Plan of Distribution	“At the market offering” that may be made from time to time through our sales agent, Cowen. See “Plan of Distribution” on page S-13.
Use of Proceeds	We intend to use the net proceeds from this offering, if any, for general corporate purposes, which may include, among other things, working capital and funding research and development, and capital expenditures including clinical program progression. See “Use of Proceeds” on page S-11.
Risk Factors	You should read the “Risk Factors” section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to purchase shares of our common stock.
Nasdaq Global Select Market Symbol	“ANNX”

The number of shares of common stock to be outstanding after this offering is based on 38,560,854 shares of common stock outstanding as of December 31, 2021 and excludes the following:

- 5,662,824 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2021, with a weighted average exercise price of \$16.98 per share;
- 1,862,155 shares of our common stock issuable upon exercise of stock options outstanding that we granted after December 31, 2021 and through the date of this prospectus supplement, with a weighted-average exercise price of \$6.96 per share;
- 711,120 shares of our common stock issued after December 31, 2021 and through the date of this prospectus supplement upon exercise of outstanding stock options pursuant to 10b5-1 plans, with a weighted-average exercise price of \$6.94 per share;
- 50,000 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of December 31, 2021;
- 338,670 shares of our common stock issuable upon the vesting of restricted stock units outstanding that we granted after December 31, 2021;
- 2,039,951 shares of our common stock reserved for future issuance under our 2020 Incentive Award Plan as of December 31, 2021, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan; and
- 729,775 shares of our common stock reserved for future issuance under our Employee Stock Purchase Plan as of December 31, 2021, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan.

RISK FACTORS

Our business involves significant risks, some of which are described below. You should carefully review the risks and uncertainties described below and under the section titled “Risk Factors” contained in our Annual Report on Form 10-K for the year ended December 31, 2021, as updated by our subsequent filings under the Exchange Act, each of which is incorporated by reference in this prospectus supplement in their entirety, together with other information in this prospectus supplement and the accompanying prospectus, and the information and documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our common stock. If any of the following risks actually occur, it could harm our business, prospects, operating results and financial condition and future prospects. In such event, the market price of our common stock could decline and you could lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

Risks Relating to this Offering

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

Our management will have broad discretion over the use of proceeds from this offering. We intend to use the net proceeds, if any, from this offering for general corporate purposes, which may include, among other things, working capital and funding research and development, and capital expenditures including clinical program progression. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or enhance the value of our common stock.

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

The price per share of our common stock being offered may be higher than the net tangible book value per share of our common stock outstanding prior to this offering. If the share price is higher, then upon your purchase of shares you will suffer immediate and potentially substantial dilution, which would be calculated based on the difference between the as adjusted net tangible book value per share of our common stock after giving effect to any sales pursuant to this offering and the share price at which you purchase your shares. To the extent that outstanding options are exercised or outstanding restricted stock units are settled, investors purchasing our common stock in this offering may experience further dilution.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we expect to in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering.

The actual number of shares we will issue under the sales agreement, at any one time or in total, is uncertain.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver a placement notice to Cowen at any time throughout the term of the sales agreement. The number of

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shares that are sold by Cowen after delivering a placement notice will fluctuate based on the market price of our common stock during the sales period and limits we set with Cowen. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares that will be ultimately issued.

The common stock offered hereby will be sold in “at the market offerings,” and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, supplement, the accompany prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, based upon current expectations that involve risks and uncertainties. In some cases, you can identify forward-looking statements by terminology such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potentially,” “predict,” “should,” “will” or the negative of these terms or other similar expressions. These forward-looking statements include, but are not limited to, statements about:

- our expectations regarding the potential market size and size of the potential patient populations for our product candidates and any future product candidates, if approved for commercial use;
- our clinical and regulatory development plans;
- our expectations with regard to the results of our clinical studies, preclinical studies and research and development programs, including the timing and availability of data from such studies;
- the timing of commencement of future nonclinical studies and clinical trials and research and development programs;
- our ability to acquire, discover, develop and advance product candidates into, and successfully complete, clinical trials;
- our intentions and our ability to establish collaborations and/or partnerships;
- the timing or likelihood of regulatory filings and approvals for our product candidates;
- our commercialization, marketing and manufacturing capabilities and expectations;
- our intentions with respect to the commercialization of our product candidates;
- the pricing and reimbursement of our product candidates, if approved;
- the potential effects of COVID-19 on our preclinical and clinical programs and business;
- the implementation of our business model and strategic plans for our business and product candidates, including additional indications for which we may pursue;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, including the projected terms of patent protection;
- estimates of our expenses, future revenue, capital requirements, our needs for additional financing and our ability to obtain additional capital;
- our use of proceeds from this offering;
- our future financial performance; and
- developments and projections relating to our competitors and our industry, including competing products.

These forward-looking statements are based on management’s current expectations, estimates, forecasts and projections about our business and the industry in which we operate and management’s beliefs and assumptions and are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this prospectus may turn out to be inaccurate and you should not rely upon forward-looking statements as predictions of future events. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled “Risk Factors” in this prospectus

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and the documents incorporated by reference into this prospectus and elsewhere in this prospectus and therein. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time and it is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Potential investors are urged to consider these factors carefully in evaluating the forward-looking statements. These forward-looking statements speak only as of the date of this prospectus. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this prospectus. See “Where You Can Find More Information” and “Information Incorporated by Reference.”

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$100 million from time to time. The amount of proceeds from this offering will depend upon the number of shares of our common stock sold and the market price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the sales agreement with Cowen as a source of financing. We intend to use the net proceeds, if any, from this offering for general corporate purposes, which may include, among other things, increasing our working capital and funding research and development, and capital expenditures including clinical program progression.

The amounts and timing of our actual expenditures will depend on numerous factors, including our development and commercialization efforts with respect to our product candidates, as well as the amount of cash used in our operations. We therefore cannot estimate with certainty the amount of net proceeds to be used for the purposes described above. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds, if any, from this offering in short-term, investment-grade, interest-bearing securities.

DIVIDEND POLICY

We have never declared or paid, and do not anticipate declaring or paying in the foreseeable future, any cash dividends on our capital stock. Any future determination as to the declaration and payment of dividends, if any, will be at the discretion of our board of directors, subject to applicable laws and will depend on then existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects, and other factors our board of directors may deem relevant.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Cowen, under which we may issue and sell from time to time up to \$100,000,000 of our common stock through or to Cowen as our sales agent or principal. Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act.

Cowen will offer our common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our common stock being made through Cowen under the sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party’s sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent will be an amount up to 3.0% of the gross sales price of the shares sold through it pursuant to the sales agreement. We have also agreed to reimburse Cowen up to \$50,000 of Cowen’s actual outside legal expenses incurred by Cowen in connection with this offering. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$750,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on Nasdaq on each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the second business day that is also a trading day following the date on which any sales were made 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 sales of our common stock on our behalf, Cowen will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to Cowen will be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, Cowen will not engage in any transactions that stabilize our common stock.

Our common stock is listed on the Nasdaq Global Select Market and trades under the symbol “ANNX.” The transfer agent of our common stock is Computershare, Inc.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

LEGAL MATTERS

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Latham & Watkins LLP, Menlo Park, California. Cowen and Company, LLC is being represented in connection with this offering by Cooley LLP, New York, New York.

EXPERTS

The consolidated financial statements of Annexon, Inc. as of December 31, 2021 and 2020, and for each of the years in the two-year period ended December 31, 2021, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2021 have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. The audit report covering the December 31, 2021 financial statements refers to a change to the accounting for leases.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act, of which this prospectus forms a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement and the accompanying prospectus certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement and the accompanying prospectus, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus supplement and the accompanying prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

We file reports, proxy statements and other information with the SEC under the Exchange Act. The SEC maintains an Internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that website is <http://www.sec.gov>.

INFORMATION INCORPORATED BY REFERENCE

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

This prospectus incorporates by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 1, 2022;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2020 from our [Definitive Proxy Statement](#) on Schedule 14A, filed with the SEC on April 22, 2021;
- our Current Reports on Form 8-K (other than information furnished rather than filed), filed with the SEC on [January 4, 2022](#), [January 20, 2022](#) (other than Items 7.01 and 9.01), [February 3, 2022](#) and [February 22, 2022](#); and

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- the description of our common stock which is registered under Section 12 of the Exchange Act, in our registration statement on [Form 8-A](#), filed on July 21, 2020, including any amendment or reports filed for the purposes of updating this 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 and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

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

Annexon, Inc.
1400 Sierra Point Parkway, Bldg C, Suite 200
Brisbane, California 94005
(650) 822-5500
Attention: Investor Relations

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

ANNEXON

biosciences

Up to \$100,000,000

Common Stock

PROSPECTUS SUPPLEMENT

Cowen

, 2022

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following is an estimate (other than the SEC registration fee and the FINRA filing fee) of the expenses (all of which are to be paid by the registrant) that we may incur in connection with the securities being registered hereby.

SEC registration fee	\$ 29,450(1)
FINRA filing fee	\$225,500
Printing expenses	\$ (2)
Legal fees and expenses	\$ (2)
Accounting fees and expenses	\$ (3)
Blue Sky, qualification fees and expenses	\$ (2)
Transfer agent fees and expenses	\$ (2)
Trustee fees and expenses	\$ (2)
Warrant agent fees and expenses	\$ (2)
Miscellaneous	\$ (2)
Total	<u>\$ (2)(4)</u>

- (1) Previously paid. This amount includes the registration fee of \$10,910 previously paid in connection with the offering, issuance and sale of up to \$100,000,000 of the registrant's common stock pursuant to this registration statement and a sales agreement, dated as of August 16, 2021, by and between the registrant and Cowen and Company, LLC. The \$300,000,000 of shares of common stock registered pursuant to this registration statement includes \$100,000,000 of shares of common stock, or the Unsold Shares, registered pursuant to Registration Statement No. 333-258863 filed on August 16, 2021. Pursuant to Rule 415(a)(6) under the Securities Act of 1933, as amended, the filing fees previously paid in connection with the Unsold Shares will continue to be applied to the Unsold Shares.
- (2) These fees and expenses are calculated based on the securities offered and the number of issuances and accordingly cannot be estimated at this time.
- (3) These fees and expenses cannot be estimated at this time.
- (4) An estimate of the aggregate expenses in connection with the sale and distribution of securities being offered will be included in the applicable prospectus supplement.

Item 15. Indemnification of Directors and Officers

As permitted by Section 102 of the Delaware General Corporation Law, we have adopted provisions in our amended and restated certificate of incorporation and amended and restated bylaws that limit or eliminate the personal liability of our directors for a breach of their fiduciary duty of care as a director. The duty of care generally requires that, when acting on behalf of the corporation, directors exercise an informed business judgment based on all material information reasonably available to them. Consequently, a director will not be personally liable to the registrant or the registrant's stockholders for monetary damages for breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to the registrant or the registrant's stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any act related to unlawful stock repurchases, redemptions or other distributions or payment of dividends; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not affect the availability of equitable remedies such as injunctive relief or rescission. The registrant's amended and restated certificate of incorporation also authorizes the registrant to indemnify the registrant's officers, directors and other agents to the fullest extent permitted under Delaware law.

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As permitted by Section 145 of the Delaware General Corporation Law, the registrant's amended and restated bylaws provide that:

- the registrant may indemnify our directors, officers and employees to the fullest extent permitted by the Delaware General Corporation Law, subject to limited exceptions;
- the registrant may advance expenses to our directors, officers and employees in connection with a legal proceeding to the fullest extent permitted by the Delaware General Corporation Law, subject to limited exceptions; and
- the rights provided in our amended and restated bylaws are not exclusive.

The registrant's amended and restated certificate of incorporation and the registrant's amended and restated bylaws provide for the indemnification provisions described above and elsewhere herein. The registrant has entered or will enter into, and intend to continue to enter into, separate indemnification agreements with the registrant's directors and officers that may be broader than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements generally require the registrant, among other things, to indemnify the registrant's officers and directors against certain liabilities that may arise by reason of their status or service as directors or officers, other than liabilities arising from willful misconduct. These indemnification agreements also generally require the registrant to advance any expenses incurred by the directors or officers as a result of any proceeding against them as to which they could be indemnified. These indemnification provisions and the indemnification agreements may be sufficiently broad to permit indemnification of the registrant's officers and directors for liabilities, including reimbursement of expenses incurred, arising under the Securities Act of 1933, as amended, or the Securities Act.

The registrant has purchased and currently intends to maintain insurance on behalf of each and every person who is or was a director or officer of the registrant against any loss arising from any claim asserted against him or her and incurred by him or her in any such capacity, subject to certain exclusions.

The underwriting agreement between the registrant and the underwriters to be filed as Exhibit 1.1 to this registration statement provides for the indemnification by the underwriters of the registrant and the registrant's officers and directors who sign this registration statement for specified liabilities, including matters arising under the Securities Act.

Item 16. Exhibits

<u>Exhibit Number</u>	<u>Exhibit Description</u>	<u>Incorporated by Reference to Filings Indicated</u>			<u>Provided Herewith</u>
		<u>Form</u>	<u>Exhibit No.</u>	<u>Filing Date</u>	
1.1*	Form of Underwriting Agreement.				
1.2	Sales Agreement, dated August 16, 2021, by and between Annexon, Inc. and Cowen and Company, LLC	10-Q	10.1	8/16/21	
3.1	Amended and Restated Certificate of Incorporation.	8-K	3.1	7/28/20	
3.2	Amended and Restated Bylaws.	8-K	3.2	7/28/20	
4.1	Reference is made to Exhibits 3.1 through 3.2 .				
4.2	Form of Common Stock Certificate.	S-1	4.2	7/2/20	
4.3*	Form of Preferred Stock Certificate.				
4.4	Form of Indenture.	S-3	4.4	8/16/21	
4.5*	Form of Note.				
4.6*	Form of Warrant.				

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<u>Exhibit Number</u>	<u>Exhibit Description</u>	<u>Incorporated by Reference to Filings Indicated</u>			<u>Provided Herewith</u>
		<u>Form</u>	<u>Exhibit No.</u>	<u>Filing Date</u>	
4.7*	Form of Warrant Agreement.				
4.8*	Form of Unit Agreement.				
4.9	Amended and Restated Investors' Rights Agreement, dated as of June 30, 2020, by and among Annexon, Inc. and the investors listed therein.	S-1	10.1	7/2/20	
5.1	Opinion of Latham & Watkins LLP.				X
23.1	Consent of Independent Registered Public Accounting Firm.				X
23.2	Consent of Latham & Watkins LLP (included in Exhibit 5.1).				X
24.1	Powers of Attorney (incorporated by reference to the signature page hereto).				X
25.1*	Statement of Eligibility on Form T-1 under the Trust Indenture Act of 1939, as amended, of the trustee, as trustee under the indenture filed herewith.				
107.1	Filing Fee Table.	S-3	107.1	3/1/22	

* To be filed by amendment or incorporated by reference in connection with the offering of the securities.

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the

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registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

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

(j) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act (the "Act") in accordance with the rules and regulations prescribed by the SEC under Section 305(b)(2) of the Act.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Post-Effective Amendment No. 2 to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Brisbane, California, on March 1, 2022.

ANNEXON, INC.

By: /s/ Douglas Love
Douglas Love, Esq.
Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this Post-Effective Amendment No. 2 to the Registration Statement has been signed below by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ Douglas Love, Esq.</u> Douglas Love, Esq.	President and Chief Executive Officer <i>(Principal Executive Officer)</i>	March 1, 2022
<u>/s/ Jennifer Lew</u> Jennifer Lew	Executive Vice President and Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i>	March 1, 2022
<u>*</u> Thomas G. Wiggans	Chairperson of the Board of Directors	March 1, 2022
<u>*</u> William H. Carson, M.D.	Director	March 1, 2022
<u>*</u> Jung E. Choi	Director	March 1, 2022
<u>*</u> Bettina M. Cockroft, M.D.	Director	March 1, 2022
<u>*</u> Muneer Satter	Director	March 1, 2022
<u>*</u> William D. Waddill	Director	March 1, 2022

*By: /s/ Jennifer Lew
Jennifer Lew
Attorney-in-Fact

LATHAM & WATKINS^{LLP}

140 Scott Drive
Menlo Park, California 94025
Tel: +1.650.328.4600 Fax: +1.650.463.2600
www.lw.com

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March 1, 2022

Annexon, Inc.
1400 Sierra Point Parkway, Bldg C, Suite 200
Brisbane, CA 94005

Re: Post-Effective Amendment No. 2 to the Registration Statement on Form S-3

To the addressee set forth above:

We have acted as special counsel to Annexon, Inc., a Delaware corporation (the “*Company*”), in connection with its filing on the date hereof with the Securities and Exchange Commission (the “*Commission*”) of a Post-Effective Amendment No. 2 to the registration statement on Form S-3 filed by the Company on August 16, 2021 (Registration No. 333-258863) (as amended, the “*Registration Statement*”), including a base prospectus (the “*Base Prospectus*”), which provides that it will be supplemented by one or more prospectus supplements (each such prospectus supplement, together with the Base Prospectus, a “*Prospectus*”), under the Securities Act of 1933, as amended (the “*Act*”), relating to the registration for issue and sale by the Company of up to \$300,000,000 aggregate offering amount of (i) shares of the Company’s common stock, par value \$0.001 per share (the “*Common Stock*”), (ii) shares of one or more series of the Company’s preferred stock, par value \$0.001 per share (the “*Preferred Stock*”), (iii) one or more series of the Company’s debt securities (collectively, “*Debt Securities*”) to be issued under an indenture to be entered into between the Company, as issuer, and a trustee (a form of which is included as Exhibit 4.4 to the Registration Statement) and one or more board resolutions, supplements thereto or officer’s certificates thereunder (such indenture, together with the applicable board resolution, supplement or officer’s certificate pertaining to the applicable series of Debt Securities, the “*Applicable Indenture*”), (iv) warrants (“*Warrants*”) and (v) units (“*Units*”), plus any additional Common Stock, Preferred Stock, Debt Securities, Warrants and Units that may be registered pursuant to any subsequent registration statement that the Company may hereafter file with the Commission pursuant to Rule 462(b) under the Act in connection with the offering by the Company contemplated by the Registration Statement. The Common Stock, Preferred Stock, Debt Securities, Warrants and Units are referred to herein collectively as the “*Securities*.”

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We also have acted as special counsel to the Company in connection with the sale through Cowen and Company, LLC as the sales agent (the “**Sales Agent**”) from time to time by the Company of shares of Common Stock (the “**Sales Agreement Shares**”) having an aggregate offering price of up to \$100,000,000 pursuant to the Registration Statement, the Base Prospectus and the related prospectus supplement for the sale of the Sales Agreement Shares included in the Registration Statement (the Base Prospectus and such prospectus supplement, collectively, the “**Sales Agreement Prospectus**”), and that certain Sales Agreement dated as of August 16, 2021 between the Sales Agent and the Company (the “**Sales Agreement**”).

This opinion is being furnished in connection with the requirements of Item 601(b)(5) of Regulation S-K under the Act, and no opinion is expressed herein as to any matter pertaining to the contents of the Registration Statement or related applicable Prospectus or the Sales Agreement Prospectus, other than as expressly stated herein with respect to the issuance of the Securities, including the issuance of the Sales Agreement Shares.

As such counsel, we have examined such matters of fact and questions of law as we have considered appropriate for purposes of this letter. With your consent, we have relied upon certificates and other assurances of officers of the Company and others as to factual matters without having independently verified such factual matters. We are opining herein as to the General Corporation Law of the State of Delaware (the “**DGCL**”), and with respect to the opinions set forth in paragraphs 3 through 5 below, the internal laws of the State of New York, and we express no opinion with respect to the applicability thereto, or the effect thereon, of the laws of any other jurisdiction or, in the case of Delaware, any other laws, or as to any matters of municipal law or the laws of any local agencies within any state.

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

1. When an issuance of Common Stock has been duly authorized by all necessary corporate action of the Company, upon issuance, delivery and payment therefor in an amount not less than the par value thereof in the manner contemplated by the applicable Prospectus and by such corporate action, and in total amounts and numbers of shares that do not exceed the respective total amounts and numbers of shares (a) available under the certificate of incorporation and (b) authorized by the board of directors in connection with the offering contemplated by the applicable Prospectus, such shares of Common Stock will be validly issued, fully paid and nonassessable. In rendering the foregoing opinion, we have assumed that the Company will comply with all applicable notice requirements regarding uncertificated shares provided in the DGCL.

2. When a series of Preferred Stock has been duly established in accordance with the terms of the Company’s certificate of incorporation and authorized by all necessary corporate action of the Company, upon issuance, delivery and payment therefor in an amount not less than the par value thereof in the manner contemplated by the applicable Prospectus and by such corporate action, and in total amounts and numbers of shares that do not exceed the respective total amounts and numbers of shares (a) available under the certificate of incorporation and (b) authorized by the board of directors in connection with the offering contemplated by the applicable Prospectus, such shares of such series of Preferred Stock will be validly issued, fully paid and nonassessable. In rendering the foregoing opinion, we have assumed that the Company will comply with all applicable notice requirements regarding uncertificated shares provided in the DGCL.

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3. When the Applicable Indenture has been duly authorized, executed and delivered by all necessary corporate action of the Company, and when the specific terms of a particular series of Debt Securities have been duly established in accordance with the terms of the Applicable Indenture and authorized by all necessary corporate action of the Company and such Debt Securities have been duly executed, authenticated, issued and delivered against payment therefor in accordance with the terms of the Applicable Indenture and in the manner contemplated by the applicable Prospectus and by such corporate action, such Debt Securities will be legally valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

4. When the applicable warrant agreement has been duly authorized, executed and delivered by all necessary corporate action of the Company, and when the specific terms of a particular issuance of Warrants have been duly established in accordance with the terms of the applicable warrant agreement and authorized by all necessary corporate action of the Company, and such Warrants have been duly executed, authenticated, issued and delivered against payment therefor in accordance with the terms of the applicable warrant agreement and in the manner contemplated by the applicable Prospectus and by such corporate action (assuming the securities issuable upon exercise of such Warrants have been duly authorized and reserved for issuance by all necessary corporate action), such Warrants will be the legally valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

5. When the applicable unit agreement has been duly authorized, executed and delivered by all necessary corporate action of the Company, and when the specific terms of a particular issuance of Units have been duly authorized in accordance with the terms of the applicable unit agreement and authorized by all necessary corporate action of the Company, and such Units have been duly executed, authenticated, issued and delivered against payment therefor in accordance with the terms of the applicable unit agreement and in the manner contemplated by the applicable Prospectus and by such corporate action (assuming the securities issuable upon exercise of such Units have been duly authorized and reserved for issuance by all necessary corporate action), such Units will be the legally valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

6. Upon the completion of all Corporate Proceedings (as defined below) relating to the Sales Agreement Shares, when the Sales Agreement Shares shall have been duly registered on the books of the transfer agent and registrar therefor in the name or on behalf of the purchasers, and have been issued by the Company against payment therefor (not less than par value) in accordance with the Corporate Proceedings and the terms of the Sales Agreement, the issuance and sale of the Sales Agreement Shares will have been duly authorized by all necessary corporate action of the Company, and the Sales Agreement Shares will be validly issued, fully paid and nonassessable. In rendering the foregoing opinion, we have assumed that (i) the Company will comply with all applicable notice requirements regarding uncertificated shares

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provided in the DGCL, (ii) upon the issuance of any of the Sales Agreement Shares, the total number of shares of Common Stock issued and outstanding will not exceed the total number of shares of Common Stock that the Company is then authorized to issue under the Company's certificate of incorporation and (iii) certain terms of the Sales Agreement Shares to be issued by the Company from time to time will be authorized and approved by the board of directors of the Company or one or more committees thereof established by the board of directors of the Company with the authority to issue and sell Sales Agreement Shares pursuant to the Sales Agreement in accordance with the DGCL, the Company's certificate of incorporation, the by-laws of the Company and certain resolutions of the board of directors of the Company and one or more committees thereof (with such approvals referred to herein as the "**Corporate Proceedings**") prior to issuance thereof.

Our opinions are subject to: (i) the effect of bankruptcy, insolvency, reorganization, preference, fraudulent transfer, moratorium or other similar laws relating to or affecting the rights and remedies of creditors; (ii) the effect of general principles of equity, whether considered in a proceeding in equity or at law (including the possible unavailability of specific performance or injunctive relief), concepts of materiality, reasonableness, good faith and fair dealing and the discretion of the court before which a proceeding is brought; (iii) the invalidity under certain circumstances under law or court decisions of provisions providing for the indemnification of or contribution to a party with respect to a liability where such indemnification or contribution is contrary to public policy; and (iv) we express no opinion as to (a) any provision for liquidated damages, default interest, late charges, monetary penalties, make-whole premiums or other economic remedies to the extent such provisions are deemed to constitute a penalty, (b) consents to, or restrictions upon, governing law, jurisdiction, venue, arbitration, remedies or judicial relief, (c) waivers of rights or defenses, (d) any provision requiring the payment of attorneys' fees, where such payment is contrary to law or public policy, (e) any provision permitting, upon acceleration of any Debt Securities, collection of that portion of the stated principal amount thereof which might be determined to constitute unearned interest thereon, (f) the creation, validity, attachment, perfection, or priority of any lien or security interest, (g) advance waivers of claims, defenses, rights granted by law, or notice, opportunity for hearing, evidentiary requirements, statutes of limitation, trial by jury or at law, or other procedural rights, (h) waivers of broadly or vaguely stated rights, (i) provisions for exclusivity, election or cumulation of rights or remedies, (j) provisions authorizing or validating conclusive or discretionary determinations, (k) grants of setoff rights, (l) proxies, powers and trusts, (m) provisions prohibiting, restricting, or requiring consent to assignment or transfer of any right or property, (n) any provision to the extent it requires that a claim with respect to a security denominated in other than U.S. dollars (or a judgment in respect of such a claim) be converted into U.S. dollars at a rate of exchange at a particular date, to the extent applicable law otherwise provides, and (o) the severability, if invalid, of provisions to the foregoing effect.

With your consent, we have assumed (a) that each of the Debt Securities, Warrants, Units, Applicable Indenture, warrant agreements and unit agreements (collectively, the "**Documents**") will be governed by the internal laws of the State of New York, (b) that each of the Documents has been or will be duly authorized, executed and delivered by the parties thereto, (c) that each of the Documents constitutes or will constitute legally valid and binding obligations of the parties thereto other than the Company, enforceable against each of them in accordance

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with their respective terms, and (d) that the status of each of the Documents as legally valid and binding obligations of the parties will not be affected by any (i) breaches of, or defaults under, agreements or instruments, (ii) violations of statutes, rules, regulations or court or governmental orders, or (iii) failures to obtain required consents, approvals or authorizations from, or to make required registrations, declarations or filings with, governmental authorities.

This opinion is for your benefit in connection with the Registration Statement and may be relied upon by you and by persons entitled to rely upon it pursuant to the applicable provisions of the Act. We consent to your filing this opinion as an exhibit to the Registration Statement and to the reference to our firm contained in each of the Prospectus and the Sales Agreement Prospectus under the heading "Legal Matters." We further consent to the incorporation by reference of this letter and consent into any registration statement or post-effective amendment to the Registration Statement filed pursuant to Rule 462(b) under the Act with respect to the Securities. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission thereunder.

Sincerely,

/s/ Latham & Watkins LLP

Consent of Independent Registered Public Accounting Firm

We consent to the use of our report dated March 1, 2022, with respect to the consolidated financial statements of Annexon, Inc., and the effectiveness of internal control over financial reporting, incorporated herein by reference and to the reference to our firm under the heading “Experts” in the prospectus.

/s/ KPMG LLP

San Francisco, California

March 1, 2022