

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM S-3

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933



GENOCEA BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation or organization)

51-0596811

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

**100 Acorn Park Drive, Cambridge, MA 02140
(617) 876-8191**

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

**William Clark
President and Chief Executive Officer
100 Acorn Park Drive, 5th Floor
Cambridge, MA 02140
(617) 876-8191**

(Name, address, and telephone number of agent for service)

Please send copies of all communications to:

Marc A. Rubenstein
Ropes & Gray LLP
Prudential Tower
800 Boylston Street
Boston, MA 02199-3600
(617) 951-7000

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 upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

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

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

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by a 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 Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered⁽¹⁾	Proposed Maximum Offering Price per Unit⁽²⁾	Proposed Maximum Aggregate Offering Price⁽²⁾	Amount of Registration Fee⁽²⁾⁽³⁾
Common Stock, \$0.001 par value per share	(4)	(5)	(5)	—
Preferred Stock, \$0.001 par value per share	(4)	(5)	(5)	—
Warrants	(4)	(5)	(5)	—
Units	(4)	(5)	(5)	—
Total	\$ 300,000,000		\$ 300,000,000	\$ 32,730

- (1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), the shares being registered hereunder include such indeterminate number of shares of common stock and preferred stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends or similar transactions.
- (2) The proposed maximum per unit and aggregate offering price per class of security and proposed maximum aggregate offering price has been calculated pursuant to Rule 457(o) under the Securities Act.
- (3) Pursuant to Rule 415(a)(6) and Rule 457(p) under the Securities Act, the registrant will offset the filing fee by \$22,891 associated with the unsold securities under its registration statement on Form S-3 (No. 333-225086) initially filed with the Securities and Exchange Commission on May 21, 2018 (the "Prior Registration Statement") against the total filing fee of \$32,730 that would otherwise be due in connection with this registration statement. Pursuant to Rule 415(a)(6), the offering of unsold securities under the Prior Registration Statements will be deemed terminated as of the date of effectiveness of this registration statement.
- (4) There are being registered hereunder such indeterminate number of shares of common stock and preferred stock, such indeterminate number of warrants to purchase common stock and/or preferred stock and such indeterminate number of units to be sold by the registrant which together shall have an aggregate initial offering price not to exceed \$300,000,000. Any securities registered hereunder may be sold separately or in combination with the other securities registered hereunder. The proposed maximum offering price will be determined, from time to time, by the registrant in connection with the issuance by the registrant of the securities registered hereunder. The securities registered include such indeterminate number of shares of common stock and preferred stock and amount of debt securities as may be issued upon conversion of or exchange for preferred stock that provide for conversion or exchange, upon exercise of warrants or pursuant to the anti-dilution provisions of any such securities.
- (5) The proposed maximum offering price per unit and aggregate offering price per class of security will be determined from time to time by the registrant in connection with the issuance by the registrant of the securities registered hereunder and is not specified as to each class of security pursuant to General Instruction II.D. of Form S-3 under 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 Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

This registration statement contains one prospectus and two prospectus supplements:

- a basic prospectus which covers the offering, issuance and sale of up to \$300,000,000 of common stock, preferred stock, warrants or units of Genocea Biosciences, Inc. by us;
- a prospectus supplement covering the offering, issuance and sale of up to \$35,808,111 of our common stock that may be issued and sold under a sales agreement with Cowen and Company, LLC ("Cowen"); and
- a prospectus supplement covering the offering, issuance and sale of up to \$23,972,805 of our common stock that may be issued and sold to Lincoln Park Capital Fund, LLC ("Lincoln Park") under a purchase agreement entered into on October 23, 2019.

The basic prospectus immediately follows this explanatory note. The sales agreement and purchase agreement prospectus supplements immediately follow the basic prospectus. Upon termination of the sales agreement with Cowen or the purchase agreement with Lincoln Park, any portion of the \$35,808,111 included in the prospectus supplement that is not sold pursuant to the sales agreement or the \$23,972,805 included in the prospectus supplement that is not sold pursuant to the purchase agreement, respectively, will be available for sale in other offerings pursuant to the base prospectus, and if no shares are sold under the Cowen agreement or the Lincoln Park agreement, the full \$300,000,000 of securities may be sold in other offerings pursuant to the base prospectus and a corresponding prospectus supplement.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated April 29, 2021

PROSPECTUS

\$300,000,000



GENOCEA BIOSCIENCES, INC.

Common Stock

Preferred Stock

Warrants

We may offer and sell from time to time, in one or more series or issuances and on terms that we will determine at the time of the offering, any combination of the securities described in this prospectus, up to an aggregate amount of \$300.0 million.

We will provide specific terms of any offering in a supplement to this prospectus. Any prospectus supplement may also add, update, or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you purchase any of the securities offered hereby.

These securities may be offered and sold in the same offering or in separate offerings; to or through underwriters, dealers, and agents; or directly to purchasers. The names of any underwriters, dealers, or agents involved in the sale of our securities and their compensation will be described in the applicable prospectus supplement.

Our common stock is traded on The Nasdaq Capital Market under the symbol "GNCA." On April 26, 2021, the closing price of our common stock was \$2.73.

Investing in our securities involves risks. See "Risk Factors" on page 3, and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

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

Prospectus dated , 2021

TABLE OF CONTENTS

	<u>Page</u>
ABOUT THIS PROSPECTUS	1
ABOUT THE COMPANY	2
RISK FACTORS	3
FORWARD-LOOKING STATEMENTS	4
USE OF PROCEEDS	5
PLAN OF DISTRIBUTION	6
DESCRIPTION OF COMMON STOCK	8
DESCRIPTION OF PREFERRED STOCK	11
DESCRIPTION OF WARRANTS	12
DESCRIPTION OF UNITS	13
LEGAL MATTERS	14
EXPERTS	14
WHERE YOU CAN FIND MORE INFORMATION	14
INCORPORATION OF DOCUMENTS BY REFERENCE	14

You should rely only on the information contained in, or incorporated by reference into, this prospectus. We have not authorized anyone to give you information different from that contained in this prospectus. We are not making an offer to sell these securities in any jurisdiction where the offer is not permitted. The information contained in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of when this prospectus is delivered or when any sale of our securities occurs. Our business, financial condition, results of operations and prospects may have changed since that date.

ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission (the "SEC") using a "shelf" registration process. Under this shelf registration process, we may offer to sell any combination of the securities described in this prospectus in one or more offerings up to a total dollar amount of \$300.0 million. Each time we sell securities under this shelf registration, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the applicable prospectus supplement, including all documents incorporated herein by reference, together with additional information described under "Where You Can Find More Information" below.

This prospectus does not include all of the information that is in the registration statement. We omitted certain parts of the registration statement from this prospectus as permitted by the SEC. We refer you to the registration statement and its exhibits for additional information about us and the securities that may be sold under this prospectus.

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

"Genocea," the "Company," "we," "us," "our" and similar names refer to Genocea Biosciences, Inc. unless we state otherwise or the context otherwise requires.

ABOUT THE COMPANY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus. The summary may not contain all the information that you should consider before investing in our common stock. You should read the entire prospectus carefully, including "Risk Factors" contained in this prospectus and the documents incorporated by reference herein, before making an investment decision.

Overview

We are a biopharmaceutical company dedicated to discovering and developing novel cancer immunotherapies using our proprietary ATLAS™ platform. The ATLAS platform can profile each patient's CD4⁺ and CD8⁺ T cell immune responses to every potential target or "antigen" identified by next-generation sequencing of that patient's tumor. ATLAS zeroes in on both antigens that activate anti-tumor T cell responses and inhibitory antigens, Inhibigens™, that drive pro-tumor immune responses. We believe this approach ensures that cancer immunotherapies, such as vaccines and cellular therapies, focus T cell responses on the tumor targets most vulnerable to T cell targeting. Consequently, we believe that ATLAS may enable more immunogenic and efficacious cancer immunotherapies.

Corporate Information

We were incorporated under the laws of the State of Delaware in August 2006. Our principal executive offices are located at 100 Acorn Park Drive, 5th Floor, Cambridge, Massachusetts 02140, and our telephone number is (617) 876-8191. Genocea® and the Genocea logo are registered trademarks.

RISK FACTORS

An investment in our common stock involves risks. Prior to making a decision about investing in our common stock, you should consider carefully the risks together with all of the other information contained or incorporated by reference in this prospectus, including any risk factors described in any supplements to this prospectus, in our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q, any Current Reports on Form 8-K and in our subsequent filings with the SEC. Each of the referenced risks and uncertainties could adversely affect our business, prospects, operating results and financial condition, as well as adversely affect the value of an investment in our securities. Additional risks not known to us or that we believe are immaterial may also adversely affect our business, operating results and financial condition and the value of an investment in our securities.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and any information incorporated by reference into this prospectus or such prospectus supplement may contain certain “forward-looking statements.” You can generally identify these forward-looking statements by forward-looking words such as “believe,” “anticipate,” “expect,” “intend,” “plan,” “will,” “may,” “estimate,” “could,” “continue,” “ongoing,” “predict,” “potential,” “likely,” “seek” and other similar expressions, as well as variations or negatives of these words. You can also identify forward-looking statements by the fact that they do not relate strictly to historical or current facts. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes to differ materially from current expectations. These statements are likely to relate to, among other things, the timing, progress and success of our ongoing and planned preclinical studies or clinical trials, the expected timing of regulatory review of our product candidates and our ability to finance contemplated development activities and fund operations for a specified period of time.

Forward-looking statements are not guarantees of future performance and our actual results could differ materially from the results discussed in the forward-looking statements we make. In particular, you should consider the numerous risks described in the risk factors incorporated by reference to our most recent Annual Report on Form 10-K, our subsequent Quarterly Reports on Form 10-Q and any Current Reports on Form 8-K we file after the date of this prospectus, together with any amendments or supplements thereto, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and the risk factors contained in any applicable prospectus supplement or free writing prospectus. See “Where You Can Find More Information.”

As a result of these and other factors, we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. The forward-looking statements contained in this prospectus reflect our views as of the date hereof. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement, we intend to use the net proceeds we receive from our sale of the securities covered by this prospectus primarily for preclinical and clinical development of our lead product candidates, discovery, research and development of other product candidates and other general corporate purposes. Additional information on the use of net proceeds we receive from the sale of securities covered by this prospectus may be set forth in the prospectus supplement relating to the specific offering.

PLAN OF DISTRIBUTION

We may sell securities in any of the ways described below or in any combination:

- to or through underwriters or dealers;
- through one or more agents;
- directly to purchasers or to a single purchaser; or
- in "at the market offerings", within the meaning of Rule 415(a)(4) of the Securities Act of 1933, as amended (the "Securities Act") to or through a market maker or into an existing trading market, or an exchange or otherwise.

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

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

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

The prospectus supplement will describe the terms of the offering of the securities, including the following:

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

Any offering price and any discounts or concessions allowed or re-allowed or paid to dealers will be specified in the applicable prospectus supplement and may be changed from time to time.

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

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

Agents, underwriters and other third parties described above may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution from us with respect to payments which the agents, underwriters or other third parties may be required to make in respect thereof. Agents, underwriters and such other third parties may be customers of, engage in transactions with, or perform services for us in the ordinary course of business. We may also use underwriters or such other third parties with whom we have a material relationship. We will describe the nature of any such relationship in the applicable prospectus supplement.

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

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale. Any underwriters involved in the sale of the securities may qualify as "underwriters" within the meaning of Section 2(a)(11) of the Securities Act. In addition, the underwriters' commissions, discounts or concessions may qualify as underwriters' compensation under the Securities Act and the rules of the Financial Industry Regulatory Authority.

Our common stock is listed on The Nasdaq Capital Market. Underwriters may make a market in our common stock, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the development, maintenance or liquidity of any trading market for the securities.

Certain persons participating in an offering may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with rules and regulations under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a short covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

DESCRIPTION OF COMMON STOCK

The following summary of the terms of our common stock does not purport to be complete and is qualified in its entirety by reference to our fifth amended and restated certificate of incorporation and amended and restated by-laws, both of which are on file with the SEC as exhibits to previous filings, and the applicable provisions of the Delaware General Corporation Law. We refer in this section to our fifth amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated by-laws as our by-laws.

General

Our authorized capital stock consists of 170,000,000 shares of our common stock, par value \$0.001 per share. As of March 31, 2021, we had 54,368,582 shares of common stock outstanding.

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

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

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or by-laws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Anti-Takeover Effects of Our Certificate of Incorporation and Our By-Laws

Our certificate of incorporation and by-laws contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the company unless such takeover or change in control is approved by the board of directors.

These provisions include:

Classified Board. Our certificate of incorporation provides that our board of directors is divided into three classes of directors, with the classes as nearly equal in number as possible. As a result, approximately one-third of our board of directors will be elected each year. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board. Our certificate of incorporation also provides that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors. Our board of directors currently consists of seven members.

Action by Written Consent; Special Meetings of Stockholders. Our certificate of incorporation provides that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our certificate of incorporation and the by-laws also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors. Except as described above, stockholders are not permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors. Our certificate of incorporation provides that our directors may be removed only for cause by the affirmative vote of at least 75% of the voting power of our outstanding shares of capital stock, voting together as a single class. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Advance Notice Procedures. Our by-laws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting are only able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although the by-laws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the by-laws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Super Majority Approval Requirements. The Delaware General Corporation Law generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless either a corporation's certificate of incorporation or by-laws requires a greater percentage. Our certificate of incorporation and by-laws provide that the affirmative vote of holders of at least 75% of the total votes eligible to be cast in the election of directors is required to amend, alter, change or repeal the by-laws. This requirement of a supermajority vote to approve amendments to our by-laws could enable a minority of our stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares. Our authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum. Our certificate of incorporation provides that, subject to limited exceptions, the state or federal courts located in the State of Delaware are the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our by-laws, or (iv) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Listing

Our common stock is listed on The Nasdaq Capital Market under the symbol "GNCA."

DESCRIPTION OF PREFERRED STOCK

Under the terms of our certificate of incorporation, our board of directors is authorized to issue up to 25,000,000 shares of our preferred stock, par value \$0.001 per share, in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. No shares of preferred stock are currently outstanding. It is not possible to state the actual effect of the issuance of any shares of preferred stock upon the rights of the holders of common stock until the board of directors determines the specific rights of the holders of preferred stock. However, effects of the issuance of preferred stock include restricting dividends on common stock, diluting the voting power of common stock, impairing the liquidation rights of common stock, and making it more difficult for a third party to acquire us, which could have the effect of discouraging a third party from acquiring, or deterring a third party from paying a premium to acquire, a majority of our outstanding voting stock.

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

- the title and stated value;
- the number of shares offered, the liquidation preference per share and the purchase price;
- the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption, if applicable;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price (or how it will be calculated) and conversion period;
- voting rights, if any, of the preferred stock;
- a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of the Company; and
- any material limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the Company.

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

Transfer Agent and Registrar

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

DESCRIPTION OF WARRANTS

We may issue warrants to purchase shares of our common stock or preferred stock in one or more series together with other securities or separately, as described in each applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the applicable warrant agreements and the applicable prospectus supplement for the warrants. As of March 31, 2021, we had warrants outstanding that represent the right to acquire 51,001,641 shares of common stock.

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

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

Transfer Agent and Registrar

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

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 United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

LEGAL MATTERS

The validity of the issuance of the securities offered hereby will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. Additional legal matters may be passed on 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 Genoclea Biosciences, Inc. appearing in Genoclea Biosciences, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2020, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website at www.sec.gov that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including us.

We maintain a website at www.genoclea.com. Information contained in, or accessible through, our website is not a part of, and is not incorporated into, this prospectus, and you should not consider it part of this prospectus.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” into this prospectus the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus. We incorporate by reference into this prospectus the documents listed below and any future filings made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information “furnished” under Items 2.02, 7.01 or 9.01 on Form 8-K or other information “furnished” to the SEC which is not deemed filed and not incorporated in this prospectus, until the termination of the offering of securities described in the applicable prospectus supplement. We hereby incorporate by reference the following documents:

- our Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the SEC on February 22, 2021;
- 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, as filed with the SEC on April 29, 2021;
- our Current Reports on Form 8-K filed with the SEC on April 14, 2021; and
- description of our Common Stock contained in our Registration Statement on Form 8-A, as filed with the SEC on January 30, 2014, as supplemented by the description of our common stock contained in Exhibit 4.8 in our Annual Report on Form 10-K for the year ended December 31, 2019, as filed with the SEC on February 13, 2020, including any amendment or report filed for the purpose of updating such description.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus modifies, supersedes or replaces such statement.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Investor Relations
100 Acorn Park Drive, 5th Floor
Cambridge, Massachusetts 02140
(617) 876-8191
email address: ir@genoclea.com

Copies of these filings are also available, without charge, on the SEC’s website at www.sec.gov and on our website at www.genoclea.com as soon as reasonably practicable after they are filed electronically with the SEC. The information contained on our website is not a part of this prospectus.

\$300,000,000



GENOCEA BIOSCIENCES, INC.

Common Stock

Preferred Stock

Warrants

PROSPECTUS

, 2021

We have not authorized any dealer, salesperson or other person to give any information or represent anything not contained in this prospectus. You must not rely on any unauthorized information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not offer to sell any shares in any jurisdiction where it is unlawful. Neither the delivery of this prospectus, nor any sale made hereunder, shall create any implication that the information in this prospectus is correct after the date hereof.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated April 29, 2021

PROSPECTUS SUPPLEMENT

(To Prospectus dated , 2021)

\$35,808,111



GENOCEA BIOSCIENCES, INC.

Common Stock

We have entered into a sales agreement (the "Sales Agreement") with Cowen and Company, LLC ("Cowen"), relating to shares of our common stock offered by this prospectus supplement. In accordance with the terms of the Sales Agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$50,000,000. As of the date of this prospectus supplement, we had issued and sold shares of our common stock having an aggregated offering price of \$14,191,889 pursuant to the Sales Agreement and a prior prospectus and related prospectus supplement. Accordingly, we may offer and sell shares of our common stock having an aggregate offering price of up to \$35,808,111 pursuant to the Sales Agreement and this prospectus supplement.

Our common stock is traded on The Nasdaq Capital Market under the symbol "GNCA." On April 26, 2021, the closing price of our common stock was \$2.73.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made in sales deemed to be "at the market offerings" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended (the "Securities Act"). Cowen is not required to sell any specific amount of securities, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Cowen and us. 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 sold pursuant to the Sales Agreement will be an amount equal to 3.0% of the gross proceeds of any shares of common stock sold under the Sales Agreement. 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 Exchange Act of 1934, as amended ("the Exchange Act").

Investing in our common stock involves risks. See "Risk Factors" on page S-4, and under similar headings in the other documents that are incorporated by reference into this prospectus supplement.

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

Cowen

, 2021

TABLE OF CONTENTS

	Page
ABOUT THIS PROSPECTUS	S-1
SUMMARY	S-2
THE OFFERING	S-3
RISK FACTORS	S-4
FORWARD-LOOKING STATEMENTS	S-5
USE OF PROCEEDS	S-6
DILUTION	S-7
PLAN OF DISTRIBUTION	S-8
LEGAL MATTERS	S-9
EXPERTS	S-9
WHERE YOU CAN FIND MORE INFORMATION	S-9
INCORPORATION OF DOCUMENTS BY REFERENCE	S-9

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and certain other matters relating to us and our business. The second part, the accompanying prospectus, contains and incorporates by reference important business and financial information about us, a description of our common stock and certain other information about us and this offering. This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the Securities and Exchange Commission (the "SEC"), using a "shelf" registration process. Both this prospectus supplement and the accompanying prospectus include or incorporate by reference important information about us, our common stock and other information you should know before investing. You should read both this prospectus supplement and the accompanying prospectus, including all documents incorporated herein and therein by reference, together with the additional information described under "Where You Can Find More Information" herein and in the accompanying prospectus before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus we may provide to you in connection with this offering. We have not, and the sales agent has not, authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying 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 supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do 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 supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

This prospectus supplement may add to, update or change the information in the accompanying prospectus or the documents incorporated by reference herein and therein. If information in this prospectus supplement is inconsistent with information in the accompanying prospectus or the documents incorporated by reference herein and therein, this prospectus supplement will apply and will supersede that information in the accompanying prospectus or the documents incorporated by reference herein and therein.

"Genocea," the "Company," "we," "us," "our" and similar names refer to Genocea Biosciences, Inc. unless we state otherwise or the context otherwise requires.

SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement. The summary may not contain all the information that you should consider before investing in our common stock. You should read the entire prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein, before making an investment decision. You should also carefully consider the matters discussed in the section titled “Risk Factors” in this prospectus supplement, in the accompanying prospectus and in other periodic reports incorporated by reference herein and the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operation” and the financial statements and the notes to those financial statements incorporated by reference in this prospectus supplement before investing in our common stock.

Overview

We are a biopharmaceutical company dedicated to discovering and developing novel cancer immunotherapies using our proprietary ATLAS™ platform. The ATLAS platform can profile each patient's CD4⁺ and CD8⁺ T cell immune responses to every potential target or “antigen” identified by next-generation sequencing of that patient's tumor. ATLAS zeroes in on both antigens that activate anti-tumor T cell responses and inhibitory antigens, Inhibigens™, that drive pro-tumor immune responses. We believe this approach ensures that cancer immunotherapies, such as vaccines and cellular therapies, focus T cell responses on the tumor targets most vulnerable to T cell targeting. Consequently, we believe that ATLAS may enable more immunogenic and efficacious cancer immunotherapies.

Corporate Information

We were incorporated under the laws of the State of Delaware in August 2006. Our principal executive offices are located at 100 Acorn Park Drive, 5th Floor, Cambridge, Massachusetts 02140, and our telephone number is (617) 876-8191. Genocea® and the Genocea logo are registered trademarks.

THE OFFERING

Common stock offered by us	Shares of common stock having an aggregate offering price of up to \$35.8 million.
Common stock to be outstanding after this offering	Up to 13,116,524 shares, assuming sales at a price of \$2.73 per share, which was the closing price on The Nasdaq Capital Market on April 26, 2021. Actual number of shares issued will vary depending on the price at which shares may be sold from time to time under this offering.
Manner of offering	"At the market offering" that may be made from time to time through our agent, Cowen and Company, LLC. See "Plan of Distribution" on page S-8.
Use of proceeds	If we receive all \$35.8 million of gross proceeds of the sale of shares of our common stock under this prospectus, we anticipate our net proceeds, after deducting estimated commissions and expenses payable by us, will be approximately \$34.7 million. We intend to use the net proceeds from this offering primarily for preclinical and clinical development of our lead product candidates, and the discovery, research and development of other product candidates and other corporate purposes. See "Use of Proceeds" on page S-6.
Nasdaq Capital Market symbol	GNCA
Risk factors	See "Risk Factors" beginning on page S-4 of this prospectus for a discussion of factors that you should read and consider before investing in our securities.

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 54,368,582 shares outstanding as of March 31, 2021. The number of shares outstanding as of March 31, 2021 as used throughout this prospectus, unless otherwise indicated, excludes:

- 3,839,107 shares of common stock issuable upon exercise of stock options outstanding at March 31, 2021 at a weighted-average exercise price of \$5.30 per share;
- 2,433,823 shares of common stock issuable upon vesting of restricted stock units outstanding at March 31, 2021;
- 51,001,641 shares of common stock issuable upon the exercise of warrants outstanding at March 31, 2021 at a weighted-average exercise price of \$2.26 per share;
- 659,653 shares of common stock reserved for future issuance under our Amended and Restated 2014 Equity Incentive Plan at March 31, 2021; and
- 141,337 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan at March 31, 2021.

RISK FACTORS

An investment in our common stock involves risks. Prior to making a decision about investing in our common stock, you should consider carefully the risks together with all of the other information contained or incorporated by reference in this prospectus supplement, including any risks described in the section entitled "Risk Factors" contained in any supplements to this prospectus supplement, in our Annual Report on Form 10-K for the year ended December 31, 2020 and in our subsequent filings with the SEC. Each of the referenced risks and uncertainties could adversely affect our business, prospects, operating results and financial condition, as well as adversely affect the value of an investment in our securities. Additional risks not known to us or that we believe are immaterial may also adversely affect our business, operating results and financial condition and the value of an investment in our securities.

Risks Relating to this Offering

We may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

We currently intend to use the net proceeds of this offering, if any, for preclinical and clinical development of our lead product candidates, discovery, research and development of other product candidates and for other general corporate purposes. This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from clinical trials, as well as any third party intellectual property or other assets that we may opportunistically identify and seek to license or acquire or any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. Because the number and variability of factors that will determine our use of the proceeds from this offering, their ultimate use may vary substantially from their currently intended use. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our operating results or enhance the value of our common stock. See "Use of Proceeds."

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

Because the prices per share at which shares of our common stock are sold in this offering may be substantially higher than the book value per share of our common stock, you may suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. The shares sold in this offering, if any, will be sold from time to time at various prices. After giving effect to the sale of our common stock in the maximum aggregate offering amount of \$35.8 million at an assumed offering price of \$2.73 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on April 26, 2021, and after deducting estimated offering commissions and estimated fees payable by us, our net tangible book value as of March 31, 2021 would have been \$34.9 million, or \$0.52 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.52 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$2.21 per share to new investors who purchase our common stock in the offering. See "Dilution" for a more detailed discussion of the dilution you may incur in connection with this offering.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and any information incorporated by reference into this prospectus supplement contain certain “forward-looking statements.” You can generally identify these forward-looking statements by forward-looking words such as “believe,” “anticipate,” “expect,” “intend,” “plan,” “will,” “may,” “estimate,” “could,” “continue,” “ongoing,” “predict,” “potential,” “likely,” “seek” and other similar expressions, as well as variations or negatives of these words. You can also identify forward-looking statements by the fact that they do not relate strictly to historical or current facts. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes to differ materially from current expectations. These statements are likely to relate to, among other things, the timing, progress and success of our ongoing and planned preclinical studies or clinical trials, the expected timing of regulatory review of our product candidates and our ability to finance contemplated development activities and fund operations for a specified period of time.

These risks and uncertainties include:

- our estimates regarding the timing and amount of funds we require to conduct clinical trials for GEN-011, to continue preclinical studies for our other product candidates and to continue our investments in immuno-oncology;
- our estimates regarding the timing and costs of manufacturing GEN-011;
- our estimates regarding the timing of GEN-011 patient enrollment and dosing;
- our estimates regarding GEN-011 third-party manufacturing capacity;
- our estimates regarding the timing and amount of funds we require to perform monitoring activities to support the GEN-009 clinical trial;
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the timing of, and our ability to, obtain and maintain regulatory approvals for our product candidates;
- the effect of the novel coronavirus (COVID-19) pandemic on the economy generally and on our business and operations specifically, including our research and development efforts, our clinical trials and our employees, and the potential disruptions in supply chains and to our third party manufacturers, including the availability of materials and equipment;
- the potential benefits of strategic partnership agreements and our ability to enter into strategic partnership arrangements;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our manufacturing methods and product candidates;
- the rate and degree of market acceptance and clinical utility of any approved product candidate;
- our ability to quickly and efficiently identify and develop product candidates; and
- our commercialization, marketing and manufacturing capabilities and strategy.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and investors should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in or incorporated by reference into this prospectus supplement, particularly in the “Risk Factors” section in this prospectus supplement, the risk factors set forth under the section entitled “Risk Factors” incorporated by reference into this prospectus supplement from our Annual Report on Form 10-K for the year ended December 31, 2020, and any risk factors contained in our subsequent filings with the SEC that are incorporated by reference in this prospectus supplement, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or collaborations or strategic partnerships we may enter into.

This prospectus supplement, the accompanying prospectus, and the other documents that we have filed with the SEC that are incorporated herein by reference should be read completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

USE OF PROCEEDS

If we receive all \$35.8 million of gross proceeds from the sale of the shares of our common stock under this prospectus supplement, we anticipate that the net proceeds we will receive from this offering will be approximately \$34.7 million, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. The amount of the 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 additional shares under or fully utilize the Sales Agreement with Cowen as a source of financing.

We currently estimate that we will use the net proceeds from this offering as follows:

- for preclinical and clinical development of our lead product candidates, and the discovery, research and development of other product candidates; and
- the balance to fund working capital, capital expenditures and other general corporate purposes.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from clinical trials, as well as any third party intellectual property or other assets that we may opportunistically identify and seek to license or acquire or any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending our use of the net proceeds from this offering described above, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities.

DILUTION

Our net tangible book value as of March 31, 2021 was approximately \$0.2 million, or \$0.00 per share of common stock. Net tangible book value per share is calculated by subtracting our total liabilities from our total tangible assets, which is total assets less intangible assets, and dividing this amount by the number of shares of common stock outstanding. After giving effect to the sale by us of the full \$35.8 million of common stock that may be offered in this offering at an assumed offering price of \$2.73 per share, which was the closing price of our common stock on the Nasdaq Capital Market on April 26, 2021, and after deducting estimated offering commissions and expenses payable by us, our as-adjusted net tangible book value as of March 31, 2021 would have been approximately \$34.9 million, or \$0.52 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.52 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$2.21 per share to new investors. The following table illustrates this hypothetical per share dilution:

Assumed offering price per share	\$	2.73
Net tangible book value per share as of March 31, 2021	—	
Increase per share attributable to new investors	0.52	
As-adjusted net tangible book value per share after this offering		0.52
Net dilution per share to new investors	\$	2.21

The table above assumes for illustrative purposes that an aggregate of 13.1 million shares of our common stock are sold at a price of \$2.73 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on April 26, 2021, for aggregate gross proceeds of \$35.8 million. The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$2.73 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$35.8 million is sold at that price, would increase our adjusted net tangible book value per share after the offering to \$0.55 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$3.18 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$2.73 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$35.8 million is sold at that price, would decrease our adjusted net tangible book value per share after the offering to \$0.46 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$1.27 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only and will adjust based on the actual public offering price and the actual number of shares that we sell in the offering.

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 54,368,582 shares outstanding as of March 31, 2021. The number of shares outstanding as of March 31, 2021 as used throughout this prospectus supplement, unless otherwise indicated, excludes:

- 3,839,107 shares of common stock issuable upon exercise of stock options outstanding at March 31, 2021 at a weighted-average exercise price of \$5.30 per share;
- 2,433,823 shares of common stock issuable upon vesting of restricted stock units outstanding at March 31, 2021;
- 51,001,641 shares of common stock issuable upon the exercise of warrants outstanding at March 31, 2021 at a weighted-average exercise price of \$2.26 per share;
- 659,653 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan at March 31, 2021; and
- 141,337 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan at March 31, 2021.

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 \$35,808,111 of our common stock through Cowen as our sales agent. 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 under the Securities Act. If authorized by us in writing, Cowen may purchase shares of our common stock as principal.

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 equals 3.0% of the gross sales price of the shares sold through it pursuant to the Sales Agreement.

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 The Nasdaq Capital Market 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 Capital Market and trades under the symbol “GNCA.” The transfer agent of our common stock is Computershare Trust Company, N.A.

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 the securities offered hereby will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. Cowen and Company, LLC is being represented in connection with this offering by Duane Morris LLP, New York, New York.

EXPERTS

The consolidated financial statements of Genocea Biosciences, Inc. appearing in Genocea Biosciences, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2020, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the common stock we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person to provide you with different information. We are not making an offer of common stock in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date on the front page of this prospectus supplement, regardless of the time of delivery of this prospectus supplement or any sale of common stock offered by this prospectus supplement.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website at www.sec.gov that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including us.

We maintain a website at www.genocea.com. Information contained in, or accessible through, our website is not a part of, and is not incorporated into, this prospectus supplement, and you should not consider it part of this prospectus supplement.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” into this prospectus supplement the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus supplement. We incorporate by reference into this prospectus supplement the documents listed below and any future filings made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information “furnished” under Items 2.02, 7.01 or 9.01 on Form 8-K or other information “furnished” to the SEC which is not deemed filed and not incorporated in this prospectus supplement. We hereby incorporate by reference the following documents:

- our Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the SEC on February 22, 2021;
- 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, as filed with the SEC on April 29, 2021;
- our Current Reports on Form 8-K filed with the SEC on April 14, 2021; and
- description of our Common Stock contained in our Registration Statement on Form 8-A, as filed with the SEC on January 30, 2014, as supplemented by the description of our common stock contained in Exhibit 4.8 in our Annual Report on Form 10-K for the year ended December 31, 2019, as filed with the SEC on February 13, 2020, including any amendment or report filed for the purpose of updating such description.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus supplement will be deemed modified, superseded or replaced for purposes of this prospectus supplement. Any statement so modified, superseded or replaced shall not be deemed, except as so modified, superseded or replaced, to constitute a part of this prospectus supplement.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Investor Relations
100 Acorn Park Drive, 5th Floor
Cambridge, Massachusetts 02140
(617) 876-8191
email address: ir@genoccea.com

Copies of these filings are also available, without charge, on the SEC's website at www.sec.gov and on our website at www.genoccea.com as soon as reasonably practicable after they are filed electronically with the SEC. The information contained on our website is not a part of this prospectus supplement.

\$35,808,111



GENOCEA BIOSCIENCES, INC.

Common Stock

PROSPECTUS SUPPLEMENT

Cowen

, 2021

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated April 29, 2021

PROSPECTUS SUPPLEMENT

(To Prospectus dated , 2021)

\$23,972,805



GENOCEA BIOSCIENCES, INC.

Common Stock

We have entered into a purchase agreement (the "Purchase Agreement") with Lincoln Park Capital Fund, LLC ("Lincoln Park") on October 23, 2019, relating to shares of our common stock offered by this prospectus supplement. In accordance with the terms of the Purchase Agreement, we may offer and sell up to \$30,000,000 of shares of common stock that may be sold from time to time, at our sole discretion, to Lincoln Park over the next twelve months in accordance with the Purchase Agreement.

Our common stock is traded on The Nasdaq Capital Market under the symbol "GNCA." On April 26, 2021, the closing price of our common stock was \$2.73.

Through the date hereof, we have sold shares of our common stock under the Purchase Agreement for an aggregate purchase price of \$3,527,195 in addition to the 289,966 shares of common stock issued to Lincoln Park in consideration for entering into the Purchase Agreement and \$2,500,000 of shares issued at an initial purchase price of \$2.587 per share. Accordingly, we may offer and sell shares of our common stock having an aggregate price of up to \$23,972,805 pursuant to the Purchase Agreement and this prospectus supplement.

Investing in our common stock involves risks. See "Risk Factors" on page S-7, and under similar headings in the other documents that are incorporated by reference into this prospectus supplement.

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

, 2021

TABLE OF CONTENTS

	Page
ABOUT THIS PROSPECTUS	S-1
SUMMARY	S-2
THE OFFERING	S-3
RISK FACTORS	S-7
FORWARD-LOOKING STATEMENTS	S-8
USE OF PROCEEDS	S-9
DILUTION	S-10
PLAN OF DISTRIBUTION	S-11
LEGAL MATTERS	S-12
EXPERTS	S-12
WHERE YOU CAN FIND MORE INFORMATION	S-12
INCORPORATION OF DOCUMENTS BY REFERENCE	S-12

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and certain other matters relating to us and our business. The second part, the accompanying prospectus, contains and incorporates by reference important business and financial information about us, a description of our common stock and certain other information about us and this offering. This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the Securities and Exchange Commission (the "SEC"), using a "shelf" registration process. Both this prospectus supplement and the accompanying prospectus include or incorporate by reference important information about us, our common stock and other information you should know before investing. You should read both this prospectus supplement and the accompanying prospectus, including all documents incorporated herein and therein by reference, together with the additional information described under "Where You Can Find More Information" herein and in the accompanying prospectus before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus we may provide to you in connection with this offering. We have not, and the sales agent has not, authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying 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 supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do 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 supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

This prospectus supplement may add to, update or change the information in the accompanying prospectus or the documents incorporated by reference herein and therein. If information in this prospectus supplement is inconsistent with information in the accompanying prospectus or the documents incorporated by reference herein and therein, this prospectus supplement will apply and will supersede that information in the accompanying prospectus or the documents incorporated by reference herein and therein.

"Genocea," the "Company," "we," "us," "our" and similar names refer to Genocea Biosciences, Inc. unless we state otherwise or the context otherwise requires.

SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement. The summary may not contain all the information that you should consider before investing in our common stock. You should read the entire prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein, before making an investment decision. You should also carefully consider the matters discussed in the section titled “Risk Factors” in this prospectus supplement, in the accompanying prospectus and in other periodic reports incorporated by reference herein and the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operation” and the financial statements and the notes to those financial statements incorporated by reference in this prospectus supplement before investing in our common stock.

Overview

We are a biopharmaceutical company dedicated to discovering and developing novel cancer immunotherapies using our proprietary ATLAS™ platform. The ATLAS platform can profile each patient's CD4⁺ and CD8⁺ T cell immune responses to every potential target or “antigen” identified by next-generation sequencing of that patient's tumor. ATLAS zeroes in on both antigens that activate anti-tumor T cell responses and inhibitory antigens, Inhibigens™, that drive pro-tumor immune responses. We believe this approach ensures that cancer immunotherapies, such as vaccines and cellular therapies, focus T cell responses on the tumor targets most vulnerable to T cell targeting. Consequently, we believe that ATLAS may enable more immunogenic and efficacious cancer immunotherapies.

Corporate Information

We were incorporated under the laws of the State of Delaware in August 2006. Our principal executive offices are located at 100 Acorn Park Drive, 5th Floor, Cambridge, Massachusetts 02140, and our telephone number is (617) 876-8191. Genocea® and the Genocea logo are registered trademarks.

THE OFFERING

Common stock offered by us	Shares of common stock having an aggregate offering price of up to \$23,972,805.
Common stock to be outstanding after this offering	Up to 2,508,857 shares, assuming sales at a price of \$2.73 per share, which was the closing price on The Nasdaq Capital Market on April 26, 2021. The actual number of shares issued will vary depending on the sales prices under this offering, but will not be greater than 5,227,323 shares representing 19.99% of the shares of Common Stock outstanding on the date of the Purchase Agreement, unless in accordance with Nasdaq rules.
Use of proceeds	We intend to use the net proceeds from this offering primarily for preclinical and clinical development of our lead product candidates, and the discovery, research and development of other product candidates and other corporate purposes. See "Use of Proceeds" on page S-9.
Nasdaq Capital Market symbol	GNCA
Risk factors	See "Risk Factors" beginning on page S-7 of this prospectus for a discussion of factors that you should read and consider before investing in our securities.

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 54,368,582 shares outstanding as of March 31, 2021. The number of shares outstanding as of March 31, 2021 as used throughout this prospectus, unless otherwise indicated, excludes:

- 3,839,107 shares of common stock issuable upon exercise of stock options outstanding at March 31, 2021 at a weighted-average exercise price of \$5.30 per share;
- 2,433,823 shares of common stock issuable upon vesting of restricted stock units outstanding at March 31, 2021;
- 51,001,641 shares of common stock issuable upon the exercise of warrants outstanding at March 31, 2021 at a weighted-average exercise price of \$2.26 per share;
- 659,653 shares of common stock reserved for future issuance under our Amended and Restated 2014 Equity Incentive Plan at March 31, 2021; and
- 141,337 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan at March 31, 2021.

Agreements with Lincoln Park Capital Fund, LLC

On October 23, 2019, we entered into a Purchase Agreement with Lincoln Park, which provides that, upon the terms and subject to the conditions and limitations set forth therein, we have the right to sell to Lincoln Park up to \$30,000,000 (including the initial purchase of \$2,500,000) of shares of our common stock at our discretion as described below. As consideration for entering into the Purchase Agreement, we agreed to issue 289,966 shares of our common stock to Lincoln Park as a commitment fee (the "Commitment Shares").

We are filing this prospectus supplement to cover the offer and sale of up to \$23,972,805 of shares of our common stock, which reflects the common stock available under the Purchase Agreement following the issuance and sale of (i) \$2,500,000 of shares that Lincoln Park purchased as the initial purchase under the Purchase Agreement (the "Initial Purchase") at a purchase price of \$2.587 per share, (ii) \$3,527,195 additional shares of our common stock sold pursuant to the Purchase Agreement and a prior prospectus and related prospectus supplement and (ii) the 289,966 Commitment Shares.

Under the Purchase Agreement, from time to time on any trading day we select, we have the right, in our sole discretion, subject to the conditions and limitations in the Purchase Agreement, to direct Lincoln Park to purchase up to 100,000 shares of our common stock (each such purchase, a “Regular Purchase”) over the 30-month term of the Purchase Agreement; provided, however, that such limit may be increased to up to 150,000 shares if the last closing sale price of our common stock is at least \$4.50 on the purchase date, and may be increased to up to 200,000 shares if the last closing sale price of our common stock is at least \$6.00 on the purchase date (each subject to adjustment for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction as provided in the Purchase Agreement). The purchase price for shares of common stock to be purchased by Lincoln Park will be the equal to lesser of (i) the lowest sale price on the purchase date, as reported by The Nasdaq Capital Market (“Nasdaq”), or (ii) the arithmetic average of the three lowest closing sale prices for our common stock during the ten trading days prior to the purchase date. Lincoln Park’s obligation under each Regular Purchase shall not exceed \$2,000,000; provided that we may agree with Lincoln Park to increase the share limit for any Regular Purchase.

We can also direct Lincoln Park to purchase additional amounts as accelerated purchases (each an “Accelerated Purchase”), under certain circumstances and provided the last closing sale price of our common stock is at least \$1.00 per share, in an amount up to the lesser of (i) three times the number of shares purchased pursuant to such Regular Purchase or (ii) 30% of the trading volume on such Accelerated Purchase date. The purchase price for the Accelerated Purchase is the lower of:

- the closing sale price for the common stock on the date of sale; and
- ninety-seven percent (97%) of the volume weighted average price of the common stock on Nasdaq on the date of sale.

In the event we have directed Lincoln Park to purchase shares of our common stock in the full amount available for an Accelerated Purchase, on the date of such Accelerated Purchase (which is the business day following the corresponding Regular Purchase), we may also direct Lincoln Park to purchase an additional amount of our common stock under the same terms set forth above for an Accelerated Purchase.

There is no upper or lower limit on the price per share that Lincoln Park must pay for our common stock under the Purchase Agreement.

Other than as described above, there are no trading volume requirements or restrictions under the Purchase Agreement. We will control the timing and amount of any sales of our common stock to Lincoln Park. We may at any time, in our sole discretion terminate the Purchase Agreement without fee, penalty or cost, upon one trading day written notice.

The Purchase Agreement limits our sales of shares of common stock to Lincoln Park to 5,227,323 shares of common stock, representing 19.99% of the shares of common stock outstanding on the date of the Purchase Agreement (which number of shares shall be reduced, on a share-for-share basis, by the number of shares of common stock issued or issuable pursuant to any transaction or series of transactions that may be aggregated with the transactions contemplated by the Purchase Agreement under applicable Nasdaq rules (the “Exchange Cap”), unless (i) shareholder approval is obtained to issue more than such amount or (ii) the average price of all applicable sales of our common stock to Lincoln Park under the Purchase Agreement equals or exceeds the closing price of our common stock on The Nasdaq Capital Market immediately preceding the signing of the Purchase Agreement as calculated in accordance with the applicable rules of The Nasdaq Capital Market.

The Purchase Agreement also prohibits us from directing Lincoln Park to purchase any shares of common stock if those shares, when aggregated with all other shares of our common stock then beneficially owned by Lincoln Park and its affiliates, would result in Lincoln Park and its affiliates having beneficial ownership, at any single point in time, of more than 9.99% of the then total outstanding shares of our common stock, as calculated pursuant to Section 13(d) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and Rule 13d-3 thereunder.

The Purchase Agreement does not limit our ability to raise capital from other sources at our sole discretion, provided, however, that we shall not enter into any “Variable Rate Transaction” as defined in the Purchase Agreement, including the issuance of any floating conversion rate or variable priced equity-like securities during the 30 months after the date of the Purchase Agreement.

Events of default under the Purchase Agreement include the following:

- the effectiveness of the registration statement, of which this prospectus supplement and accompanying prospectus are a part, lapses for any reason (including, without limitation, the issuance of a stop order), or this prospectus supplement and accompanying prospectus are unavailable for sale by us or the resale by Lincoln Park of our common stock offered hereby, and such lapse or unavailability continues for a period of ten consecutive business days or for more than an aggregate of thirty business days in any 365-day period;
- the suspension of our common stock from trading or the failure of our common stock to be listed on Nasdaq for a period of one business day;

- the delisting of our common stock from Nasdaq; provided, however, that our common stock is not immediately thereafter trading on the New York Stock Exchange, the Nasdaq Global Market, the Nasdaq Global Select Market, the NYSE American, the NYSE Arca, the OTC Bulletin Board, or the OTCQX or OTCQB operated by the OTC Markets Group, Inc. (or nationally recognized successor to any of the foregoing);
- the failure for any reason by the transfer agent to issue the securities offered hereby to Lincoln Park within three business days after the applicable purchase date on which Lincoln Park is entitled to receive such securities;
- any breach of the representations and warranties or covenants contained in the Purchase Agreement or any related agreements with Lincoln Park if such breach would reasonably be expected to have a material adverse effect and such breach is not cured within five trading days;
- our insolvency or our participation or threatened participation in insolvency or bankruptcy proceedings by or against us, as more fully described in the Purchase Agreement;
- if at any time we are not eligible to transfer our common stock electronically via DWAC; or
- if at any time after the commencement date, the Exchange Cap is reached, to the extent it is applicable.

Lincoln Park does not have the right to terminate the Purchase Agreement upon any of the events of default set forth above. During an event of default, all of which are outside the control of Lincoln Park, shares of our common stock cannot be sold by us or purchased by Lincoln Park under the terms of the Purchase Agreement.

We have the right to terminate the Purchase Agreement at any time, at no cost to us. In the event of bankruptcy proceedings by or against us, the Purchase Agreement will automatically terminate without action of any party.

Concurrently with entering into the Purchase Agreement, we also entered into a registration rights agreement with Lincoln Park (the "Registration Rights Agreement"), pursuant to which we agreed to file a prospectus supplement relating to the sale of the shares of common stock to be issued to Lincoln Park under the Purchase Agreement pursuant to the registration statement of which this prospectus supplement forms a part or a new registration statement and use reasonable best efforts to keep such registration statement effective until the earlier of (i) the date on which Lincoln Park shall have sold all the shares under the Purchase Agreement and (ii) the earlier of (A) 180 days following the first day of the month immediately following the 30 month anniversary of the commencement date and (B) the nine months following the termination of the Purchase Agreement.

The above description of the Purchase Agreement and the Registration Rights Agreement is qualified in its entirety by reference to the Purchase Agreement and the Registration Rights Agreement, which were filed with the Current Report on Form 8-K, filed October 24, 2019 and is incorporated by reference into this prospectus supplement.

The following table sets forth the amount of gross proceeds we would receive from Lincoln Park from our sale of shares to Lincoln Park under the Purchase Agreement at varying purchase prices:

Assumed Average Purchase Price Per Share	Number of Registered Shares to be Issued if Full Purchase ⁽¹⁾⁽²⁾	Percentage of Outstanding Shares After Giving Effect to the Issuance to Lincoln Park ⁽³⁾	Proceeds from the Sale of Shares to Lincoln Park Under the Purchase Agreement ⁽³⁾
\$ 2.00	2,508,857	4.41 %	\$ 5,017,714
\$ 2.73 ⁽⁴⁾	2,508,857	4.41 %	\$ 6,849,180
\$ 3.00	2,508,857	4.41 %	\$ 7,526,571
\$ 4.00	2,508,857	4.41 %	\$ 10,035,428
\$ 5.00	2,508,857	4.41 %	\$ 12,544,285
\$ 6.00	2,508,857	4.41 %	\$ 15,053,142
\$ 7.00	2,508,857	4.41 %	\$ 17,561,999
\$ 8.00	2,508,857	4.41 %	\$ 20,070,856
\$ 9.00	2,508,857	4.41 %	\$ 22,579,713
\$ 9.56	2,507,615	4.41 %	\$ 23,972,799

1. Includes the total number of shares which we would have sold under the Purchase Agreement at the corresponding assumed purchase price set forth in the adjacent column, up to the aggregate purchase price of \$23,972,805.

2. The Purchase Agreement prohibits us from issuing or selling to Lincoln Park under the Purchase Agreement (i) shares of our common stock in excess of the Exchange Cap, unless we obtain stockholder approval to issue shares in excess of the Exchange Cap or the average price of all applicable sales of our common stock to Lincoln Park under the Purchase Agreement equal or exceed the closing price of our common stock on the Nasdaq Capital Market immediately preceding the signing of the Purchase Agreement as calculated in accordance with the applicable rules of the Nasdaq Capital Market, and (ii) any shares of our common stock if those shares, when aggregated with all other shares of our common stock then beneficially owned by Lincoln Park and its affiliates, would exceed the Beneficial Ownership Cap of 9.99%.
3. The denominator is based on 54,368,582 shares outstanding as of March 31, 2021 and the number of shares set forth in the adjacent column which we would have sold to Lincoln Park. The numerator is based on the number of shares which we may issue to Lincoln Park under the Purchase Agreement (that are the subject of this offering) at the corresponding assumed purchase price set forth in the adjacent column.
4. The closing sale price of our common stock on April 26, 2021.

RISK FACTORS

An investment in our common stock involves risks. Prior to making a decision about investing in our common stock, you should consider carefully the risks together with all of the other information contained or incorporated by reference in this prospectus supplement, including any risks described in the section entitled "Risk Factors" contained in any supplements to this prospectus supplement, in our Annual Report on Form 10-K for the year ended December 31, 2020 and in our subsequent filings with the SEC. Each of the referenced risks and uncertainties could adversely affect our business, prospects, operating results and financial condition, as well as adversely affect the value of an investment in our securities. Additional risks not known to us or that we believe are immaterial may also adversely affect our business, operating results and financial condition and the value of an investment in our securities.

Risks Relating to this Offering

We may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

We currently intend to use the net proceeds of this offering, if any, for preclinical and clinical development of our lead product candidates, discovery, research and development of other product candidates and for other general corporate purposes. This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from clinical trials, as well as any third party intellectual property or other assets that we may opportunistically identify and seek to license or acquire or any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. Because the number and variability of factors that will determine our use of the proceeds from this offering, their ultimate use may vary substantially from their currently intended use. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our operating results or enhance the value of our common stock. See "Use of Proceeds."

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

Because the prices per share at which shares of our common stock are sold in this offering may be substantially higher than the book value per share of our common stock, you may suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. The shares sold in this offering, if any, will be sold from time to time at various prices. After giving effect to the sale of our common stock in the maximum aggregate offering amount of \$23,972,805 at an assumed offering price of \$2.73 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on April 26, 2021, our net tangible book value as of March 31, 2021 would have been \$7.0 million, or \$0.12 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.12 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$2.61 per share to new investors who purchase our common stock in the offering. See "Dilution" for a more detailed discussion of the dilution you may incur in connection with this offering.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and any information incorporated by reference into this prospectus supplement contain certain “forward-looking statements.” You can generally identify these forward-looking statements by forward-looking words such as “believe,” “anticipate,” “expect,” “intend,” “plan,” “will,” “may,” “estimate,” “could,” “continue,” “ongoing,” “predict,” “potential,” “likely,” “seek” and other similar expressions, as well as variations or negatives of these words. You can also identify forward-looking statements by the fact that they do not relate strictly to historical or current facts. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes to differ materially from current expectations. These statements are likely to relate to, among other things, the timing, progress and success of our ongoing and planned preclinical studies or clinical trials, the expected timing of regulatory review of our product candidates and our ability to finance contemplated development activities and fund operations for a specified period of time.

These risks and uncertainties include:

- our estimates regarding the timing and amount of funds we require to conduct clinical trials for GEN-011, to continue preclinical studies for our other product candidates and to continue our investments in immuno-oncology;
- our estimates regarding the timing and costs of manufacturing GEN-011;
- our estimates regarding the timing of GEN-011 patient enrollment and dosing;
- our estimates regarding GEN-011 third-party manufacturing capacity;
- our estimates regarding the timing and amount of funds we require to perform monitoring activities to support the GEN-009 clinical trial;
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the timing of, and our ability to, obtain and maintain regulatory approvals for our product candidates;
- the effect of the novel coronavirus (COVID-19) pandemic on the economy generally and on our business and operations specifically, including our research and development efforts, our clinical trials and our employees, and the potential disruptions in supply chains and to our third party manufacturers, including the availability of materials and equipment;
- the potential benefits of strategic partnership agreements and our ability to enter into strategic partnership arrangements;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our manufacturing methods and product candidates;
- the rate and degree of market acceptance and clinical utility of any approved product candidate;
- our ability to quickly and efficiently identify and develop product candidates; and
- our commercialization, marketing and manufacturing capabilities and strategy.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and investors should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in or incorporated by reference into this prospectus supplement, particularly in the “Risk Factors” section in this prospectus supplement, the risk factors set forth under the section entitled “Risk Factors” incorporated by reference into this prospectus supplement from our Annual Report on Form 10-K for the year ended December 31, 2020, and any risk factors contained in our subsequent filings with the SEC that are incorporated by reference in this prospectus supplement, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or collaborations or strategic partnerships we may enter into.

This prospectus supplement, the accompanying prospectus, and the other documents that we have filed with the SEC that are incorporated herein by reference should be read completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

USE OF PROCEEDS

If we receive all \$24.0 million of gross proceeds from the sale of the shares of our common stock under this prospectus supplement, we anticipate that the net proceeds we will receive from this offering will be approximately \$24.0 million, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. The amount of the 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 Purchase Agreement with Lincoln Park as a source of financing.

We currently estimate that we will use the net proceeds from this offering as follows:

- for preclinical and clinical development of our lead product candidates, and the discovery, research and development of other product candidates; and
- the balance to fund working capital, capital expenditures and other general corporate purposes.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from clinical trials, as well as any third party intellectual property or other assets that we may opportunistically identify and seek to license or acquire or any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending our use of the net proceeds from this offering described above, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities.

DILUTION

Our net tangible book value as of March 31, 2021 was approximately \$0.2 million, or \$0.00 per share of common stock. Net tangible book value per share is calculated by subtracting our total liabilities from our total tangible assets, which is total assets less intangible assets, and dividing this amount by the number of shares of common stock outstanding. After giving effect to the sale by us of the full \$24.0 million of common stock that may be offered in this offering at an assumed offering price of \$2.73 per share, which was the closing price of our common stock on the Nasdaq Capital Market on April 26, 2021, and after deducting estimated offering commissions and expenses payable by us, our as-adjusted net tangible book value as of March 31, 2021 would have been approximately \$7.0 million, or \$0.12 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.12 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$2.61 per share to new investors. The following table illustrates this hypothetical per share dilution:

Assumed offering price per share	\$	2.73
Net tangible book value per share as of March 31, 2021	—	
Increase per share attributable to new investors	0.12	
As-adjusted net tangible book value per share after this offering		0.12
Net dilution per share to new investors	\$	2.61

The table above assumes for illustrative purposes that an aggregate of 2,508,857 shares of our common stock are sold at a price of \$2.73 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on April 26, 2021, for aggregate gross proceeds of \$24.0 million. The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$2.73 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$24.0 million is sold at that price, would increase our adjusted net tangible book value per share after the offering to \$0.17 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$3.56 per share. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$2.73 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$24.0 million is sold at that price, would decrease our adjusted net tangible book value per share after the offering to \$0.08 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$1.65 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only and will adjust based on the actual public offering price and the actual number of shares that we sell in the offering.

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 54,368,582 shares outstanding as of March 31, 2021. The number of shares outstanding as of March 31, 2021 as used throughout this prospectus supplement, unless otherwise indicated, excludes:

- 3,839,107 shares of common stock issuable upon exercise of stock options outstanding at March 31, 2021 at a weighted-average exercise price of \$5.30 per share;
- 2,433,823 shares of common stock issuable upon vesting of restricted stock units outstanding at March 31, 2021;
- 51,001,641 shares of common stock issuable upon the exercise of warrants outstanding at March 31, 2021 at a weighted-average exercise price of \$2.26 per share;
- 659,653 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan at March 31, 2021; and
- 141,337 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan at March 31, 2021.

PLAN OF DISTRIBUTION

Pursuant to this prospectus supplement and the accompanying prospectus, we are offering up to \$23,972,805 in shares of our common stock that have been or may be issued by us directly to Lincoln Park under the Purchase Agreement. This prospectus supplement and the accompanying prospectus also cover the resale of these shares by Lincoln Park to the public, including the resale of shares to the public by Lincoln Park sold to Lincoln Park pursuant to the Purchase Agreement and a prior prospectus and related prospectus supplement.

The Purchase Agreement provides that, upon the terms and subject to the conditions set forth therein, Lincoln Park is committed to purchase an aggregate of up to \$30,000,000 of shares of our common stock (including the initial purchase of \$2,500,000) over the 30-month term of the Purchase Agreement. As of the date of this prospectus supplement, we had issued and sold shares of our common stock having an aggregate offering price of \$3,527,195 in addition to the 289,966 shares of common stock issued to Lincoln Park in consideration for entering into the Purchase Agreement and \$2,500,000 shares issued at an initial purchase price of \$2.587 per share pursuant to a prior prospectus and related prospectus supplement and prospectus. Accordingly, we may offer and sell shares of our common stock having an aggregate offering price of up to \$23,972,805 pursuant to the Purchase Agreement and this prospectus supplement. See “The Offering—Agreements with Lincoln Park Capital Fund, LLC”.

Lincoln Park is an “underwriter” within the meaning of Section 2(a)(11) of the Securities Act. Lincoln Park has informed us that it will use an unaffiliated broker-dealer to effectuate all sales, if any, of the common stock that it may purchase from us pursuant to the Purchase Agreement. Such sales will be made on the Nasdaq Capital Market at prices and at terms then prevailing or at prices related to the then current market price. Each such unaffiliated broker-dealer will be an underwriter within the meaning of Section 2(a)(11) of the Securities Act. Lincoln Park has informed us that each such broker-dealer will receive commissions from Lincoln Park that will not exceed customary brokerage commissions.

We know of no existing arrangements between Lincoln Park and any other stockholder, broker, dealer, underwriter, or agent relating to the sale or distribution of the shares offered by this Prospectus. At the time a particular offer of shares is made, a prospectus supplement, if required, will be distributed that will set forth the names of any agents, underwriters, or dealers and any compensation from the selling stockholder, and any other required information.

We will pay all of the expenses incident to the registration, offering, and sale of the shares to Lincoln Park. We have agreed to indemnify Lincoln Park and certain other persons against certain liabilities in connection with the offering of shares of common stock offered hereby, including liabilities arising under the Securities Act or, if such indemnity is unavailable, to contribute amounts required to be paid in respect of such liabilities.

Lincoln Park represented to us that at no time prior to the date of the Purchase Agreement has Lincoln Park or its agents, representatives or affiliates engaged in or effected, in any manner whatsoever, directly or indirectly, any short sale (as such term is defined in Rule 200 of Regulation SHO of the Exchange Act) of our common stock or any hedging transaction. Lincoln Park agreed that during the term of the Purchase Agreement, it, its agents, representatives or affiliates will not enter into or effect, directly or indirectly, any of the foregoing transactions.

We have advised Lincoln Park that it is required to comply with Regulation M promulgated under the Exchange Act. With certain exceptions, Regulation M precludes the selling stockholder, any affiliated purchasers, and any broker-dealer or other person who participates in the distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase any security which is the subject of the distribution until the entire distribution is complete. Regulation M also prohibits any bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of the shares offered by this prospectus supplement.

Our common stock is listed on The Nasdaq Capital Market and trades under the symbol “GNCA.” The transfer agent of our common stock is Computershare Trust Company, N.A.

LEGAL MATTERS

The validity of the issuance of the securities offered hereby will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts.

EXPERTS

The consolidated financial statements of Genoclea Biosciences, Inc. appearing in Genoclea Biosciences, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2020, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the common stock we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person to provide you with different information. We are not making an offer of common stock in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date on the front page of this prospectus supplement, regardless of the time of delivery of this prospectus supplement or any sale of common stock offered by this prospectus supplement.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website at www.sec.gov that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including us.

We maintain a website at www.genoclea.com. Information contained in, or accessible through, our website is not a part of, and is not incorporated into, this prospectus supplement, and you should not consider it part of this prospectus supplement.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” into this prospectus supplement the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus supplement. We incorporate by reference into this prospectus supplement the documents listed below and any future filings made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information “furnished” under Items 2.02, 7.01 or 9.01 on Form 8-K or other information “furnished” to the SEC which is not deemed filed and not incorporated in this prospectus supplement. We hereby incorporate by reference the following documents:

- our Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the SEC on February 22, 2021;
- 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, as filed with the SEC on April 29, 2021;
- our Current Reports on Form 8-K filed with the SEC on April 14, 2021; and
- description of our Common Stock contained in our Registration Statement on Form 8-A, as filed with the SEC on January 30, 2014, as supplemented by the description of our common stock contained in Exhibit 4.8 in our Annual Report on Form 10-K for the year ended December 31, 2019, as filed with the SEC on February 13, 2020, including any amendment or report filed for the purpose of updating such description.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus supplement will be deemed modified, superseded or replaced for purposes of this prospectus supplement. Any statement so modified, superseded or replaced shall not be deemed, except as so modified, superseded or replaced, to constitute a part of this prospectus supplement.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Investor Relations
100 Acorn Park Drive, 5th Floor
Cambridge, Massachusetts 02140
(617) 876-8191
email address: ir@genoccea.com

Copies of these filings are also available, without charge, on the SEC's website at www.sec.gov and on our website at www.genoccea.com as soon as reasonably practicable after they are filed electronically with the SEC. The information contained on our website is not a part of this prospectus supplement.

\$23,972,805



GENOCEA BIOSCIENCES, INC.

Common Stock

PROSPECTUS SUPPLEMENT

, 2021

S-14

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth an estimate of the fees and expenses relating to the issuance and distribution of the securities being registered hereby, other than underwriting discounts and commissions, all of which shall be borne by the Registrant. All of such fees and expenses, except for the SEC registration fee, are estimated:

SEC registration fee	\$	32,730
Legal fees and expenses		*
Accounting fees and expenses		*
Miscellaneous fees and expenses		*
Total		

* These fees are calculated based on the number of issuances and the amount of securities offered and accordingly cannot be estimated at this time. The applicable prospectus supplement will set forth the estimated aggregate amount of expenses payable in respect of any offering of securities.

Item 15. Indemnification of Officers and Directors.

Section 102 of the Delaware General Corporation Law permits a corporation to eliminate the personal liability of its directors or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his or her duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our certificate of incorporation provides that no director shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the Delaware General Corporation Law prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the Delaware General Corporation Law provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he or she is party or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnification for such expenses which the Court of Chancery or such other court shall deem proper.

Our certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding whether civil, criminal, administrative or investigative (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful.

Our certificate of incorporation also provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee or, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred by him or her or on his or her behalf in connection therewith. If we don't assume the defense, expenses must be advanced to an Indemnitee under certain circumstances.

We have entered into indemnification agreements with our directors. In general, these agreements provide that we will indemnify the director to the fullest extent permitted by law for claims arising in his or her capacity as a director of our company or in connection with his or her service at our request for another corporation or entity. The indemnification agreements also provide for procedures that will apply in the event that a director makes a claim for indemnification and establish certain presumptions that are favorable to the director.

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

Item 16. Exhibits.

Exhibit Number	Description of Document
1.1*	Form of Underwriting Agreement
1.2	Sales Agreement, dated March 2, 2015 by and between the Company and Cowen and Company, LLC (incorporated by reference to Exhibit 1.2 to the Company's Registration Statement on Form S-3, File No. 333-202406, filed on March 2, 2015)
1.3	Amendment No. 1 to Sales Agreement dated March 8, 2015 by and between the Company and Cowen and Company, LLC (incorporated by reference to Exhibit 1.3 to the Company's Registration Statement on Form S-3, File No. 333-203981, filed on May 8, 2015)
1.4	Purchase Agreement, dated as of October 23, 2019, by and between Genocea Biosciences, Inc. and Lincoln Park Capital Fund, LLC (incorporated by reference to Exhibit 99.1 to the Company's Current Report on Form 8-K, File No. 001-36289, filed on October 24, 2019)
4.1	Fifth Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, File No. 001-36289, filed on February 12, 2014)
4.2	Certificate of Amendment to the Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, File No. 001-36289, filed on June 25, 2018)
4.3	Certificate of Amendment to the Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, File No. 001-36289, filed on May 21, 2019)
4.4	Certificate of Amendment to Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, File No. 001-36289, filed on June 2, 2020)
4.5	Certificate of Correction to the Certificate of Amendment to the Restated Certificate of Incorporation of Genocea Biosciences, Inc. (incorporated by reference to Exhibit 3.5 to the Company's Quarterly Report on Form 10-Q, File No. 001-36289, filed on July 23, 2020)
4.6	Amended and Restated By-laws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K, File No. 001-36289, filed on February 12, 2014)
4.7	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1, File No. 333-193043, filed on December 23, 2013)
4.8	Fourth Amended and Restated Registration Rights Agreement (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-1, File No. 333-193043, filed on December 23, 2013)

Exhibit Number	Description of Document
4.9	Registration Rights Agreement, dated as of October 23, 2019, by and between Genocea Biosciences, Inc. and Lincoln Park Capital Fund, LLC (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K, File No. 001-36289, filed on October 24, 2019).
4.10*	Form of Common Stock Warrant Agreement and Warrant Certificate
4.11*	Form of Preferred Stock Warrant Agreement and Warrant Certificate
5.1	Opinion of Ropes & Gray LLP (filed herewith)
5.2	Opinion of Ropes & Gray LLP relating to the sales agreement (filed herewith)
5.3	Opinion of Ropes & Gray LLP relating to the purchase agreement (filed herewith)
23.1	Consent of Ropes & Gray LLP (included in Exhibit 5.1)
23.2	Consent of Ropes & Gray LLP (included in Exhibit 5.2)
23.3	Consent of Ropes & Gray LLP (included in Exhibit 5.3)
23.4	Consent of Ernst & Young LLP (filed herewith)
24.1	Power of Attorney (included on signature page)

* To be filed if necessary, subsequent to the effectiveness of this registration statement by an amendment to this registration statement or incorporated by reference pursuant to a Current Report on Form 8-K in connection with the offering of securities.

Item 17. Undertakings.

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;
 - (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 the undertakings set forth in paragraphs (1)(i), (1)(ii) and (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 ("the Exchange Act") that are incorporated by reference in this registration statement or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of this registration statement.
- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
 - (i) 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

- (ii) 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.
- (5) 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.
- (6) 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 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

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 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 of 1933 and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in Cambridge, Massachusetts, on the 29th day of April 2021.

GENOCEA BIOSCIENCES, INC.

By: /s/ WILLIAM CLARK

William Clark

President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints William D. Clark and Diantha Duvall as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place, and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and to file the same, with all exhibits thereto, and other documents in connection therewith with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ WILLIAM CLARK</u> William D. Clark	President and Chief Executive Officer and Director (Principal Executive Officer)	April 29, 2021
<u>/s/ DIANTHA DUVALL</u> Diantha Duvall	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	April 29, 2021
<u>/s/ KENNETH BATE</u> Kenneth Bate	Director	April 29, 2021
<u>/s/ ALI BEHBAHANI</u> Ali Behbahani	Director	April 29, 2021
<u>/s/ KATRINE BOSLEY</u> Katrine Bosley	Director	April 29, 2021
<u>/s/ MICHAEL HIGGINS</u> Michael Higgins	Director	April 29, 2021
<u>/s/ GISELA SCHWAB</u> Gisela Schwab, M.D.	Director	April 29, 2021
<u>/s/ GEORGE SIBER</u> George Siber, M.D.	Director	April 29, 2021

Exhibit 5.1

April 29, 2021

Genocea Biosciences, Inc.
Cambridge Discovery Park
100 Acorn Park Drive, 5th Floor
Cambridge, MA 02140

Re: Registration of Securities by Genocea Biosciences, Inc.

Ladies and Gentlemen:

We have acted as counsel to Genocea Biosciences, Inc. (the "Company") in connection with the registration statement on Form S-3 (the "Registration Statement") filed on the date hereof by the Company with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Securities Act"), relating to the registration under the Securities Act and the proposed issuance and sale from time to time pursuant to Rule 415 under the Securities Act of:

- (i) shares of the Company's common stock, \$0.001 par value per share (the "Common Stock");
- (ii) warrants representing the right to receive or the obligation to sell, upon exercise, a number of shares of Common Stock, and/or shares of Preferred Stock (the "Warrants");
- (iii) shares of preferred stock of the Company, \$0.001 par value per share (the "Preferred Stock");
- (iv) units (the "Units"), each representing ownership of a Unit, securing a holder's obligation to purchase Common Stock, Preferred Stock or Warrants.

The Common Stock, the Warrants, the Preferred Stock and the Units are referred to herein collectively as the "Securities."

In connection with this opinion letter, we have examined such certificates, documents and records and have made such investigation of fact and such examination of law as we have deemed appropriate in order to enable us to render the opinions set forth herein. In conducting such investigation, we have relied, without independent verification, upon certificates or officers of the Company, public officials and other appropriate persons.

The opinions expressed below are limited to the laws of the Commonwealth of Massachusetts and the Delaware General Corporation Law.

Based upon and subject to the foregoing and the assumptions, qualifications and limitations set forth below, we are of the opinion that:

1. When (i) the issuance and sale of any shares of Common Stock have been duly authorized by all necessary corporate action of the Company and (ii) such shares have been issued and delivered against payment of the purchase price therefor (in an amount in excess of the par value thereof) in accordance with the applicable purchase, underwriting or other agreement, and as contemplated by the Registration Statement, such shares of Common Stock will be validly issued, fully paid and nonassessable. The Common Stock covered in the opinion in this paragraph includes any shares of Common Stock that may be issued upon exercise, conversion or exchange pursuant to the terms of any other Securities.
2. When (i) the terms of any Warrants and their issuance and sale have been duly authorized by all necessary corporate action of the Company and (ii) such Warrants have been duly executed, countersigned and delivered in accordance with the applicable warrant agreement and against payment of the purchase price therefor in accordance with the applicable purchase, underwriting or other agreement, and as contemplated by the Registration Statement, such Warrants will constitute valid and binding obligations of the Company enforceable against the Company in accordance with their terms.

3. When (i) the terms of any Preferred Stock of a particular series and their issuance and sale have been duly authorized by all necessary corporate action of the Company, (ii) a certificate of designations with respect to such series of Preferred Stock has been duly adopted by the Company and filed with the Secretary of State of the State of Delaware, and (iii) such shares of Preferred Stock have been issued and delivered against payment of the purchase price therefor (in an amount in excess of the par value thereof) in accordance with the applicable purchase, underwriting or other agreement, and as contemplated by the Registration Statement, such shares of Preferred Stock will be validly issued, fully paid, and nonassessable. The Preferred Stock covered in the opinion in this paragraph includes any shares of Preferred Stock that may be issued upon exercise, conversion or exchange pursuant to the terms of any other Securities.
4. When the issuance and terms of any Units and their issuance and sale have been duly authorized by all necessary corporate action of the Company and (ii) such Units have been duly executed and delivered in accordance with the applicable purchase, underwriting or other agreement, and as contemplated by the Registration Statement, such Units will constitute valid and binding obligations of the Company enforceable against the Company in accordance with their respective terms.

In rendering the opinions set forth above, we have assumed that (i) the Registration Statement will have become effective under the Securities Act, a prospectus supplement will have been prepared and filed with the Commission describing the Securities offered thereby and such Securities will have been issued and sold in accordance with the terms of such prospectus supplement; (ii) a definitive purchase, underwriting, or similar agreement, and any applicable warrant, pursuant to which such Securities may be issued, will have been duly authorized, executed and delivered by the Company and the other parties thereto, and the specific terms of such Securities will have been duly established in conformity with the applicable agreement and the certificate of incorporation and bylaws of the Company (if applicable); (iii) at the time of the issuance of any Securities, the Company will be a validly existing corporation under the law of its jurisdiction of incorporation; (iv) the number of shares of Common Stock issued pursuant to the Registration Statement, together with the number of shares outstanding or reserved at the time of issuance, will not exceed the respective number of shares authorized by the Company's certificate of incorporation in effect at the time of such issuance; and (v) all the foregoing actions to be taken by the Company will have been taken so as not to violate any applicable law and so as to comply with any requirement or restriction imposed by any court or governmental or regulatory body having jurisdiction over the Company or any of its property.

Our opinions set forth above are subject to (a) bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance and similar laws affecting the rights and remedies of creditors generally and (b) general principles of equity.

We hereby consent to the filing of this opinion letter as an exhibit to the Registration Statement and to the use of our name therein and in the related prospectus under the caption "Legal Matters." In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Sections 7 of the Securities Act or the rules and regulations of the Commission thereunder.

Very truly yours,

/s/ Ropes & Gray LLP
Ropes & Gray LLP

Exhibit 5.2

April 29, 2021

Genocea Biosciences, Inc.
Cambridge Discovery Park
100 Acorn Park Drive, 5th Floor
Cambridge, MA 02140

Re: Registration Statement on Form S-3

Ladies and Gentlemen:

This opinion is furnished to you in connection with the registration statement on Form S-3 (the "Registration Statement") filed on the date hereof with the Securities and Exchange Commission, the base prospectus dated the date hereof (the "Base Prospectus") and the prospectus supplement dated the date hereof related to the offering by Genocea Biosciences, Inc., a Delaware corporation (the "Company"), of up to \$35,808,111 of shares (the "Shares") of the Company's common stock, par value \$0.001 per share (the "Common Stock") (collectively with the Base Prospectus, the "Prospectus"). We understand that the Shares will be sold pursuant to a Sales Agreement, dated March 2, 2015, and amended March 8, 2015, by and between the Company and Cowen and Company LLC (the "Agreement") as described in the Prospectus.

We have acted as counsel for the Company in connection with the issuance of the Shares. For purposes of this opinion, we have examined such documents, records and certificates and have made such investigation of fact and such examination of law as we have deemed appropriate in order to enable us to render the opinions set forth herein. In conducting such investigation, we have relied, without independent verification, upon certificates of officers of the Company, public officials and other appropriate persons.

The opinions expressed below are limited to the Delaware General Corporation Law.

Based upon and subject to the foregoing, we are of the opinion that when the Shares are issued out of the Company's duly authorized Common Stock and sold in accordance with the terms of the Agreement against payment of the consideration set forth therein, the Shares will be duly authorized, validly issued, fully paid and non-assessable.

We hereby consent to your filing this opinion as an exhibit to the Registration Statement and to the use of our name under the caption "Legal Matters" in the Prospectus contained therein. In giving such consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act of 1933, as amended, or the rules and regulations of the Securities and Exchange Commission thereunder.

Very truly yours,

/s/ Ropes & Gray LLP
Ropes & Gray LLP

Exhibit 5.3

April 29, 2021

Genocea Biosciences, Inc.
Cambridge Discovery Park
100 Acorn Park Drive, 5th Floor
Cambridge, MA 02140

Re: Registration Statement on Form S-3

Ladies and Gentlemen:

This opinion is furnished to you in connection with the registration statement on Form S-3 (the "Registration Statement") filed on the date hereof with the Securities and Exchange Commission, the base prospectus dated the date hereof (the "Base Prospectus") and the prospectus supplement dated the date hereof related to the offering by Genocea Biosciences, Inc., a Delaware corporation (the "Company"), of up to \$23,972,805 of shares (the "Shares") of the Company's common stock, par value \$0.001 per share (the "Common Stock") (collectively with the Base Prospectus, the "Prospectus"). We understand that the Shares will be sold pursuant to a Purchase Agreement, dated October 23, 2019 by and between the Company and Lincoln Park Capital Fund, LLC (the "Agreement") as described in the Prospectus.

We have acted as counsel for the Company in connection with the issuance of the Shares. For purposes of this opinion, we have examined such documents, records and certificates and have made such investigation of fact and such examination of law as we have deemed appropriate in order to enable us to render the opinions set forth herein. In conducting such investigation, we have relied, without independent verification, upon certificates of officers of the Company, public officials and other appropriate persons.

The opinions expressed below are limited to the Delaware General Corporation Law.

Based upon and subject to the foregoing, we are of the opinion that when the Shares are issued out of the Company's duly authorized Common Stock and sold in accordance with the terms of the Agreement against payment of the consideration set forth therein, the Shares will be duly authorized, validly issued, fully paid and non-assessable.

We hereby consent to your filing this opinion as an exhibit to the Registration Statement and to the use of our name under the caption "Legal Matters" in the Prospectus contained therein. In giving such consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act of 1933, as amended, or the rules and regulations of the Securities and Exchange Commission thereunder.

Very truly yours,

/s/ Ropes & Gray LLP
Ropes & Gray LLP

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” in this Registration Statement (Form S-3) and related Prospectus of Genocera Biosciences, Inc. for the registration of up to \$300,000,000 of its common stock, preferred stock, warrants and units and to the incorporation by reference therein of our report dated February 22, 2021, with respect to the consolidated financial statements of Genocera Biosciences, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2020, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
April 29, 2021