

PROSPECTUS SUPPLEMENT
(To Prospectus dated June 5, 2018)

\$50,000,000



Common Stock

We have entered into a sales agreement with Cowen and Company, LLC ("Cowen"), relating to shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$50,000,000.

Our common stock is traded on the Nasdaq Capital Market under the symbol "GNCA." On November 7, 2019, the closing price of our common stock was \$2.36.

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% 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").

Through the date hereof, we have sold shares of our common stock under the sales agreement for an aggregate purchase price of \$4.1 million, which leaves \$45.9 million of our common stock available under the sales agreement.

Investing in our common stock involves risks, including those described in the "Risk Factors" section beginning on page S-4 of this prospectus supplement and the section captioned "Item 1A-Risk Factors" in our most recently filed annual report on Form 10-K or quarterly report on Form 10-Q which is 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 and accompanying prospectus. Any representation to the contrary is a criminal offense.

Cowen

November 8, 2019

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the common stock we are offering. The second part, the accompanying prospectus dated June 5, 2018, gives more general information about our securities. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectuses we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled "Where You Can Find More Information" and "Incorporation of Certain Information by Reference."

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any free writing prospectuses we have authorized for use in connection with this offering. If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement. Neither we nor any of the sales agents has authorized anyone to provide you with different or additional information. Under no circumstances should the delivery to you of this prospectus supplement and the accompanying prospectus or any sale made pursuant to this prospectus supplement create any implication that the information contained in this prospectus supplement or the accompanying prospectus is correct as of any time after the respective dates of such information.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and in any free writing prospectuses we may provide to you in connection with this offering. We have not, and Cowen 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 outside the United States. This prospectus supplement and the accompanying prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus 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.

"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 and the accompanying 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 supplement and the accompanying prospectus carefully, including "Risk Factors" contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein, before making an investment decision.

Overview

We are a biopharmaceutical company that was incorporated in Delaware on August 16, 2006 and have a principal place of business in Cambridge, Massachusetts. We seek to discover and develop novel cancer immunotherapies using our ATLAS™ proprietary discovery platform. The ATLAS platform profiles each patient's CD4⁺ and CD8⁺ T cell immune responses to every potential target or "antigen" in that patient's tumor. We believe that this approach optimizes antigen selection for immunotherapies such as cancer vaccines and cellular therapies. Consequently, we believe that ATLAS could lead to more immunogenic and efficacious cancer immunotherapies.

Our most advanced program is GEN-009, a personalized neoantigen cancer vaccine, for which we are conducting a Phase 1/2a clinical trial. The GEN-009 program uses ATLAS to identify neoantigens, or immunogenic tumor mutations unique to each patient, for inclusion in each patient's GEN-009 vaccine. We are also advancing GEN-011, a neoantigen-specific adoptive T cell therapy program that also relies on ATLAS, targeting an investigational new drug application in the first half of 2020.

Our principal executive offices are located at 100 Acorn Park Drive, Cambridge, MA 02140, and our telephone number is (617) 876-8191. Our website address is: www.genocoea.com. We have included our website address as a factual reference and do not intend it to be an active link to our website. The information that can be accessed through our website is not part of this prospectus supplement or the accompanying prospectus, and investors should not rely on any such information in deciding whether to purchase our common stock.

THE OFFERING

Common stock offered by us	Shares of common stock having an aggregate offering price of up to \$50.0 million.
Common stock to be outstanding after this offering	Up to 47,336,130 shares, assuming sales at a price of \$2.36 per share, which was the closing price on the Nasdaq Capital Market on November 7, 2019. 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 \$50.0 million of gross proceeds of the sale of shares of our common stock under this prospectus supplement, we anticipate our net proceeds, after deducting commissions and estimated expenses payable by us, will be approximately \$48.3 million. We intend to use the net proceeds from this offering primarily to support the continued advancement of both GEN-009 and GEN-011 as well as for other research and general 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 supplement for a discussion of factors that you should read and consider before investing in our securities.

The number of shares of common stock outstanding after the offering as reflected above is based on 26,149,689 shares of common stock outstanding on September 30, 2019. The number of shares of common stock outstanding after this offering as reflected above excludes:

- 1,397,523 shares of our common stock issuable upon exercise of options outstanding as of September 30, 2019 at a weighted average exercise price of \$11.72 per share;
- 5,131,399 shares of our common stock issuable upon exercise of warrants outstanding as of September 30, 2019 at a weighted average exercise price of \$7.77 per share;
- 204,375 shares of our common stock issuable upon conversion of preferred stock outstanding as of September 30, 2019;
- 171,012 shares of our common stock reserved for issuance under our Amended and Restated 2014 Equity Incentive Plan as of September 30, 2019; and
- 264,860 shares of our common stock reserved for issuance under our 2014 Employee Stock Purchase Plan, as amended, as of September 30, 2019.

RISK FACTORS

Any investment in our common stock involves a high degree of risk. You should consider carefully the risks described below and discussed under the section captioned "Risk Factors" contained in our annual report on Form 10-K for the year ended December 31, 2018, and in our subsequent quarterly reports on Form 10-Q as updated by our subsequent filings under the Exchange Act, each of which is incorporated by reference in this prospectus supplement in their entirety, together with other information in this prospectus supplement and accompanying prospectus, and the information and documents incorporated by reference in this prospectus supplement, and any free writing prospectus that we have authorized for use in connection with this offering before you make a decision to invest in our common stock. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities. The discussion of risks includes or refers to forward-looking statements; you should read the explanation of the qualifications and limitations on such forward-looking statements discussed elsewhere in this prospectus supplement.

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, primarily to support the continued advancement of both GEN-009 and GEN-011 as well as for other research and 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 \$50.0 million at an assumed offering price of \$2.36 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on November 7, 2019, and after deducting offering commissions and estimated fees payable by us, our net tangible book value as of September 30, 2019 would have been \$78.3 million, or \$1.65 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.50 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$0.71 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.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus and the other documents we have filed with the SEC that are incorporated herein by reference contain forward-looking statements that involve risks and uncertainties. All statements, other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. In particular, you should consider the numerous risks described in our Annual Report on Form 10-K for the year ended December 31, 2018 and any subsequent Quarterly Reports on Form 10-Q, each incorporated by reference in this prospectus supplement, and in the "Risk Factors" section of this prospectus supplement and in the accompanying prospectus. See "Where You Can Find More Information."

Although we believe the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, level of activity, performance or achievements. You should not rely upon forward-looking statements as predictions of future events. Unless required by law, we will not undertake and we specifically disclaim any obligation to release publicly the result of any revisions which may be made to any forward-looking statements to reflect events or circumstances after the date of such statements or to reflect the occurrence of events, whether or not anticipated. In that respect, we wish to caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made.

This prospectus supplement, the accompanying prospectus and the other documents incorporated by reference herein include statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third party research, surveys and studies are reliable, we have not independently verified such data.

These risks and uncertainties include, among other things:

- our estimates regarding the timing and amount of funds we require to initiate clinical trials for GEN-009 and to continue our investments in immunology;
- our estimate for when we will require additional funding;
- our plans to commercialize GEN-009 and our other product candidates;
- the timing of, and our ability to, obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any approved product candidate;
- the potential benefits of strategic partnership agreements and our ability to enter into strategic partnership arrangements;
- our ability to quickly and efficiently identify and develop product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
and
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing.

USE OF PROCEEDS

If we receive all \$50.0 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 \$48.3 million, after deducting the 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 sales agreement with Cowen as a source of financing.

We currently estimate that we will use the net proceeds from this offering primarily to support the continued advancement of both GEN-009 and GEN-011 as well as for other research and 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 September 30, 2019 was approximately \$30.0 million, or \$1.15 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 \$50.0 million of common stock that may be offered in this offering at an assumed offering price of \$2.36 per share, which was the closing price of our common stock on the Nasdaq Capital Market on November 7, 2019, and after deducting offering commissions and estimated expenses payable by us, our as-adjusted net tangible book value as of September 30, 2019 would have been approximately \$78.3 million, or \$1.65 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.50 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$0.71 per share to new investors. The following table illustrates this hypothetical per share dilution:

Assumed offering price per share	\$	2.36
Net tangible book value per share as of September 30, 2019	\$	1.15
Increase per share attributable to new investors	\$	0.50
As-adjusted net tangible book value per share after this offering	\$	1.65
Net dilution per share to new investors	\$	0.71

The table above assumes for illustrative purposes that an aggregate of 21,186,441 shares of our common stock are sold at a price of \$2.36 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on November 7, 2019, for aggregate gross proceeds of \$50.0 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 \$2.36 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$50.0 million is sold at that price, would increase our adjusted net tangible book value per share after the offering to \$1.91 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$1.45 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease in the price at which the shares are sold to \$0.50 per share, assuming all of our common stock in the aggregate amount of \$50.0 million is sold at that price, would decrease our adjusted net tangible book value per share after the offering to \$0.62 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$(0.12) per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of 100,000 shares in the number of shares offered by us from the assumed number of shares set forth above would decrease our as adjusted net tangible book value after this offering by approximately \$0.2 million, or approximately \$0.00 per share, and the dilution per share to new investors would remain the same, assuming that the assumed public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated 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 shown above to be outstanding is based on 26,149,689 shares of our common stock outstanding as of September 30, 2019 that will be outstanding immediately after this offering and excludes:

- 1,397,523 shares of our common stock issuable upon exercise of options outstanding as of September 30, 2019 at a weighted average exercise price of \$11.72 per share;
- 5,131,399 shares of our common stock issuable upon exercise of warrants outstanding as of September 30, 2019 at a weighted average exercise price of \$7.77 per share;
- 204,375 shares of our common stock issuable upon conversion of preferred stock outstanding as of September 30, 2019;
- 171,012 shares of our common stock reserved for issuance under our Amended and Restated 2014 Equity Incentive Plan as of September 30, 2019; and
- 264,860 shares of our common stock reserved for issuance under our 2014 Employee Stock Purchase Plan, as amended, as of September 30, 2019.

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 \$50.0 million 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.

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. We have also agreed to reimburse Cowen up to \$50,000 of Cowen’s actual outside legal expenses incurred by Cowen in connection with this offering. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$200,000.

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

Cowen will provide written confirmation to us following the close of trading on 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.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus supplement and the accompanying prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the shares of common stock offered hereby, we refer you to the registration statement and the exhibits and schedules filed thereto. Statements contained in this prospectus supplement and the accompanying prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. The SEC maintains an internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the SEC. The address of that site is www.sec.gov.

We are subject to the informational requirements of the Exchange Act, and, in accordance with the Exchange Act, are required to file annual, quarterly and current reports, proxy and information statements and other information with the SEC. Such annual, quarterly and current reports, proxy and information statements and other information can be reviewed by accessing the SEC website provided above. This information is also available on the investor relations section of our website, which is located at www.genoce.com. Information on, or accessible through, our website is not part of this prospectus supplement and the accompanying prospectus.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" into this prospectus supplement and the accompanying 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 supplement and the accompanying prospectus, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus supplement and the accompanying prospectus. We incorporate by reference into this prospectus supplement and the accompanying 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 supplement and the accompanying prospectus, until the termination of the offering of securities described 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, 2018, as filed with the SEC on February 28, 2019;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2018 from our definitive proxy statement on Schedule 14A, as filed with the SEC on March 29, 2019;
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2019, as filed with the SEC on April 30, 2019, June 30, 2019, as filed with the SEC on July 25, 2019, and September 30, 2019 as filed with the SEC on October 24, 2019;
- Our Current Reports on Form 8-K filed with the SEC on February 12, 2019, February 28, 2019, May 21, 2019 and October 24, 2019; and
- Description of our common stock contained in our Registration Statement on Form 8-A, as filed with the SEC on January 30, 2014, 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 and the accompanying prospectus will be deemed modified, superseded or replaced for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained in this prospectus supplement or the accompanying 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@genoce.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.genocea.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 and the accompanying prospectus.

LEGAL MATTERS

The validity of the issuance of the securities offered pursuant to this prospectus 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 financial statements of Genocera Biosciences, Inc. appearing in Genocera Biosciences, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2018, 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 incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

PROSPECTUS

\$200,000,000



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 \$200.0 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 Global Market under the symbol "GNCA." On May 21, 2018, the closing price of our common stock was \$0.94.

As of May 21, 2018, the aggregate market value of our outstanding common stock held by non-affiliates, or public float, was approximately \$70.0 million based on 61,366,484 shares of outstanding common stock, at a price of \$1.14 per share, which was the last reported sale price of our common stock on the Nasdaq Global Market on March 26, 2018. We have offered approximately \$3.0 million of securities pursuant to General Instruction I.B.6. of Form S-3 during the prior 12 calendar month period that ends on and includes the date of this prospectus. Pursuant to General Instruction I.B.6. of Form S-3, in no event will we sell securities registered on this registration statement in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below \$75.0 million.

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 June 5, 2018

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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 \$200.0 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.

SUMMARY

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 that seeks to discover and develop novel cancer vaccines through its AnTigen Lead Acquisition System ("ATLAS") proprietary discovery platform. The ATLAS platform is designed to recall a patient's pre-existing CD4+ and CD8+ T cell immune responses to their tumor to identify neoantigens and antigens for inclusion in vaccines that are designed to act through T cell (or cellular) immune responses. We believe that using ATLAS to identify neoantigens and antigens for inclusion in cancer vaccines could lead to more immunogenic and efficacious cancer vaccines.

Currently, all of our research programs and product candidates in active development are at the preclinical stage. Our most advanced program is our preclinical immuno-oncology program, GEN-009, a neoantigen cancer vaccine. The GEN-009 program uses ATLAS to identify patient neoantigens, or newly formed antigens unique to each patient, that are associated with that individual's tumor. We are also exploring partnering opportunities in the development of cancer vaccines targeting tumor-associated antigens and a vaccine targeting cancers caused by Epstein-Barr Virus.

We have one Phase 3-ready product candidate, GEN-003, an investigational immunotherapy for the treatment of genital herpes. In September 2017, we announced that we are exploring strategic alternatives to maximize value for GEN-003 through sale, partnership or other means. Consequently, substantially all GEN-003 spending and activities were ceased.

We were incorporated in the state of Delaware in August 2006 as Genoceia, Inc., and we subsequently changed our name to Genoceia Biosciences, Inc. Our principal executive offices are located at Cambridge Discovery Park, 100 Acorn Park Drive, 5th Floor, Cambridge, Massachusetts 02140, and our telephone number is (617) 876-8191. Our Internet website is www.genoceia.com.

RISK FACTORS

Investing in our securities involves a high degree of risk. See "Item 1A—Risk Factors" in our most recent Annual Report on Form 10-K and in any subsequent Quarterly Report on Form 10-Q incorporated by reference in this prospectus, in any other documents we file with the SEC that are deemed incorporated by reference into this prospectus and the "Risk Factors" section in the applicable prospectus supplement for a discussion of the factors you should carefully consider before deciding to purchase our securities. Before you invest in our securities, you should carefully consider these risks as well as other information we include or incorporate by reference into this prospectus and the applicable prospectus supplement. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities. The discussion of risks includes or refers to forward-looking statements; you should read the explanation of the qualifications and limitations on such forward-looking statements discussed elsewhere in this prospectus.

FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the other documents we have filed with the SEC that are incorporated herein by reference, contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. In particular, you should consider the numerous risks described in our Annual Report on Form 10-K for the year ended December 31, 2017 and any subsequent Quarterly Reports on Form 10-Q, each incorporated by reference in this prospectus, and in the "Risk Factors" section in the applicable prospectus supplement. See "Where You Can Find More Information."

Although we believe the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, level of activity, performance or achievements. You should not rely upon forward-looking statements as predictions of future events. Unless required by law, we will not undertake and we specifically disclaim any obligation to release publicly the result of any revisions which may be made to any forward-looking statements to reflect events or circumstances after the date of such statements or to reflect the occurrence of events, whether or not anticipated. In that respect, we wish to caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made.

This prospectus and the other documents incorporated by reference herein include statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third party research, surveys and studies are reliable, we have not independently verified such data.

These risks and uncertainties include, among other things:

- our estimates regarding the timing and amount of funds we require to initiate clinical trials for GEN-009 and to continue our investments in immuno-oncology;
- our estimate for when we will require additional funding;
- our plans to commercialize GEN-009 and our other product candidates;
- the timing of, and our ability to, obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any approved product candidate;
- the potential benefits of strategic partnership agreements and our ability to enter into strategic partnership arrangements;
- our ability to quickly and efficiently identify and develop product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;

- our intellectual property position; and
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing.

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 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.

RATIO OF COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS TO EARNINGS

The following table sets forth our historical ratios of earnings to fixed charges and preferred stock dividends for the periods indicated. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus.

	Three Months Ended March 31, 2018	Year Ended December 31,				
		2017	2016	2015	2014	2013
Ratio of combined fixed charges and preferred stock dividends to earnings(1)	—	—	—	—	—	—

(1) Earnings were inadequate to cover fixed charges and preferred dividends for the quarter ended March 31, 2018 and the years ended December 31, 2017, 2016, 2015, 2014 and 2013 by \$10.6 million, \$56.7 million, \$49.6 million, \$42.5 million, \$35.5 million and \$22.4 million, respectively.

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 reallocated or paid to dealers; and
- any securities exchanges on which the securities may be listed.

Any offering price and any discounts or concessions allowed or reallocated or paid to dealers 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 Global 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 over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with rules and regulations under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Over-allotment 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 175,000,000 shares of our common stock, par value \$0.001 per share. As of March 31, 2018, we had 83,057,643 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 six 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 be 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. The transfer agent and registrar's address is 144 Fernwood Ave, Edison, New Jersey 08837.

Listing

Our common stock is listed on the Nasdaq Global 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. As of March 31, 2018, we had 1,635 shares of preferred stock outstanding. 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 outstanding other than shares of our Series A convertible preferred stock, as described below under “Series A Convertible Preferred Stock.” 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.

Series A Convertible Preferred Stock

As of March 31, 2018, we had 1,635 shares of Series A convertible preferred stock outstanding. The following description is a summary of the material provisions of the Series A convertible preferred stock and the certificate of designation and does not purport to be complete. This summary is subject to and is qualified by reference to all the provisions of the Series A convertible preferred stock and certificate of designations. We urge you to read this document because it, and not this description, defines the rights of a holder of the Series A convertible preferred stock. A copy of the form of certificate of designation that we filed with the Secretary of State of the State of Delaware on January 18, 2018 has been incorporated by reference as an exhibit to the registration statement of which this prospectus forms a part.

Rank and Liquidation Preference. The Series A preferred stock rank pari passu on an as-converted to common stock basis with all of our common stock as to distributions of assets upon our liquidation, dissolution or winding up, whether voluntarily or involuntarily, or a “Fundamental Transaction,” as defined in the certificate of designation.

Conversion. Each share of our Series A preferred stock is convertible into 1,000 shares of our common stock (subject to adjustment as provided in the certificate of designation) at any time at the option of the holder, provided that the holder will be prohibited from converting Series A preferred stock into shares of our common stock if, as a result of such conversion, the holder, together with its affiliates, would own more than 9.99% of the total number of shares of our common stock then issued and outstanding.

Voting Rights. Shares of Series A preferred stock generally have no voting rights, except as required by law and except that the consent of holders of a majority of the outstanding Series A preferred stock is required to amend the terms of the Series A preferred stock.

Dividends. Shares of Series A preferred stock are entitled to receive dividends equal, on an as-converted to common stock basis, to and in the same form as dividends actually paid on shares of common stock when, as and if such dividends are paid on shares of common stock.

Redemption. We are not obligated to redeem or repurchase any shares of Series A preferred stock. Shares of Series A preferred stock are not otherwise entitled to any redemption rights, or mandatory sinking fund or analogous fund provisions.

Exchange Listing. The Series A preferred stock is not listed on The Nasdaq Global Market, any national securities exchange or other nationally recognized trading system. The common stock issuable upon conversion of the Series A preferred stock is currently listed on The Nasdaq Global Market.

Conversion Agent. The conversion agent is Computershare Trust Company, N.A.

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, 2018, we had warrants outstanding that represent the right to acquire 29,015,653 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.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC for the securities offered by this prospectus. This prospectus does not include all of the information contained in the registration statement. You should refer to the registration statement and its exhibits for additional information.

We are required to file annual and quarterly reports, current reports, proxy statements, and other information with the SEC. We make these documents publicly available, free of charge, on our website at www.genoccea.com as soon as reasonably practicable after filing such documents with the SEC. The information contained on our website is not part of this prospectus. You can read our SEC filings, including the registration statement, on the SEC's website at <http://www.sec.gov>. You also may read and copy any document we file with the SEC at its public reference facility at:

Public Reference Room
100 F Street N.E.
Washington, DC 20549

Please call the SEC at 1-800-732-0330 for further information on the operation of the public reference facilities.

INCORPORATION OF CERTAIN 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, 2017, as filed with the SEC on February 16, 2018;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2017 from our definitive proxy statement on Schedule 14A, as filed with the SEC on April 24, 2018;
- Our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2018, as filed with the SEC on May 11, 2018;
- Our Current Reports on Form 8-K filed with the SEC on January 19, 2018, January 31, 2018, February 12, 2018, February 15, 2018, March 9, 2018 and April 30, 2018; and
- Description of our common stock contained in our Registration Statement on Form 8-A, as filed with the SEC on January 30, 2014, 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@genocea.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.genocea.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.

LEGAL MATTERS

The validity of the issuance of the securities offered pursuant to this prospectus will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. The validity of any securities will be passed upon for any underwriters or agents by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements of Genocea Biosciences, Inc. appearing in Genocea Biosciences, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2017, 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 incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

\$50,000,000



Common Stock

PROSPECTUS SUPPLEMENT

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November 8, 2019
