PROSPECTUS SUPPLEMENT (To Prospectus dated July 1, 2021)

Up to \$400,000,000



Common Stock

This prospectus supplement is being filed to update, amend and supplement certain information in the sales prospectus of Vaxcyte, Inc. dated July 1, 2021 (including any documents incorporated by reference therein), or the Prior ATM Sales Prospectus. The Prior ATM Sales Prospectus will no longer be in effect as of the date of this prospectus supplement.

We previously entered into an Open Market Sale AgreementSM, or the Sales Agreement, with Jefferies LLC, or Jefferies, on July 1, 2021, relating to the sale of shares of our common stock, \$0.001 par value per share, or Common Stock, offered by the Prior ATM Sales Prospectus. On February 27, 2023, we entered into an amendment to the Sales Agreement. In accordance with the terms of the Sales Agreement, as amended, or the Amended Sales Agreement, under this prospectus supplement, we may offer and sell shares of our Common Stock having an aggregate offering price of up to \$400,000,000 from time to time through Jefferies acting as our sales agent, exclusive of any amounts previously sold under the Sales Agreement. From July 2021 through the date of this prospectus supplement, we have sold 4,995,709 shares of our Common Stock totaling gross proceeds of \$137.8 million under the Prior ATM Sales Prospectus.

Our Common Stock is listed on the Nasdaq Global Select Market under the symbol "PCVX." On February 24, 2023, the last reported sale price of our Common Stock on the Nasdaq Global Select Market was \$41.70 per share.

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

Jefferies will be entitled to compensation at a commission rate of up to 3.0% of the gross proceeds of any shares of Common Stock sold under the Amended Sales Agreement. In connection with the sale of the Common Stock on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Jefferies with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act. See "Plan of Distribution" beginning on page S-14 of this prospectus supplement for additional information regarding the compensation to be paid to Jefferies.

Investing in our Common Stock involves risks. See "Risk Factors" beginning on page S-7 of this prospectus supplement and in the reports we file with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934, as amended, incorporated by reference in this prospectus supplement, before making a decision to invest in our Common Stock.

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

Jefferies

The date of this prospectus supplement is February 27, 2023.

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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 this offering and the securities offered hereby, and also adds to and updates information contained in the accompanying prospectus and the documents incorporated into each by reference. The second part is the accompanying prospectus, which provides more general information, some of which may not apply to this offering of Common Stock. This prospectus supplement is deemed to be incorporated by reference into the accompanying prospectus solely for the purpose of this offering. When we refer only to the "prospectus," we are referring to both parts combined.

To the extent the information contained in this prospectus supplement differs from or conflicts with the information contained in the accompanying prospectus or any document incorporated by reference, the information in this prospectus supplement will control. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference into the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

Before buying any of the Common Stock that we are offering, we urge you to carefully read this prospectus, together with the information incorporated by reference as described under the headings "Where You Can Find More Information" and "Incorporation by Reference" in this prospectus. These documents contain important information that you should consider when making your investment decision.

You should rely only on the information contained in or incorporated by reference in this prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the sales agent has not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the sales agent is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, the documents incorporated by reference in this prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus, the documents incorporated by reference in this prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

Unless the context otherwise requires, all references in this prospectus supplement to "we," "us," "our," "our company" and "Vaxcyte" refer to Vaxcyte, Inc.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference may include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all the information you should consider before investing in our Common Stock. You should read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus (including the documents incorporated by reference herein and therein), including the factors described under the heading "Risk Factors" in this prospectus supplement and documents incorporated by reference and the financial and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, as well as the information included in any free writing prospectus that we have authorized for use in connection with this offering, before making an investment decision.

Overview

We are a clinical-stage vaccine innovation company engineering high-fidelity vaccines to protect humankind from the consequences of bacterial diseases. We are developing broad-spectrum conjugate and novel protein vaccines to prevent or treat bacterial infectious diseases. We are re-engineering the way highly complex vaccines are made through modern synthetic techniques, including advanced chemistry and the XpressCF™ cell-free protein synthesis platform, exclusively licensed from Sutro Biopharma, Inc., or Sutro Biopharma. Unlike conventional cell-based approaches, our system for producing difficult-to-make proteins and antigens is intended to accelerate our ability to efficiently create and deliver high-fidelity vaccines with enhanced immunological benefits.

Vaccines are one of the most successful and cost-effective global health interventions and prevent millions of deaths worldwide each year. Routine pediatric vaccinations are estimated to prevent 20 million cases of disease each year, saving over \$180 billion in direct and societal costs in the United States alone. Adult vaccination rates are lower than pediatric vaccination rates, but new technologies are driving adult vaccine development, which in turn is fueling the growth of the overall vaccine market. Given the critical role vaccines play in preventing disease from childhood to adulthood, the global vaccine market is large, durable and growing. Therefore, there are areas of unmet medical need, including vaccines that can provide broader protection than currently marketed vaccines and novel vaccines that target pathogens for which there are no currently approved vaccines. We are driven to eradicate or treat invasive bacterial infections, which have serious and costly health consequences when left unchecked.

We carefully select our target disease areas and vaccine candidates based on the following criteria: areas of significant unmet medical need, well-defined commercial landscape and efficient market adoption, acceptable biological risk and established clinical pathways. We are leveraging our scalable cell-free protein synthesis platform to develop potentially superior and novel conjugate and protein vaccine candidates for adult and pediatric indications using these criteria.

Our pipeline includes:

- Pneumococcal conjugate vaccine, or PCV, candidates that we believe are among the most broad-spectrum PCV candidates currently in development, targeting the approximately \$7 billion global pneumococcal vaccine market. Pneumococcal disease is an infection caused by Streptococcus pneumoniae, or pneumococcus, bacteria. It can result in invasive pneumococcal disease, or IPD, including meningitis and bacteremia, and non-invasive pneumococcal disease, including pneumonia, otitis media and sinusitis.
 - Our lead vaccine candidate, VAX-24, is a 24-valent, broad-spectrum investigational PCV being developed for the prevention of IPD. VAX-24 is intended to improve upon the standard-of-care

PCV vaccines for both children and adults by covering the serotypes that are responsible for most of the pneumococcal disease currently in circulation.

- VAX-24 Adult Program: On October 24, 2022, we announced positive topline results from both the Phase 1 and Phase 2 portions of a clinical proof-of-concept study evaluating the safety, tolerability and immunogenicity of VAX-24 in 800 healthy adults aged 18-64. The Phase 1 portion of the study evaluated the safety and tolerability of a single injection of VAX-24 at three dose levels, 1.1mcg, 2.2mcg and 2.2mcg/4.4mcg, and compared to PCV20 in 64 healthy adults 18-49 years of age. The Phase 2 portion evaluated the safety, tolerability and immunogenicity of a single injection of VAX-24 at the same three dose levels and compared to a single injection of Prevnar 20™, or PCV20, in 771 healthy adults 50-64 years of age. In this study, VAX-24 met the primary safety and tolerability objectives, demonstrating a safety profile similar to PCV20, for all doses studied. In this study, VAX-24 met or exceeded the established regulatory immunogenicity standards for all 24 serotypes at the conventional 2.2mcg dose, which we intend to move forward into a Phase 3 program. At this dose, VAX-24 met the standard opsonophagocytic activity, or OPA, response non-inferiority criteria for all 20 serotypes common with PCV20, of which 16 achieved higher immune responses. Additionally, at all three doses, VAX-24 met the standard superiority criteria for all four serotypes unique to VAX-24. VAX-24 has the potential to cover an additional 10-28 percent of strains causing IPD in adults over the current standard-of-care PCVs. We have a separate Phase 2 study in approximately 200 healthy adults aged 65 and older for which we have completed enrollment, and we anticipate announcing topline safety, tolerability and immunogenicity results from this study in the second quarter of 2023. We anticipate final results with the six-month safety data from both Phase 2 adult studies in the first half of 2023 and expect to hold regulatory interactions with the U.S. Food and Drug Administration, or FDA, in the second half of 2023 to inform the Phase 3 program. We expect topline safety, tolerability and immunogenicity data from the Phase 3 pivotal, non-inferiority study in adults in 2025. The FDA has granted Fast Track and Breakthrough Therapy designations for VAX-24 in adults.
- VAX-24 Pediatric Program: In late February 2023, we announced that the FDA cleared the VAX-24 IND application for the prevention of IPD in infants. We plan to initiate the infant Phase 2 study in the second quarter of 2023, with topline safety, tolerability and immunogenicity data following the primary three-dose immunization series expected by 2025. The study design will include a primary immunization series consisting of three doses followed by a subsequent booster dose.
- Our second PCV candidate, VAX-31 (formerly VAX-XP), builds on what has been established with VAX-24 and is designed to expand the breadth of coverage to 31 strains without compromising immunogenicity due to carrier suppression. VAX-31 was designed to provide coverage for approximately 95% of IPD currently circulating in the adult U.S. population. We anticipate submitting an IND application to the FDA for VAX-31 in adults in the second half of 2023. We expect topline safety, tolerability and immunogenicity data from a Phase 1/2 study in adults in 2024.
- VAX-A1, a novel conjugate vaccine candidate designed to prevent disease caused by Group A Streptococcus, or Group A Strep. Group A Strep is pervasive globally and causes 700 million cases of illness annually, including pharyngitis, or strep throat, and certain severe invasive infections such as sepsis, necrotizing fasciitis and toxic shock syndrome. There is currently no vaccine against Group A Strep, which is one of the leading infectious disease-related causes of death and disability worldwide and a significant contributor to the prescription of antibiotics in the very young. We believe we have demonstrated preclinical proof of concept for VAX-A1, the data for which were published in December 2020. We nominated the final vaccine candidate for VAX-A1 in the first quarter of 2021 and

initiated IND-enabling activities in the second half of 2021. We continue to advance the development of VAX-A1 and intend to provide further information about the anticipated timing of an IND application as the program progresses.

- VAX-PG, a novel protein vaccine candidate targeting the keystone pathogen responsible for periodontitis, a chronic oral inflammatory
 disease affecting an estimated 65 million adults in the United States. We believe we have generally demonstrated preclinical proof of
 concept for a periodontitis protein vaccine, the data for which was published in February 2019. We nominated a final vaccine
 candidate for VAX-PG in the fourth quarter of 2022 and continue to progress the program. Our initial goal is to develop a therapeutic
 vaccine to slow or stop disease progression; however, the results from clinical trials may inform the potential adoption of prophylactic
 immunization.
- VAX-GI, a new vaccine program designed to prevent Shigella, a bacterial illness that affects an estimated 188 million people
 worldwide each year and results in approximately 164,000 deaths annually, mostly among children under five years of age in low- and
 middle-income settings.
- We have other discovery-stage programs that leverage our cell-free protein synthesis platform, which, if proven successful in preclinical studies, could also be advanced into IND-enabling activities and clinical studies.

Our modern synthetic techniques, including advanced chemistry and the XpressCF cell-free protein synthesis platform, offer several advantages over conventional cell-based protein expression methods, which we believe enable us to generate superior, novel, more broad-spectrum and/or more immunogenic vaccines. In the context of conjugate vaccines, we believe we can add more antigenic strains without compromising the overall immune response. In particular, our ability to specify the attachment point of antigens, including polysaccharides, on protein carriers represents a significant improvement over the random conjugation that occurs with conventional technologies. This site-specific conjugation is designed to ensure that B-cell and/or T-cell epitopes are optimally exposed, maximizing the immune response, whereas random conjugation blocks these critical immunogenic epitopes, which dampens the immune response and may lead to a phenomenon known as carrier suppression.

We believe this precise control of conjugation chemistry enables us to design broader-spectrum conjugate vaccine candidates using carrier-sparing conjugates that use less protein carrier without sacrificing immunogenicity. We are also able to design novel conjugate vaccine candidates using standard amounts of protein carrier to generate heightened immunogenicity. Beyond conjugate vaccines, we believe we can also design novel protein vaccine candidates based on well-appreciated but highly complex antigens that currently cannot be made using conventional technologies to address diseases for which there are no available vaccines. In addition, our platform enables us to rapidly screen vaccine candidates, requiring less effort than conventional chemistry which allows us to produce and iterate conjugate candidates, thereby dramatically accelerating the development cycle of designing, producing and testing vaccine candidates.

Corporate Information

We were incorporated under the laws of the state of Delaware in November 2013 as SutroVax, Inc. and changed our name to Vaxcyte, Inc. in May 2020. Our principal executive offices are located at 825 Industrial Road, Suite 300, San Carlos, California 94070. Our telephone number is (650) 837-0111. Our website address is https://www.vaxcyte.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus supplement and the accompanying prospectus.

Vaxcyte, the Vaxcyte logo and our other registered or common law trade names, trademarks or service marks appearing in this prospectus supplement and the accompanying prospectus are the property of Vaxcyte, Inc. or exclusively licensed for Vaxcyte's use.

THE OFFERING

Common Stock offered by us

Shares of our Common Stock having an aggregate offering price of up to \$400.0 million.

Common Stock to be outstanding immediately after this offering

Up to 89,062,996 shares (as more fully described in the notes following this table), assuming sales of 9,592,326 shares of our Common Stock in this offering at an offering price of \$41.70 per share, which was the last reported sale price of our Common Stock on the Nasdaq Global Select Market on February 24, 2023. The actual number of shares issued will vary depending on the sales price under this offering.

Plan of distribution

"At-the-market offering" that may be made from time to time through the sales agent, Jefferies. See "Plan of Distribution" on page S-14 of this prospectus supplement.

Use of proceeds

We currently intend to use the net proceeds from this offering, if any, together with our existing cash, cash equivalents and investments, to fund the advancement of our current vaccine candidates VAX-24, VAX-31, VAX-A1 and VAX-PG; to fund ongoing research and the potential development of our discovery-stage programs; and for other general corporate purposes, including working capital, operating expenses and capital expenditures, as well as potential expansion of our research pipeline. See the section titled "Use of Proceeds" for additional information.

Risk factors

Investing in our Common Stock involves significant risks. Before making an investment decision, please read the information contained in and incorporated by reference under the heading "Risk Factors" on page S-7 of this prospectus supplement, and under similar headings in other documents that are incorporated by reference into this prospectus supplement.

The Nasdaq Global Select Market symbol

"PCVX"

The number of shares of our Common Stock that will be outstanding after this offering is based on 79,470,670 shares of our Common Stock outstanding as of December 31, 2022, and excludes:

- 7,752,204 shares of our Common Stock issuable upon the exercise of options to purchase shares of our Common Stock outstanding as of December 31, 2022, with a weighted-average exercise price of \$18.62 per share;
- 456,766 shares of our Common Stock issuable upon settlement of restricted stock units outstanding as of December 31, 2022;
- 4,679,598 shares of our Common Stock reserved for future issuance under our 2020 Equity Incentive Plan as of December 31, 2022, as well as any annual evergreen increases in the number of shares reserved for future issuance under this plan;
- 1,539,314 shares of our Common Stock reserved for future issuance under our 2020 Employee Stock Purchase Plan as of December 31, 2022, as well as any annual evergreen increases in the number of shares reserved for future issuance under this plan; and
- 6,250,000 shares of our Common Stock issuable upon the exercise of pre-funded warrants outstanding as of December 31, 2022 at an exercise price of \$0.001 per share.

Subsequent to December 31, 2022 and through the date of this prospectus supplement:

- we granted stock options to purchase 78,946 shares of our Common Stock with a weighted-average exercise price of \$45.67 per share:
- we reserved an additional 3,973,533 shares of common stock for future issuance under our 2020 Equity Incentive Plan pursuant to the annual evergreen increase;
- we reserved an additional 794,706 shares of common stock for future issuance under our 2020 Employee Stock Purchase Plan pursuant to the annual evergreen increase; and
- we sold 507,136 shares of our Common Stock for total gross proceeds of approximately \$23.0 million under the Sales Agreement.

Unless otherwise indicated, the information in this prospectus supplement assumes no exercise of the outstanding options or warrants or the vesting of outstanding restricted stock units described above.

RISK FACTORS

Investing in our Common Stock involves a high degree of risk. Before making a decision to invest in our Common Stock, you should consider carefully the risks and uncertainties described under the heading "Risk Factors" contained or incorporated by reference in this prospectus, including the risk factors incorporated by reference herein from our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as may be updated by our subsequent annual reports, quarterly reports and other filings we make with the SEC. The risks described in these documents are not the only ones we face. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could harm our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be harmed. This could cause the trading price of our Common Stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below titled "Special Note Regarding Forward-Looking Statements."

Additional Risks Related to the Offering

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section titled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short- and intermediate-term, interest-bearing instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

If you purchase our Common Stock in this offering, you may experience immediate and substantial dilution in the net tangible book value of your shares.

The offering price per share in this offering may exceed the net tangible book value per share of our Common Stock outstanding prior to this offering. Assuming that an aggregate of 9,592,326 shares of our Common Stock are sold at a price of \$41.70 per share, the last reported sale price of our Common Stock on the Nasdaq Global Select Market on February 24, 2023, for aggregate gross proceeds of approximately \$400.0 million, and after deducting commissions and estimated offering expenses payable by us, you would experience immediate dilution of \$26.64 per share, representing the difference between our as adjusted net tangible book value per share as of February 24, 2023 after giving effect to this offering and the assumed public offering price. The exercise of outstanding stock options or warrants or the vesting of outstanding restricted stock units would result in further dilution of your investment. See the section titled "Dilution" below for a more detailed illustration of the dilution you would incur if you participate in this offering. Because the sales of the shares offered hereby will be made directly into the market or in negotiated transactions, the prices at which we sell these shares will vary and these variations may be significant. Purchasers of the shares we sell, as well as our existing stockholders, will experience significant dilution if we sell shares at prices significantly below the price at which they invested.

Future sales or issuances of our Common Stock in the public markets, or the perception of such sales, could depress the trading price of our Common Stock.

The sale of a substantial number of shares of our Common Stock or other equity-related securities in the public markets, or the perception that such sales could occur, could depress the market price of our Common Stock and

impair our ability to raise capital through the sale of additional equity securities. We may sell large quantities of our Common Stock at any time pursuant to this prospectus supplement or in one or more separate offerings. We cannot predict the effect that future sales of Common Stock or other equity-related securities would have on the market price of our Common Stock.

It is not possible to predict the actual number of shares we will sell under the Amended Sales Agreement, or the gross proceeds resulting from those sales.

Subject to certain limitations in the Amended Sales Agreement and compliance with applicable law, we have the discretion to deliver instruction to Jefferies to sell shares of our Common Stock at any time throughout the term of the Amended Sales Agreement. The number of shares, if any, that are sold through Jefferies after our instruction will fluctuate based on a number of factors, including the market price of our Common Stock during the sales period, the limits we set with Jefferies in any instruction to sell shares, and the demand for our Common Stock during the sales period. Because the price per share of each share sold, if any, will fluctuate during this offering, it is not currently possible to predict the number of shares that will be sold or the gross proceeds to be raised in connection with those sales.

The Common Stock offered hereby will be sold in "at the market offerings," and investors who buy shares at different times will likely pay different prices.

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering, contain forward-looking statements about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein, including statements regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations, including our statements regarding the benefits and timing of the roll-out of new technology, are forward-looking statements. In some cases, you can identify forward-looking statements because they contain words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will" or "would" or the negative of these words or other similar terms or expressions. Forward-looking statements in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein, include, but are not limited to, statements about:

- · our expected uses of the net proceeds from this offering;
- our expectations regarding the potential benefits, spectrum coverage and immunogenicity of our vaccine candidates;
- our expectations regarding our preclinical study results potentially being predictive of clinical study results;
- our belief that our PCVs could receive regulatory approval based on a demonstration of non-inferiority to the standard of care using well-defined surrogate immune endpoints rather than requiring clinical field efficacy studies;
- the timing of the initiation, progress and expected results of our preclinical studies, clinical trials and our research and development programs;
- our ability to advance vaccine candidates into, and successfully complete, preclinical studies and clinical trials;
- the commercialization of our vaccine candidates, if approved;
- estimates of our total addressable market, future revenue, expenses, capital requirements and our needs for additional financing;
- our ability to compete effectively with existing competitors and new market entrants;
- our ability to establish and maintain intellectual property protection for our products or avoid claims of infringement;
- our manufacturing capabilities and the scalable nature of our manufacturing process;
- potential effects of extensive government regulation;
- the pricing, coverage and reimbursement of our vaccine candidates, if approved;
- our ability and the ability of our third-party contract manufacturers to operate and continue operations in light of the COVID-19 pandemic;
- our ability to hire and retain key personnel;
- our ability to obtain additional financing in this or future offerings; and
- the volatility of the trading price of our Common Stock.

You should not rely on forward-looking statements as predictions of future events. We have based the forward-looking statements contained in this prospectus supplement and the accompanying prospectus, including the

documents incorporated by reference herein, primarily on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. The outcome of the events described in these forward-looking statements is subject to risks, uncertainties and other factors described in the section titled "Risk Factors" and elsewhere in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein. Moreover, we operate in a very competitive and rapidly changing environment. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein. The results, events and circumstances reflected in the forward-looking statements may not be achieved or occur, and actual results, events or circumstances could differ materially from those described in the forward-looking statements.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein. While we believe that information provides a reasonable basis for these statements, that information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements.

The forward-looking statements made in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, relate only to events as of the date on which the statements are made. We undertake no obligation to update any forward-looking statements made in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein, to reflect events or circumstances after the date of this prospectus supplement, or to reflect new information or the occurrence of unanticipated events, except as required by law. 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. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments.

USE OF PROCEEDS

We may issue and sell shares of our Common Stock having aggregate sales proceeds of up to \$400.0 million from time to time. Because there is no minimum offering price for the shares that we may offer from time to time, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the Amended Sales Agreement with Jefferies as a source of financing.

The principal purposes of this offering are to increase our capitalization and financial flexibility. We currently intend to use the net proceeds we receive from this offering, if any, together with our existing cash, cash equivalents and investments, to fund the advancement of our current vaccine candidates VAX-24, VAX-31, VAX-A1 and VAX-PG; to fund ongoing research and the potential development of our discovery-stage programs; and for other general corporate purposes, including working capital, operating expenses and capital expenditures, as well as potential expansion of our research pipeline.

This expected use of the net proceeds from this offering represents our intentions based on our current plans and business conditions, which could change in the future as our plans and business conditions evolve. Further, due to the uncertainties inherent in the vaccine development process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering that may be used for the above purposes. We cannot specify with certainty all of the particular uses for the remaining net proceeds to us from this offering. We may also use a portion of the net proceeds for acquisitions or strategic investments in complementary businesses, products, services or technologies or in connection with partnering and manufacturing arrangements. However, we do not have agreements or commitments to enter into any such acquisitions or investments at this time. We will have broad discretion over how to use the net proceeds to us from this offering, and our investors will be relying on the judgment of our management regarding the application of the net proceeds of this offering. The amounts and timing of our expenditures will depend upon numerous factors including the results of our research and development efforts, the timing and success of preclinical studies and any clinical trials we may commence in the future, the timing of regulatory submissions, and the amount of cash obtained through any future collaborations.

As of the date of this prospectus supplement, we cannot predict with certainty all of the particular uses for the net proceeds from this offering or the amounts that we will actually spend on the uses set forth above. As a result, our management will have broad discretion regarding the timing and application of the net proceeds from this offering. We intend to invest the net proceeds to us from this offering that are not used as described above in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DILUTION

Our historical net tangible book value as of December 31, 2022 was \$953.6 million, or \$12.00 per share of our Common Stock. Our historical net tangible book value represents the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share represents historical net tangible book value divided by the number of shares of our Common Stock outstanding as of December 31, 2022.

After giving effect to the sale of 9,592,326 shares of Common Stock that we are offering at the assumed public offering price of \$41.70 per share, which was the last reported sale price of our Common Stock on the Nasdaq Global Select Market on February 24, 2023, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2022, would have been approximately \$1.34 billion, or approximately \$15.06 per share. This amount represents an immediate increase in as adjusted net tangible book value of \$3.06 per share to our existing stockholders and an immediate dilution in net tangible book value of approximately \$26.64 per share to new investors purchasing shares of Common Stock in this offering.

Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the price per share paid by new investors. The following table illustrates this dilution:

Assumed public offering price per share		\$ 41.70
Historical net tangible book value per share as of December 31, 2022	\$ 12.00	
Increase in as adjusted net tangible book value per share attributable to this offering	3.06	
As adjusted net tangible book value per share after this offering		15.06
Dilution per share to new investors in this offering		\$ 26.64

Each \$1.00 increase in the assumed public offering price of \$41.70 per share, which was the last reported sale price of our Common Stock on the Nasdaq Global Select Market on February 24, 2023, would increase the as adjusted net tangible book value per share after this offering by approximately \$3.17, and dilution in as adjusted net tangible book value per share to new investors by approximately \$27.53, after deducting commissions and estimated offering expenses payable by us. Each \$1.00 decrease in the assumed public offering price of \$41.70 per share, which was the last reported sale price of our Common Stock on the Nasdaq Global Select Market on February 24, 2023, would increase the as adjusted net tangible book value per share after this offering by approximately \$2.95, and dilution in as adjusted net tangible book value per share to new investors by approximately \$25.75.

The outstanding share information in the table above is based on 79,470,670 shares of our Common Stock outstanding as of December 31, 2022, and excludes:

- 7,752,204 shares of our Common Stock issuable upon the exercise of options to purchase shares of our Common Stock outstanding as of December 31, 2022, with a weighted-average exercise price of \$18.62 per share;
- 456,766 shares of our Common Stock issuable upon settlement of restricted stock units outstanding as of December 31, 2022;
- 4,679,598 shares of our Common Stock reserved for future issuance under our 2020 Equity Incentive Plan as of December 31, 2022, as well as any annual evergreen increases in the number of shares reserved for future issuance under this plan;
- 1,539,314 shares of our Common Stock reserved for future issuance under our 2020 Employee Stock Purchase Plan as of December 31, 2022, as well as any annual evergreen increases in the number of shares reserved for future issuance under this plan; and

• 6,250,000 shares of our Common Stock issuable upon the exercise of pre-funded warrants outstanding as of December 31, 2022 at an exercise price of \$0.001 per share.

Subsequent to December 31, 2022 and through the date of this prospectus supplement:

- we granted stock options to purchase 78,946 shares of our Common Stock with a weighted-average exercise price of \$45.67 per share:
- we reserved an additional 3,973,533 shares of common stock for future issuance under our 2020 Equity Incentive Plan pursuant to the annual evergreen increase;
- we reserved an additional 794,706 shares of common stock for future issuance under our 2020 Employee Stock Purchase Plan
 pursuant to the annual evergreen increase; and
- we sold 507,136 shares of our Common Stock for total gross proceeds of approximately \$23.0 million under the Sales Agreement.

To the extent any outstanding options or warrants are exercised, outstanding restricted stock units vest, new options or other equity awards are issued under our equity incentive plans, or we issue additional equity or convertible debt securities in the future, there will be further dilution to new investors.

PLAN OF DISTRIBUTION

On July 1, 2021, we entered into the Sales Agreement with Jefferies, under which we may offer and sell shares of our Common Stock from time to time through Jefferies acting as sales agent. On February 27, 2023, we entered into an amendment to the Sales Agreement. In accordance with the Amended Sales Agreement and pursuant to this prospectus supplement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$400.0 million from time to time, exclusive of any shares sold pursuant to the Sales Agreement under the Prior ATM Sales Prospectus.

Sales of our shares of Common Stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act.

Each time we wish to issue and sell our shares of Common Stock under the Amended Sales Agreement, we will notify Jefferies of the number of shares to be issued, the dates on which such sales are anticipated to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Jefferies, unless Jefferies declines to accept the terms of such notice, Jefferies has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Jefferies under the Amended Sales Agreement to sell our shares of Common Stock are subject to a number of conditions that we must meet.

The settlement of sales of shares between us and Jefferies is generally anticipated to occur on the second trading day following the date on which the sale was made. Sales of our shares of Common Stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Jefferies may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Jefferies a commission rate of up to 3.0% of the gross proceeds of any shares of Common Stock sold under the Amended Sales Agreement. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. In addition, we have agreed to reimburse Jefferies for the fees and disbursements of its counsel, payable upon execution of the Amended Sales Agreement, in an amount not to exceed \$35,000, in addition to certain ongoing disbursements of its legal counsel, unless we and Jefferies otherwise agree. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Jefferies under the terms of the Amended Sales Agreement, will be approximately \$250,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Jefferies will provide written confirmation to us before the open on the Nasdaq Global Select Market on the day following each day on which our shares of Common Stock are sold under the Amended Sales Agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to us.

In connection with the sale of our shares of Common Stock on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain civil liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of our shares of Common Stock pursuant to the Amended Sales Agreement will terminate upon the earlier of (i) the sale of all shares of Common Stock subject to the Amended Sales Agreement and (ii) the termination of the Amended Sales Agreement as permitted therein. We and Jefferies may each terminate the Amended Sales Agreement at any time upon ten days' prior notice.

This summary of the material provisions of the Amended Sales Agreement does not purport to be a complete statement of its terms and conditions. A copy of the Amended Sales Agreement is filed as an exhibit to Form 8-K filed on February 27, 2023 and is incorporated by reference in this prospectus supplement.

Jefferies and its affiliates may in the future provide various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates, for which services they may in the future receive customary fees. In the course of its business, Jefferies may actively trade our securities for its own account or for the accounts of customers, and accordingly, Jefferies may at any time hold long or short positions in such securities.

A prospectus in electronic format may be made available on a website maintained by Jefferies, and Jefferies may distribute the prospectus electronically.

LEGAL MATTERS

The validity of the shares of Common Stock offered by this prospectus supplement will be passed upon for us by Cooley LLP, Palo Alto, California. Jefferies LLC is being represented in connection with this offering by Latham & Watkins LLP, Menlo Park, California.

EXPERTS

The financial statements of Vaxcyte, Inc. as of December 31, 2022 and 2021, and for each of the three years in the period ended December 31, 2022, incorporated by reference in this prospectus supplement by reference to Vaxcyte, Inc.'s annual report on Form 10-K for the year ended December 31, 2022, and the effectiveness of Vaxcyte, Inc.'s internal controls over financial reporting have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their reports. Such financial statements are incorporated by reference in reliance upon the reports of such firm given their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

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

Our website address is https://www.vaxcyte.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus supplement and the accompanying prospectus.

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

INCORPORATION BY REFERENCE

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

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act in this prospectus supplement and accompanying prospectus, between the date of this prospectus supplement and the termination of the offering of the securities described in this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed "filed" with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

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

- our <u>Annual Report on Form 10-K</u> for the year ended December 31, 2022, filed with the SEC on February 27, 2023;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2021 from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 20, 2022; and
- the description of our Common Stock contained in our registration statement on <u>Form 8-A</u>, filed with the SEC on June 9, 2020, as updated by <u>Exhibit 4.2</u> to our Annual Report on Form 10-K for the year ended December 31, 2020, and any amendment or report filed with the SEC for the purpose of updating the description.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus supplement but not delivered with this prospectus supplement, including exhibits which are specifically incorporated by reference into such documents. You should direct any requests for documents by writing or telephoning us at the following address and telephone number:

Vaxcyte, Inc.
Attention: Corporate Secretary
825 Industrial Road
Suite 300
San Carlos, CA 94070
(650) 837-0111

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PROSPECTUS



Common Stock Preferred Stock Debt Securities Warrants

We may offer and sell the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities pursuant to this prospectus, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, together with the documents we incorporate by reference, before you invest in any of our securities.

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

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

Our common stock is listed on the Nasdaq Global Select Market under the symbol "PCVX." On June 30, 2021, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$22.51 per share.

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

The date of this prospectus is July 1, 2021.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act of 1933, as amended, which we refer to as the "Securities Act" in this prospectus, using a "shelf" registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. We may also authorize one or more free writing prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading "Where You Can Find More Information; Incorporation by Reference."

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

When we refer to "Vaxcyte," "we," "our," "us" and the "Company" in this prospectus, we mean Vaxcyte, Inc., unless otherwise specified.

This prospectus also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the $^{\circledR}$ and $^{\intercal}$ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

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

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

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

Incorporation by Reference

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

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, between the date of this prospectus and the termination of the offering of the securities described in this prospectus. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed "filed" with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus incorporates by reference the documents set forth below that have previously been filed with the SEC (Commission No. 001-39323):

- our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 29, 2021;
- our Quarterly Report on Form 10-Q for the quarter ended on March 31, 2021, filed with the SEC on May 11, 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, filed with the SEC on April 14, 2021;
- the description of our common stock contained in our registration statement on <u>Form 8-A</u>, filed with the SEC on June 9, 2020, as updated by <u>Exhibit 4.2</u> to our Annual Report on Form 10-K for the year ended December 31, 2020, and any amendment or report filed with the SEC for the purpose of updating the description; and

• our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on <u>January 25, 2021</u>, <u>March 25, 2021</u> and <u>June 3, 2021</u>.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Vaxcyte, Inc. Attention: Corporate Secretary 353 Hatch Drive Foster City, CA 94404 (650) 837-0111

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

THE COMPANY

We are a next-generation vaccine company seeking to improve global health by developing superior and novel vaccines designed to prevent or treat some of the most common and deadly infectious diseases worldwide. Our cell-free protein synthesis platform enables us to design and produce protein carriers and antigens, the critical building blocks of vaccines, in ways that we believe conventional vaccine technologies currently cannot.

Vaccines are one of the most successful and cost-effective global health interventions and prevent millions of deaths worldwide each year. Routine pediatric vaccinations are estimated to prevent 20 million cases of disease each year, saving over \$180 billion in direct and societal costs in the United States alone. Adult vaccination rates are lower than pediatric vaccination rates, but new technologies are driving adult vaccine development, which in turn is fueling the growth of the overall vaccine market. Given the critical role vaccines play in preventing disease from childhood to adulthood, the global vaccine market is large, durable and growing. Nonetheless, there are areas of unmet medical need, including vaccines that can provide broader protection than currently marketed vaccines and novel vaccines that target pathogens for which there are no currently approved vaccines.

We carefully select our target disease areas and vaccine candidates to address areas of significant unmet medical need based on the following criteria: well-defined commercial landscape and efficient market adoption, low biological risk and established clinical pathways. We are leveraging our scalable cell-free protein synthesis platform to develop potentially superior and novel conjugate and protein vaccine candidates for adult and pediatric indications using these criteria.

We were incorporated under the laws of the state of Delaware in November 2013 as SutroVax, Inc. and changed our name to Vaxcyte, Inc. in May 2020. Our principal executive office is located at 353 Hatch Drive, Foster City, California 94404. Our telephone number is (650) 837-0111. Our website address is www.vaxcyte.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus.

RISK FACTORS

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

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement, as well as the documents incorporated by reference in this prospectus or any accompanying prospectus supplement, contain forward-looking statements within the meaning of Section 21E of the Exchange Act. All statements other than statements of historical facts contained in this prospectus, any accompanying prospectus supplement and the documents incorporated by reference, including statements regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations, including our statements regarding the benefits and timing of the roll-out of new technology, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus, any accompanying prospectus supplement and the documents incorporated by reference also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements because they contain words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "seek," "should," "target," "will," or "would," or the negative of these words or other similar terms or expressions. The forward-looking statements in this prospectus, any accompanying prospectus supplement and the documents incorporated by reference are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of the document containing the applicable statement and are subject to a number of risks, uncertainties and assumptions, which we discuss in greater detail in the documents incorporated by reference, including under the heading "Risk Factors" and elsewhere in this prospectus. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus, any accompanying prospectus supplement or the documents incorporated by reference, whether as a result of any new information, future events, changed circumstances or otherwise. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Secur

USE OF PROCEEDS

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

DIVIDEND POLICY

We have not declared or paid any cash dividend on our common stock. We intend to retain any future earnings and do not expect to pay cash dividends in the foreseeable future. Payment of cash dividends, if any, in the future will be at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is not complete and may not contain all the information you should consider before investing in our capital stock. This description is summarized from, and qualified in its entirety by reference to, our amended and restated certificate of incorporation, which has been publicly filed with the SEC. See "Where You Can Find More Information; Incorporation by Reference."

General

Our authorized capital stock consists of 510,000,000 shares, all with a par value of \$0.001 per share, of which:

- 500,000,000 shares are designated as common stock; and
- 10,000,000 shares are designated as preferred stock.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, including the election of directors, and do not have cumulative voting rights. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared by the board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the assets legally available for distribution to stockholders after the payment of or provision for all of our debts and other liabilities, subject to the prior rights of any preferred stock then outstanding. Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking funds provisions applicable to the common stock. All outstanding shares of common stock are duly authorized, validly issued, fully paid and nonassessable. All authorized but unissued shares of our common stock will be available for issuance by our board of directors without any further stockholder action, except as required by the listing standards of the Nasdaq Stock Market. 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.

Preferred Stock

Pursuant to our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or stock exchange listing rules), to designate and issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the designations, powers, preferences, privileges and relative participating, optional or special rights and the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, voting rights, terms of redemption and liquidation preferences, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

The preferred shares may have voting or conversion rights that could have the effect of restricting dividends on our shares of common stock, diluting the voting power of our shares of common stock, impairing the rights of our shares of common stock in the event of our dissolution, liquidation or winding-up or otherwise adversely affect the rights of holders of our shares of common stock. The issuance of preferred shares, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change of control and may adversely affect the market price of our shares of common stock and may preclude stockholders from realizing a potential premium over the market value of their shares.

Our board of directors will fix the designations, voting powers, preferences, rights, qualifications, limitations and restrictions of each series of preferred stock that we offer under this prospectus and applicable prospectus

supplements in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering.

This description will include:

- the title and stated value;
- · the number of shares we are offering;
- · the liquidation preference per share;
- · the purchase price per share;
- the dividend rate per share, dividend period and payment dates and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock or other securities of ours, including depositary shares and warrants, and, if applicable, the conversion period, the conversion price, or how it will be calculated, and under what circumstances it may be adjusted;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange period, the exchange price, or how it
 will be calculated, and under what circumstances it may be adjusted;
- voting rights, if any, of the preferred stock;
- preemption rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on issuances of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, rights, preferences, privileges, qualifications or restrictions of the preferred stock.

The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as a series) on an

amendment to our amended and restated certificate of incorporation if the amendment would change the par value or, unless the amended and restated certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Registration Rights

We are party to an amended and restated investor rights agreement that provides that certain stockholders, including certain holders of at least 5% of our outstanding capital stock, have certain registration rights as set forth below. We refer to these shares collectively as registrable securities. The registration of the registrable securities by the exercise of registration rights described below would enable the holders to sell these registrable securities without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses, other than underwriting discounts and commissions, of the registrable securities registered pursuant to the demand, piggyback and Form S-3 registration rights described below.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares such holders may include. The demand, piggyback and Form S-3 registration rights described below will expire June 16, 2023, or with respect to any particular stockholder, such time that such stockholder can sell all of its shares entitled to registration rights under Rule 144 of the Securities Act during any 90-day period.

Demand Registration Rights

At any time beginning on December 8, 2020, the holders of a majority of the registrable securities may request that we register all or a portion of their shares. We are obligated to effect only two such registrations. Such request for registration must cover shares with an anticipated aggregate offering price, net of underwriting discounts and commissions, of at least \$10.0 million.

Piggyback Registration Rights

In the event that we propose to register any of our securities under the Securities Act, either for our own account or for the account of other security holders, the holders of these registrable securities will be entitled to certain piggyback registration rights allowing the holder to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to (i) a registration statement relating to any employee benefit plans, (ii) a registration relating to a corporate reorganization or other Rule 145 transaction, (iii) a registration relating to the offer and sale of debt securities or (iv) a registration on any registration form that does not permit secondary sales, the holders of these shares are entitled to notice of the registration and have the right to include their shares in the registration, subject to limitations that the underwriters may impose on the number of shares included in the offering.

Form S-3 Registration Rights

The holders of these registrable securities can make a request that we register their shares on Form S-3 if we are qualified to file a registration statement on Form S-3 and if they reasonably anticipated aggregate gross proceeds of the shares offered would equal or exceed \$1.0 million. We will not be required to effect more than three registrations on Form S-3 within any 12-month period.

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

Some provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make the following transactions more difficult: an acquisition of us

by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Stockholder Meetings

Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president, or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

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

Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation and amended and restated bylaws eliminate the right of stockholders to act by written consent without a meeting.

Staggered Board

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors

Our amended and restated certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two thirds of the total voting power of all of our outstanding voting stock then entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting

Our amended and restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute

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

Choice of Forum

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, in the event that the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) will, to the fullest extent permitted by applicable law, be the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers, or employees to us or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or employees arising out of or pursuant to any provision of the DGCL or our certificate of incorporation or bylaws; (iv) any action or proceeding to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; (v) any action or proceeding as to which the DGCL confers jurisdiction to the Court of Chancery of the State of Delaware; or (vi) any action or proceeding asserting a claim against us or any of our current or former directors, officers or employees governed by the internal affairs doctrine. This provision does not apply to suits brought to enforce a duty or liability created by the Securities Act, the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction. Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. Our amended and restated certificate of incorporation also provides that any person or entity holding, owning, purchasing or otherwise acquiring any interest in any of our securities will be deemed to have notice of and to have consented to these choice of forum provisions. While the Delaware courts have determined that such choice of forum provisions are facially valid, it is possible that a court of law in another jurisdiction could rule that the choice of forum provisions to be contained in our amended and restated certificate of incorporation are inapplicable or unenforceable if they are challenged in a proceeding or otherwise. If a court were to find the choice of forum provision that will be contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions.

Amendment of Charter Provisions

The amendment of any of the above provisions requires approval by holders of at least two-thirds of the total voting power of all of our outstanding voting stock.

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

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, New York 11219. The transfer agent for any series of preferred stock that we may offer under this prospectus will be named and described in the prospectus supplement for that series.

Exchange Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "PCVX."

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as "discount securities," which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with "original issue discount," or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- · the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of
 any subordination;

- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- · our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple
 thereof:
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our
 obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt
 securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;

- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any, and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal

amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, of such series of debt securities due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.
- A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:
- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request;
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;
- to comply with the provisions described above under "Description of Debt Securities—Consolidation, Merger or Sale;"

- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of
 the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such
 additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the
 indenture:
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under "Description of Debt Securities—General" to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- · hold monies for payment in trust;
- · recover excess money held by the trustee;
- · compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depositary named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange of any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

DESCRIPTION OF WARRANTS

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

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

Those terms may include:

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

Holders of warrants will not be entitled to:

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

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

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any

other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

GLOBAL SECURITIES

Book-Entry, Delivery and Form

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

DTC has advised us that it is:

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

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

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

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

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depositary and its direct and indirect participants. We will maintain an office or

agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

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

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

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

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

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

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

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

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

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

- DTC notifies us that it is unwilling or unable to continue as a depositary for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depositary is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;
- · we determine, in our sole discretion, not to have such securities represented by one or more global securities; or
- an Event of Default has occurred and is continuing with respect to such series of securities, we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depositary directs. It is expected that these directions will be based upon directions received by the depositary from its participants with respect to ownership of beneficial interests in the global securities.

Euroclear and Clearstream

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

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

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

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

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

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

Other

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

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, "at-the-market" offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through one or more underwriters or dealers (acting as principal or agent), through agents, or directly to one or more purchasers.

We may distribute securities from time to time in one or more transactions:

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

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of the underwriters, dealers or agents, if any;
- the purchase price of the securities or other consideration therefor, and the proceeds, we will receive from the sale;
- · any over-allotment or other options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement. Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts. If such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. If a dealer is used in the sale of securities, we or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. To the extent required, we will set forth in the prospectus supplement the name of the dealer and the terms of the transaction. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time.

We may use underwriters, dealers or agents with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, dealer or agent, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions payable to the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, the agent will act on a best-efforts basis for the period of its appointment.

We may provide agents, underwriters and dealers with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents, underwriters or dealers may make with respect to these liabilities. Agents, underwriters and dealers, or their affiliates, may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under 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 price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or 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 stabilizing or 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.

Any underwriters that are qualified market makers on The Nasdaq Global Select Market may engage in passive market making transactions in the common stock on The Nasdaq Global Select Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

LEGAL MATTERS

Cooley LLP, Palo Alto, California, will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Vaxcyte, Inc. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements incorporated in this prospectus by reference from the Annual Report on Form 10-K have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated by reference herein. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

Up to \$400,000,000



Common Stock

PROSPECTUS SUPPLEMENT

Jefferies

February 27, 2023

Calculation of Filing Fee Tables

424(b)(5) (Form Type)

Vaxcyte, Inc.

(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Share	Maximum Aggregate Offering Price ⁽¹⁾	Fee Rate	Amount of Registration Fee ⁽²⁾
Fees to Be Paid		Common stock, par	455()					
	Equity	value \$0.001 per share	457(o) and 457(r)	_		\$400,000,000	\$0.00011020	\$44,080
	Total Offering Amounts					\$400,000,000		\$44,080
	Total Fees Previously Paid							
	Total Fee Offsets							_
	Net Fees Due							\$44,080

 ⁽¹⁾ The proposed maximum aggregate offering price is being used to calculate the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.
 (2) The registration fee relates to the Registration Statement on Form S-3ASR (File No. 333-257622) filed by the Registrant on July 2, 2021.