UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____

Commission File Number 001-39323

VAXCYTE, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**46-4233385**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
825 Industrial Road, Suite 300 San Carlos, California	**94070ca**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (650) 837-0111

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	PCVX	The Nasdaq Stock Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☒ NO ☐

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

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

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
Emerging growth company	☐		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of its Common Stock on the Nasdaq Global Select Market on June 30, 2022, the last business day of the Registrant's most recently completed second fiscal quarter, was approximately $1.1 billion. Shares of the Registrant's common stock held by each executive officer, director and holder of 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates. This calculation does not reflect a determination that certain persons are affiliates of the Registrant for any other purpose.

The number of shares of Registrant's Common Stock outstanding as of February 23, 2023 was 80,033,727.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates information by reference from the Registrant's definitive proxy statement to be filed with the U.S. Securities and Exchange Commission pursuant to Regulation 14A, not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, in connection with the Registrant's 2023 annual meeting of stockholders.

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Unless the context otherwise requires, all references in this Annual Report on Form 10-K to "we," "us," "our," "our company" and "Vaxcyte" refer to Vaxcyte, Inc.

"Vaxcyte," "eCRM," and other trademarks of ours appearing in this report are our property. This report contains additional trade names and trademarks of other companies. We do not intend our use or display of other companies' trade names or trademarks to imply an endorsement or sponsorship of us by such companies, or any relationship with any of these companies.

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains 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 Annual Report on Form 10-K, including statements regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations, 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," "seek," "should," "target," "will," or "would," or the negative of these words or other similar terms or expressions. Forward-looking statements contained in this Annual Report on Form 10-K include, but are not limited to, statements about:

- our expectations regarding the potential benefits, spectrum of 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 pneumococcal conjugate vaccine candidates 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 potential 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 future 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 and our third-party manufacturers' 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; and
- the volatility of the trading price of our common stock.

Actual events or results may differ from those expressed in forward-looking statements. You should not rely on forward-looking statements as predictions of future events. We have based the forward-looking statements contained in this Annual Report on Form 10-K 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 Annual Report on Form 10-K. 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 Annual Report on Form 10-K. 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 Annual Report on Form 10-K. 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K to reflect events or circumstances after the date of this Annual Report on Form 10-K 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.

Summary of Risks Affecting Our Business

Our business is subject to numerous risks and uncertainties, including those discussed more fully in the section titled "Risk Factors" in this Annual Report on Form 10-K. These risks include, but are not limited to, the following:

- We are in the clinical or preclinical phase of vaccine development and have a very limited operating history and no products approved for commercial sale, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- We have incurred significant net losses since inception and anticipate that we will continue to incur substantial net losses for the foreseeable future. We currently have no source of product revenue and may never achieve profitability. Our stock is a highly speculative investment.
- We will require substantial additional funding to finance our operations, which may not be available to us on acceptable terms, or at all. If we are unable to raise additional capital when needed, we could be forced to delay, reduce or terminate certain of our development programs or other operations.
- Our approach to the discovery and development of our vaccine candidates is based on novel technologies that are unproven, which may expose us to unforeseen risks, require us to modify processes, and make it difficult to predict the time and cost of vaccine candidate development and the timing to apply for and obtain regulatory approvals.
- Our vaccine candidates are in clinical or preclinical stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability. If we are unable to complete development of or commercialize our vaccine candidates or experience significant delays in doing so, our business would be materially harmed.
- The U.S. Food and Drug Administration ("FDA") may disagree with our regulatory plan, and we may fail to obtain regulatory approval of our vaccine candidates.
- Our business is highly dependent on the success of VAX-24, which is in clinical development. If we are unable to obtain approval for VAX-24 and effectively commercialize VAX-24, our business would be significantly harmed.
- Our primary competitors have significantly greater resources and experience than we do, which may make it difficult for us to successfully develop our vaccine candidates, or may result in others discovering, developing or commercializing products before or more successfully than us.
- We may not be successful in our efforts to use our cell-free protein synthesis platform to expand our pipeline of vaccine candidates and develop marketable products.

- We currently rely on third-party manufacturing and supply partners, including Lonza Ltd. and Sutro Biopharma, Inc. to supply raw materials and components for, and manufacture of, our preclinical and clinical supplies as well as our vaccine candidates. Our inability to procure necessary raw materials or to have sufficient quantities of preclinical and clinical supplies or the inability to have our vaccine candidates manufactured, including delays or interruptions at our third-party manufacturers, or our failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, would materially and adversely affect our business.
- Health epidemics, including the effects of the ongoing COVID-19 pandemic, have impacted and could continue to impact our business, including in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of potential clinical trial sites or other business operations.
- The FDA regulatory approval process is lengthy and time-consuming, and we may experience significant delays in the clinical development and regulatory approval of our vaccine candidates.
- If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

PART I

Item 1. Business.

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.

Our Approach

To address areas of significant unmet medical need, we carefully select the disease areas we target and are developing vaccine candidates based on the following criteria:

- *Well-defined commercial landscape and efficient market adoption:* We select vaccine targets that are characterized by an established patient population and significant unmet medical need. Our lead vaccine candidate, VAX-24, is a PCV intended to improve upon the standard-of-care for both children and adults by covering the serotypes that are responsible for most of the residual pneumococcal disease currently in circulation without sacrificing immunogenicity. We believe that by providing the broadest coverage of serotypes for PCVs, as well as providing novel vaccines for diseases for which there are no currently approved vaccines, we can leverage the U.S. Centers for Disease Control, or CDC, its Advisory Committee on Immunization Practices, or ACIP, and similar international advisory body recommendations to drive rapid and significant market adoption.

- *Acceptable biological risk:* We choose vaccine targets with well-understood mechanisms of action and strong precedents for positive preclinical study results that we believe will translate to positive clinical trial results. For example, conjugate vaccines have demonstrated effectiveness in both preclinical and clinical trials against a range of bacteria, including pneumococcus, meningococcus and Haemophilus influenza B. There is consistent evidence that antibodies directed against these bacteria are protective against their respective diseases.

- *Established clinical pathways:* We pursue vaccine targets that we believe have clear and established clinical development pathways in order to accelerate the potential time to market. For example, we believe that our PCVs could receive regulatory approval based on successful completion of clinical studies utilizing well-defined surrogate immune endpoints, consistent with how other PCVs have obtained regulatory approval in the past, rather than requiring clinical field efficacy studies. However, while there have been approvals granted for both PCVs and meningococcal conjugate vaccines based on surrogate immune endpoints rather than field efficacy studies, we will not be able to confirm this approach's applicability for our PCVs until we complete our interactions with the FDA prior to the initiation of our Phase 3 clinical development program. For our novel vaccine candidates, where we believe clinical field efficacy studies will be necessary, we select disease areas with high attack rates, such as Group A Strep, which may allow for more manageable study sizes. For novel protein-based therapeutic vaccine candidates, such as our periodontitis vaccine candidate, we select disease areas where we believe clinical efficacy may be evaluated based on

disease progression rather than prevention, which could allow for smaller and faster trials relative to preventative vaccines.

Our Platform

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 to develop potentially superior and novel conjugate and protein vaccine candidates for adult and pediatric indications using the above criteria by taking advantage of the following:

- *Site-Specific Conjugation.* We are able to specify the attachment point of antigens, including polysaccharides, on protein carriers to ensure optimal exposure of B-cell and/or T-cell epitopes, thereby creating protein carriers designed to have enhanced potency. We believe this precise control of conjugation chemistry enables us to create 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.

- *Production of Novel Protein Vaccines*. We can design novel protein vaccine candidates based on well-appreciated but highly complex antigens that currently cannot be made with conventional technologies to address diseases for which there are no available vaccines, and we believe we may be able to leverage our platform to rapidly respond to new or emerging pathogens. We can design and produce these “tough-to-make” antigens that conform to the target pathogens, thereby increasing the likelihood that the vaccine will elicit a protective immune response.

- *Speed, Flexibility and Scalability of the Discovery Engine.* We are able to rapidly screen vaccine candidates and produce conjugates, thereby accelerating the process of making and testing vaccine candidates. Because cell viability is not required for cell-free protein synthesis, we can utilize a broader range of reaction conditions as we seek to optimize proteins. This flexibility enables us to develop novel vaccine candidates unachievable with current technologies. Furthermore, we believe our platform can scale linearly from discovery to commercial scale.

Our Strategy

Our goal is to become a leader in the vaccines industry by using our cell-free protein synthesis platform to develop superior and/or novel vaccines to prevent or treat serious infectious diseases. Key elements of our strategy include:

- *Advance VAX-24 through clinical development and regulatory approval.* Our lead vaccine candidate, VAX-24, targets the pneumococcal vaccine market. We expect to advance VAX-24 along a well-understood clinical development pathway in an effort to obtain regulatory approval in adults and infants based on successful completion of clinical studies using previously established surrogate immune endpoints, potentially without the need to conduct clinical field efficacy studies, consistent with how other conjugate vaccines have obtained approval. In the fourth quarter of 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 healthy adults aged 18-64. 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 FDA to inform the Phase 3 program in the second half of 2023. We expect topline safety, tolerability and immunogenicity data from the Phase 3 non-inferiority study in adults in 2025. The FDA has granted Fast Track and Breakthrough Therapy designations for VAX-24 in adults. For our VAX-24 pediatric program, we announced in late February 2023 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.

- *Advance VAX-31 through IND-enabling activities, clinical development and regulatory approval.* Our second PCV candidate, VAX-31, leverages our scalable and modular platform and builds on the technical proof of concept established by 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 U.S. adult 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.

- *Establish scalable production of VAX-24 and VAX-31.* We believe high-quality and scalable manufacturing is critical to our long-term success. We have designed and developed a proprietary, scalable and portable manufacturing process that we have scaled to supply clinical volumes and believe can scale to supply initial commercial volumes of VAX-24 and VAX-31 needed to support commercial launch. For our VAX-24 program, we have completed the production of clinical trial materials for our Phase 1 and 2 studies in both adults and infants and are conducting scale-up activities to support potential regulatory approval and commercial launch. We have access to substantial manufacturing resources through our contract manufacturer, Lonza, that we believe can facilitate an independent path to market. For our next-generation VAX-31 program, for which we use the same components and core manufacturing processes established for VAX-24, we are currently conducting IND-enabling activities.

- *Create a long-lasting PCV franchise by offering the broadest-spectrum PCV available.* The two leading pneumococcal vaccine franchises to date, Prevnar and Pneumovax 23, or PPSV23, have generated over $100 billion in combined sales, have been on the market for over 40 years and 20 years, respectively, and can attribute their success to being the broadest-spectrum vaccines on the market. If approved, we believe VAX-24 may obtain an ACIP preferred recommendation and potentially replace both lesser-valent incumbents for pneumococcal disease prevention in both adult and pediatric populations because of its broader coverage. We designed VAX-24 to address the 24 pneumococcal strains covered by Prevnar and PPSV23 that drive most pneumococcal disease today with the durable, boostable immune response of a conjugate vaccine. Further, we have designed VAX-31 to address these 24 strains plus seven additional epidemiologically significant emerging strains expected to cause increasing pneumococcal disease and antibiotic resistance in the future. With these broad-spectrum vaccine candidates, we believe we are well-positioned to obtain an ACIP preferred recommendation and potentially replace the current standard of care for pneumococcal disease prevention in both adult and pediatric populations, thereby creating a long-lasting PCV franchise.

- *Advance our novel vaccine candidates and leverage our platform to expand our pipeline.*

    - *Advance VAX-A1 through IND-enabling activities, clinical development and regulatory approval*. VAX-A1 is designed to prevent Group A Strep, a pervasive disease that results in 700 million cases of illness each year and is one of the leading infectious disease-related causes of death and disability worldwide. Some of the most serious consequences of Group A Strep include flesh eating disease (necrotizing fasciitis) and invasive diseases such as sepsis and rheumatic heart disease. However, the majority of Group A Strep cases are pharyngitis, commonly known as strep throat. Pharyngitis is highly prevalent in school-age children and a significant source of antibiotic prescriptions, which further exacerbates the growing problem of antibiotic resistance globally. VAX-A1 is a conjugate vaccine candidate designed to confer broad protective immune responses against all subtypes of Group A Strep and be boostable to offer long-lasting protection from infection. We believe our data published in December 2020 demonstrated preclinical proof of concept for VAX-A1. 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 we intend to provide further information about the anticipated timing of an IND application as the program progresses.

- *Advance VAX-PG to final vaccine candidate nomination and IND-enabling activities, clinical development and regulatory approval.* VAX-PG is our novel protein vaccine candidate which targets the keystone pathogen responsible for periodontitis, a chronic oral inflammatory disease affecting an estimated 65 million adults in the United States. 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. We have established preclinical proof of concept for VAX-PG. We nominated a final vaccine candidate for VAX-PG in the fourth quarter of 2022 and we continue to progress the program.

- *Advance VAX-GI program research and development.* VAX-GI is 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.

- *Leverage our platform for other discovery stage programs.* We are also able to leverage our platform as a discovery engine given our ability to uniquely create building blocks to construct potential novel conjugate and protein vaccine candidates, and we have other discovery-stage programs which leverage this platform.

- *Continue to build a robust intellectual property portfolio.* We have developed and are continuing to develop a comprehensive intellectual property portfolio related to vaccine applications, including manufacturing, formulation and process applications as well as protection for our specific vaccine candidates. We have rights to a robust portfolio of patents and patent applications related to the XpressCF platform through our exclusive license from Sutro Biopharma. We currently have one issued U.S. patent, as well as patents issued in Japan and Mexico, and multiple pending patent applications in the United States and internationally that cover vaccine formulations, protein-antigen conjugates, methods of making conjugate vaccines with various protein-antigen conjugates and other processes related to vaccine production, enhancements of immunogenicity and methods of use.

Our Pipeline

We have utilized our cell-free protein synthesis platform to generate a pipeline of vaccine candidates that we believe, if approved, may offer important advantages over existing vaccines or for which there are no vaccines available today. The following table summarizes our current pipeline:

Global Vaccine Market (Excluding COVID-19 Vaccines)

The global vaccine market, excluding COVID-19 vaccines, was approximately $45 to $50 billion in 2022 and is expected to grow at an 10% CAGR to approximately $67 billion by 2026. The World Health Organization, or WHO, has reported that non-COVID vaccine revenues have grown at nearly twice the rate of therapeutic products over the last two decades. Conjugate vaccines, including PCVs, have historically represented the largest segment (approximately a third) of the global non-COVID vaccine market. The Prevnar franchise from Pfizer Inc., or Pfizer, comprised of Prevnar 13, or PCV13, and PCV20, was among the highest selling non-COVID vaccine products in the world in 2022, accounting for approximately 14% of global non-COVID vaccine sales.

The pediatric vaccine market is large and well-established in the United States and European Union and growing in emerging countries. The annual new birth cohort, which in the United States and Europe approached approximately 11 million in 2022, drives ongoing sales year after year. In the United States, once a new vaccine is approved by the FDA, the ACIP considers whether to recommend the use of the vaccine. New pediatric vaccines that receive a preferred recommendation from ACIP are nearly universally adopted by pediatricians and parents and are required by many schools, contributing to a national immunization rate for the diseases targeted by such vaccines of approximately 90%.

In addition, the adult vaccine market is currently undergoing rapid growth. Vaccination rates among adults have historically been lower and vary by disease, though strong initiatives are underway to increase awareness and utilization. Excluding the impact of the COVID-19 pandemic, studies estimate that 40,000 to 80,000 adults in the United States die annually of vaccine-preventable diseases, and hundreds of thousands more are hospitalized. In recent years, manufacturers have started developing more vaccines for the adult market, with Pfizer's PCV13 and PCV20, Merck & Co., Inc.'s, or Merck, Vaxneuvance, or PCV15, and GSK plc's, or GSK, Shingrix each representing successful examples. The U.S. adult pneumococcal market generated annual sales of

over $2 billion, and Shingrix, a vaccine for shingles (herpes zoster) debuted with over $1 billion in sales in 2018 as it replaced Merck's incumbent vaccine, Zostavax, after receiving an ACIP preferred recommendation, and generated over $2.5 billion in sales in 2020.

The complex development and production processes of vaccines create a high barrier to entry and long product lifecycles. In recent history, four multinational companies—GSK, Merck, Pfizer and Sanofi have been responsible for developing and introducing most new vaccines to the world. As a result of the COVID-19 pandemic, there have been a number of new entrants into the vaccines market, including multinational companies such as Johnson & Johnson, and emerging biopharmaceutical companies.

Pneumococcal Disease

Pneumococcal disease is an infection caused by *Streptococcus pneumoniae* (pneumococcus) bacteria. It can result in IPD, including meningitis and bacteremia, and non-invasive pneumococcal disease, including pneumonia, otitis media and sinusitis. The global incidence of pneumococcal disease is driven by emerging serotypes not covered by currently available vaccines. In the United States, approximately 320,000 people get pneumococcal pneumonia each year, which is estimated to result in approximately 150,000 hospitalizations and 5,000 deaths. Pneumococci also cause over 50% of all cases of bacterial meningitis in the United States. Antibiotics are used to treat pneumococcal disease, but some strains of the bacteria have developed resistance to treatments. The morbidity and mortality due to pneumococcal disease are highly significant, particularly for young children and older adults, underscoring the need for a more broad-spectrum vaccine.

Evolution of Pneumococcal Vaccines

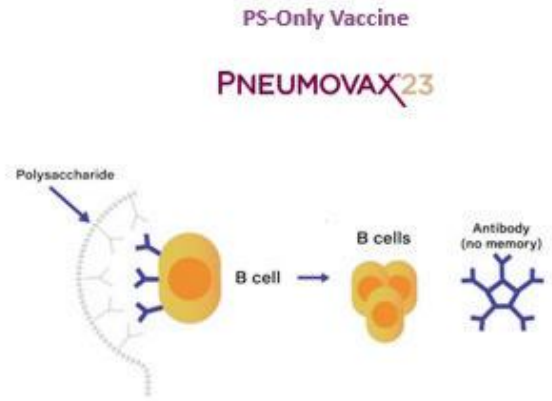
There are currently two types of vaccines targeting pneumococcal disease—polysaccharide-only vaccines and polysaccharide-conjugate vaccines. Polysaccharide vaccines contain polysaccharide antigens, which induce antibodies (B-cell responses) that bind to a bacteria's outer coating of polysaccharides and clear the bacteria. PCVs improve on polysaccharide vaccines by attaching, or conjugating, the polysaccharide antigen to a non-disease specific protein carrier. PCVs induce both an improved B-cell response and a T-cell response, resulting in a stronger and more durable immune response and longer-lasting protection, as compared to polysaccharide vaccines, which only induce a B-cell response.

Pneumococcal Polysaccharide-Only Vaccines

PPSV23, manufactured and marketed by Merck is the only pneumococcal polysaccharide vaccine widely available. PPSV23 is indicated for the prevention of pneumococcal disease in adults and was first approved in the United States in 1977, at which time it contained 14 different strains of pneumococcal bacteria. In 1983, it was replaced by the current version containing 23 different strains. PPSV23 is routinely administered to adults to provide protection against bacteremia and generates sales of over $600 million per year.

Polysaccharide vaccines induce a B-cell response only and do not induce a T-cell dependent immune response. In the absence of immunological memory responses, the resulting antibody responses are transient and cannot be boosted. Without the ability to provide long-lasting durable immunity, polysaccharide vaccines are not effective in children below two years of age. In addition, the antibody responses primarily consist of immunoglobulin M, or IgM, antibodies that, due to their size, are restricted to blood and are unable to penetrate into lung tissue to protect against pneumonia. Therefore, polysaccharide vaccines such as PPSV23 are only thought to protect against blood-borne infections, such as bacteremia. Figure 1 below illustrates polysaccharide-induced T-cell independent antibody responses.

Figure 1.



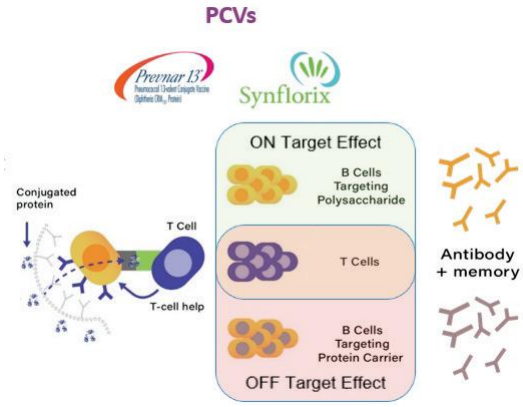
Graphics adapted from Strugnell et al, *Understanding Modern Vaccines*, Vol 1, Issue 1, 61-88.

Polysaccharide vaccines also interfere with optimal use of PCVs, as they create a hyporesponsive immune effect. In particular, absent T-cell inducement, polysaccharide vaccines actually clear the memory B-cells that are formed following primary immunization with a PCV, thereby eliminating the ability to boost with subsequent vaccination. This historically has been a significant drawback of vaccination in older adults, which consisted of the administration of a limited spectrum PCV followed by the administration of a polysaccharide vaccine. Despite these shortcomings, PPSV23 historically has been widely used primarily to provide protection against circulating strains not contained in the currently available PCV. The current standard of care, which consists of the administration of either PCV20 alone or PCV15 followed by the administration of PPSV23, in adults, or PCV13 or PCV15 in infants, continues to include the alternative of a polysaccharide vaccine.

Pneumococcal Conjugate Vaccines

PCVs overcome the limitations of polysaccharide vaccines by conjugating the polysaccharide to a more immunogenic protein carrier containing T-cell epitopes. These T-cell epitopes provide $CD4^+$ help, which is critical to the conversion of a traditional B-cell dependent immune response to a more robust combined B-cell and T-cell dependent immune response. The T-cell response causes immediate class switching of the B-cells from more rudimentary IgM antibodies prevalent with polysaccharide vaccines to more refined IgG antibodies. IgG antibodies are refined enough to penetrate into lung tissues to prevent pneumonia. Furthermore, as polysaccharide strands attach to multiple copies of the protein carrier, they create an inter-strand cross-linked matrix structure, which the immune system easily recognizes as foreign. The T-cell dependent immune response also generates memory B-cells that can be re-stimulated, creating a prime-boost immune response and enabling a more robust and durable immune response, enabling the use of PCVs in young children. Figure 2 below illustrates this immune response:

Figure 2.



The first PCV, Prevnar, was a 7-valent vaccine that was launched in the United States in 2000. It included purified capsular polysaccharides of seven serotypes of *S. pneumoniae* (4, 6B, 9V, 14, 18C, 19F and 23F), each of which was individually conjugated to a T-cell-epitope-containing, nontoxic variant of diphtheria toxin known as CRM_{197} to produce seven separate conjugates. To obtain approval, a large field efficacy study was conducted that demonstrated the vaccine's efficacy in infants. Efficacy correlated with serological immune endpoints, as measured by IgG titers (a measurement of concentration), and a seroconversion threshold (or reference antibody concentration) of protection was defined. Prevnar is credited with tremendous medical and commercial success, having dramatically reduced circulating disease in children. However, after a number of years of widespread use, IPD incidence caused by strains not contained in the vaccine started to opportunistically rise, a phenomenon called serotype replacement, which led to the need for a broader-spectrum version of the vaccine.

In the race to develop a broader-spectrum PCV than Prevnar, two vaccines were successfully developed: Synflorix, a 10-valent PCV from GSK, and PCV13, a 13-valent PCV from Wyeth (subsequently acquired by Pfizer). Based on its broader coverage of then-emerging strains, PCV13 was adopted as the standard of care in the United States and Europe. Synflorix continues to be used primarily in emerging countries.

PCV13 contains the seven serotypes originally included in Prevnar plus six more serotypes of *S. pneumoniae* (1, 3, 5, 6A, 7F and 19A) and was approved and launched in the United States in 2010. Each polysaccharide is conjugated to CRM_{197} to produce 13 individual conjugates, which are mixed into a final vaccine formulation and then adsorbed to alum. In 2010, PCV13 obtained FDA approval for the prevention of IPD in infants based on non-inferior IgG antibody responses relative to Prevnar, using the surrogate immune endpoints established by the prior Prevnar field efficacy study. While PCV13 failed to achieve non-inferiority on two of the common seven strains relative to Prevnar, it was granted approval across all 13 strains. Upon receipt of the ACIP preferred recommendation, PCV13 replaced Prevnar in the infant market as the standard of care. This also created a "catch-up" population for those children previously vaccinated with Prevnar to provide protection against the incremental serotypes covered by PCV13.

PCV13 has also received accelerated approval for the prevention of IPD and pneumonia in adults in the United States based on non-inferior OPA responses as compared to PPSV23. To fulfill a post-marketing commitment, a large-scale field efficacy study of adults in the Netherlands was completed in 2013, which showed protection against community-acquired pneumonia and concordance between OPA and protection from community-acquired pneumonia. Thus, OPA was established as a validated surrogate immune endpoint in adults to support future regulatory approvals. PCV13 subsequently received an ACIP preferred recommendation for adults 65 years and older, and the standard of care was amended to first vaccinate with PCV13, and then after a waiting period, PPSV23. This dual vaccine regimen provides some protection against the circulating strains over and above PCV13 but we believe creates coverage gaps and patient compliance and convenience challenges.

PCV13 quickly became the highest selling product in the global vaccine market. However, at the time of ACIP's recommendation in 2014, it was determined that the recommendation would be revisited in four years to evaluate the impact of PCV13 on pneumococcal disease burden in older adults. In June 2019, the ACIP downgraded its recommendation of PCV13 for older adults, given the lack of disease caused by the incorporated strains, and instead began directing physicians and patients to decide whether to vaccinate on a case-by-case basis while still recommending universal vaccination with PPSV23 due to its broader coverage.

In an effort to develop even broader-spectrum PCVs than PCV13, two vaccines were successfully developed for the adult population: PCV20, a 20-valent PCV from Pfizer, and PCV15, a 15-valent PCV from Merck.

PCV20 contains the 13 serotypes included in PCV13 plus seven more serotypes of *S. pneumoniae* (8, 10A, 11A, 12F, 15B, 22F and 33F) and was granted regulatory approval and launched in the United States in 2021 for the prevention of IPD in adults based on non-inferior OPA responses relative to PCV13 without the need for a field efficacy study. While PCV20 failed to achieve non-inferiority on serotype 8 relative to PPSV23, it was still granted approval across all 20 strains.

PCV15 contains the 13 serotypes included in PCV13 plus two more serotypes of *S. pneumoniae* (22F and 33F) and was granted regulatory approval and launched in the United States in 2021 for the prevention of IPD in adults based on non-inferior OPA responses relative to PCV13 without the need for a field efficacy study.

In October 2021, the ACIP voted to recommend universal vaccination for the use of either PCV20 alone or PCV15 with PPSV23 for routine use in adults aged 65 years and older as well as for those between the ages of 19 and 64 years with certain underlying medical conditions or other risk factors. In October 2022, the ACIP voted to recommend a dose of PCV20 for adults aged 65 years and older at least five years after the last pneumococcal vaccine dose for those who haven't previously received PCV20.

PCV15 was granted regulatory approval and launched in the United States in June 2022 for the prevention of IPD in infants. Pfizer has a Prescription Drug User Fee Act, or PDUFA, goal date of April 2023 for PCV20 in infants.

Drawbacks for Current PCVs

Routine immunization with PCVs has been effective in dramatically lowering the incidence of IPD in both adults and children in the United States and other industrialized nations. However, due to a phenomenon called serotype replacement, strains that are not covered by existing vaccines are increasing in prevalence. As published in 2020, over 71% of IPD incidence in 2017 for both children and adults was caused by strains beyond the 13 strains covered by PCV13. Efforts to improve upon current standard of care vaccines center around expanding the valency of PCVs to address the strains driving residual pneumococcal disease. However, limitations due to conventional conjugation chemistry and carrier suppression have complicated those efforts, and notwithstanding the recent approvals of PCV20 and PCV15, there remains a significant need for broader-spectrum PCVs, as evidenced by the fact that despite PCV20's broader coverage, the combination of PCV15 and PPSV23 remains universally recommended in adults, as an alternative to PCV20 alone, given its broader-spectrum coverage.

While vaccination with current PCVs has been effective in dramatically lowering the incidence of IPD in both adults and children in the United States and other industrialized nations, current PCVs suffer from the following drawbacks.

Serotype Replacement

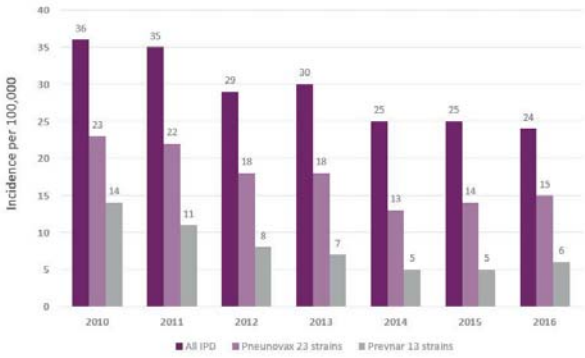
Current PCVs do not address circulating strains causing the majority of pneumococcal disease. Since its introduction, there has been a decrease in the incidence of disease attributable to the serotypes covered by PCV13 but an increase in incidence attributable to the incremental 11 strains that now cause most residual disease. Such change is driven by the void created when serotypes are taken out of circulation after widespread vaccination, which is a phenomenon known as serotype replacement. As a result of such change, broader-spectrum PCVs are required

to maintain protection against historically pathogenic strains while expanding coverage to address current circulating and emerging strains.

To date, the most comprehensive pneumococcal disease surveillance has been conducted by the CDC in the United States and by the National Institute of Health and Care Excellence, in the United Kingdom. As shown in Figure 3, IPD cases in adults in the United States initially declined after the introduction of PCV13 but have since plateaued. As published in 2020, non-covered serotypes were responsible for over 71% of IPD incidence in 2017 for both children and adults. The rate of serotype replacement has been more pronounced in the United Kingdom. Figure 4 shows the approximate IPD incidence rates in the United Kingdom caused by the incremental 11 strains over and above those in PCV13, which increased over the last three years of surveillance.

Figure 3.

US IPD Incidence in Adults ≥ 65[1]



[1] US CDC Active Bacterial Core Surveillance Annual Reports

Figure 4.

UK IPD Incidence in Adults ≥ 65[2]

[2] Ladhani et al, *Lancet Infectious Disease,* 2018 Apr.; 18(4):441-45 inclusive of unpublished raw data

While these 11 strains are covered by PPSV23, that vaccine only protects against blood-borne infections and not pneumonia, leaving patients vulnerable to infection. Although PCV20 and PCV15 address more disease-causing strains than PCV13, we believe there remains a significant need for even broader-spectrum vaccines to address a greater number of currently circulating and emerging strains.

Carrier Suppression

Technical constraints inherent to conventional conjugation chemistry limit the coverage of current PCVs due to a phenomenon known as carrier suppression. In particular, traditional conjugation methods cannot control where conjugation of the polysaccharide occurs on the protein carrier. The protein carrier used in all versions of Prevnar is CRM_{197}, a diphtheria toxin with a single point mutation rendering it non-toxic. The CRM_{197} protein contains 39 lysines, approximately 20% of which border relevant T-cell epitopes. Conventional conjugation chemistry randomly attaches the polysaccharide to any of the numerous lysines located on the protein carrier. When a polysaccharide is covalently bound to a protein carrier at a lysine residue that is co-resident with a T-cell epitope, it blocks the presentation of the T-cell epitope to the immune system, thus preventing the induction of a T-cell response. The masking of these critical epitopes prevents the conversion to a T-cell dependent immune response and negates the benefit of the protein carrier.

Meanwhile, the B-cell epitopes of both the protein carrier and the antigen are presented to the immune system, causing B-cells to the respective immunogens to compete with one another for the T-cell help engendered by unblocked T-cell epitopes. This competition for T-cell help diminishes the immune response to the polysaccharide antigen of interest, resulting in carrier suppression.

The result of carrier suppression is a decrease in the targeted immune response to the disease-specific polysaccharides, which intensifies with higher cumulative amounts of protein carrier. This phenomenon impedes the

ability to expand coverage of current PCVs and has been shown consistently when broader-spectrum versions of conventional PCVs have been compared to lesser-valent versions. When PCV13 was compared to Prevnar (Pfizer's first generation 7-valent PCV) in a well-controlled Phase 3 study in infants, the IgG antibody responses directed against the polysaccharides of interest for all seven of the common strains in each vaccine were lower for PCV13 (Figure 5). In 2020, Pfizer presented results of a well-controlled Phase 3 study in adults, aged 60 and over, where they compared PCV20 to PCV13. In that study, the OPA responses directed against the polysaccharides of interest for all thirteen of the common strains were lower for the 20-valent development candidate (Figure 6). In 2021, Pfizer presented results of a well-controlled Phase 2 in infants, where they compared PCV20 to PCV 13. In that study, the IgG Geometric Mean Concentrations, or GMCs, one month after the third dose were lower for all 13 of the common strains of the 20-valent development candidate (Figure 7).

Figure 5.

Infant Immune Responses (IGG): Prevnar 7 vs PCV13[1]

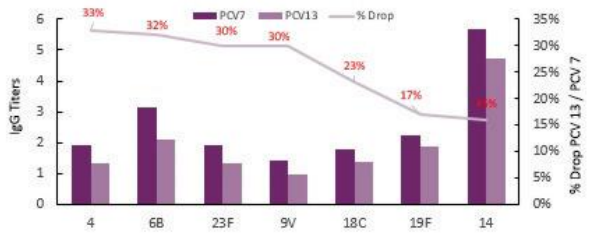


Figure 6.

Adult Immune Responses (OPA): PCV13 VS PCV20[2]

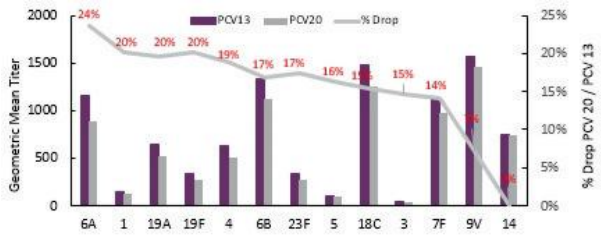
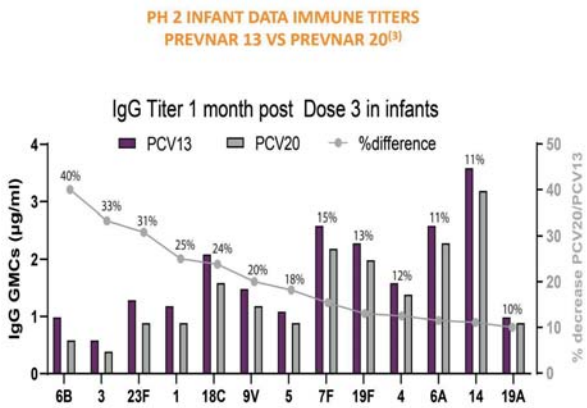


Figure 7.



[1] Yeh et al, Pediatrics. 126:e493 (2010).

[2] PCV20 BLA Clinical Review Memorandum. STN: 125731/0 June 8, 2021.

[3] Clintrials.gov NCT03512288 Phase 2 study (N=460), posted March 2, 2021.

Conventional Chemistry

The problem of carrier suppression is compounded by conventional conjugation chemistry used to make current PCVs, including PCV13, PCV20 and PCV15, which requires a higher amount of CRM_{197} protein carrier than polysaccharide antigen to complete the conjugation reaction, as well as long reaction times and harsh conditions that can damage the critical epitopes on the polysaccharide antigens. This results in a higher ratio of protein carrier to polysaccharide antigen in their monovalent conjugates (approximately 1.1 on average), as well as a much higher amount of cumulative protein carrier in the final formulation compared to the amount of any given polysaccharide antigen. For example, in the marketed PCV13 formulation, there are 34 micrograms of the protein carrier, CRM_{197}, relative to 2.2 micrograms of each polysaccharide (except serotype 6B at 4.4 micrograms), and in

the marketed PCV20 formulation, there are 51 micrograms of CRM_{197} relative to 2.2 micrograms of each polysaccharide (except serotype 6B at 4.4 micrograms). With substantially more protein carrier in the vaccine than polysaccharide antigen, the carrier suppression effect discussed above is exacerbated.

Our Solution

We are leveraging our cell-free protein synthesis platform to develop potentially superior conjugate vaccines for adult and pediatric indications. Our solution to the drawbacks with conventional conjugate vaccine techniques represents the first of three main applications of our platform.

Platform Application One: Creating Superior Conjugate Vaccines

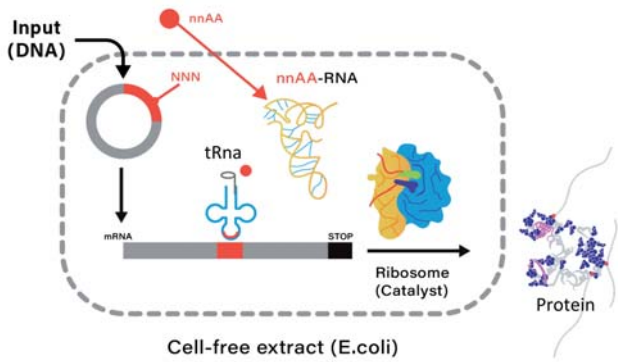
Using our cell-free protein synthesis platform, we are developing superior, novel carrier-sparing PCVs designed to have broader-spectrum coverage in an effort to address current and future residual disease in ways that conventional technologies cannot. We are able to design our investigational PCVs using site-specific conjugation in an effort to ensure optimal exposure of targeted immunogenic T-cell epitopes on protein carriers. This enables us to create broader-spectrum conjugate vaccine candidates using carrier-sparing conjugates designed to minimize carrier suppression while maintaining protective immunogenicity.

Synthesizing proteins outside of a living host cell provides us greater freedom to design and produce specific proteins of interest under optimized conditions. We separate the precise cellular machinery required for transcription, translation and energy production—the critical components for protein production—into an *Escherichia coli* (*E. coli)*-derived extract. We can then optimally express a single protein carrier by adding the plasmid-DNA encoding that protein into the extract mixture.

Site-Specific Conjugation

Within a protein carrier, we can substitute non-native amino acids, or nnAAs, for native amino acids at specific sites. These inserted nnAAs serve as conjugation anchors that permit the attachment of antigens, including polysaccharides, at a specific site on a protein carrier to ensure optimal exposure of B-cell and/or T-cell epitopes to induce the desired immune response. This precise site-specific linkage is not possible using conventional conjugation chemistry with conventional carrier proteins and affords an advantage to our conjugate vaccine candidates. Figure 8 below depicts our method of inserting nnAAs into a protein carrier, where the DNA sequence has been modified to permit nnAA incorporation into the protein at pre-selected sites using a nnAA-RNA permitting transcription and translation of the protein in the ribosome to yield the protein carrier with nnAAs site-specifically incorporated, facilitating site-specific conjugation.

Figure 8.



Most conjugate vaccines available today use a non-disease-specific protein carrier, CRM_{197}, in order to leverage T-cell epitopes to induce a T-cell dependent immune response. This traditional method produces a

heterogeneous mixture of conjugates with blocked and unblocked T-cell epitopes in a large immunogenic cross-linked matrix structure. In contrast, the precision and flexibility of cell-free protein expression, together with our ability to insert nnAAs, allow us to construct our proprietary enhanced protein carrier, or eCRM, with pre-determined conjugation sites. Our method produces homogenous conjugates that provide for the consistent exposure of T-cell epitopes and likewise form a large, immunogenic cross-linked matrix structure. By precisely conjugating polysaccharides to eCRM in a way that provides for optimal exposure of T-cell epitopes to the immune system, we can heighten immunogenicity attainable with conjugate vaccines.

The figures below illustrate the site-specific conjugation process. Figure 9 shows site-specific conjugation of the polysaccharide to the protein carrier, avoiding the T-cell epitopes. Figure 10 shows the inter-strand cross-linked matrix, which is the structure of each monovalent conjugate included in the final vaccine.

Figure 9.

Precise, Site-Specific Conjugation Sites on Proprietary eCRM Protein Carrier

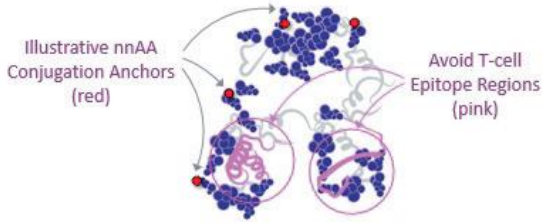
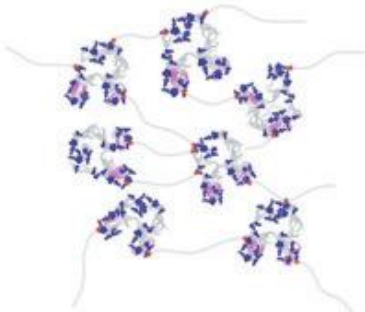


Figure 10.

Final VAX-24 Conjugates in Customary Matrix Form



We believe consistent exposure of T-cell epitopes should translate to higher potency of the protein carrier on a weight-to-weight basis. To harness this potential potency advantage, we have elected to construct conjugates with a lower ratio of protein carrier to polysaccharide than conventional PCVs. We have observed in animal models that despite having approximately half as much protein on average in each monovalent conjugate, VAX-24 had comparable immunogenicity relative to PCV13 on a strain-by-strain basis. As a result, we believe we can incorporate more monovalent conjugates to create an even more broad-spectrum vaccine with less protein carrier per conjugate in order to minimize carrier suppression.

Better Chemistry

We also employ a rapid and less harsh chemistry method called copper-free click chemistry to site-specifically conjugate the polysaccharides to eCRM. We believe this distinctive technique is a better controlled, more efficient and faster method of conjugation relative to conventional chemistry used to make traditional PCVs. The click chemistry conjugation reaction is designed to cause less damage to the critical immunogenic epitopes on the protein carrier or the target antigen.

Our PCV Franchise

We are developing broad-spectrum investigational PCVs designed to minimize carrier suppression.

VAX-24

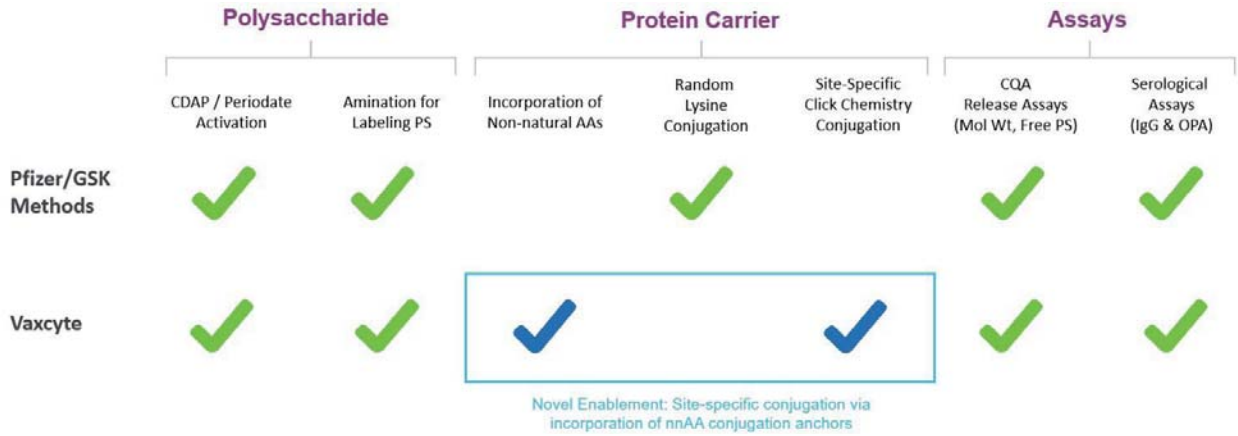
Our lead vaccine candidate, VAX-24, is designed to improve upon the standard of care by potentially covering an additional 10-28 percent of strains causing IPD in adults over the current standard-of-care PCVs. The 24 serotypes that comprise VAX-24 eclipse the coverage of all currently available conjugate and polysaccharide-only vaccines to prevent IPD. The 24 serotypes included in VAX-24 cover a significant portion of the IPD currently in circulation and are associated with high case-fatality rates, antibiotic resistance and meningitis. 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 healthy adults aged 18-64 .

VAX-24 includes 24 purified capsular polysaccharides of *S. pneumoniae* (1, 2, 3, 4, 5, 6A, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F), each of which is conjugated to eCRM to produce 24 monovalent conjugates. These conjugates are mixed into a final vaccine formulation and then adsorbed to alum.

As shown in Figure 11 below, there are critical differences between VAX-24 and other currently available PCVs relating to the protein carrier, particularly the use of site-specific conjugation and the milder reaction conditions. We achieve site-specific conjugation through the insertion of multiple nnAAs, which is not possible with the conventional chemistry used for making other PCVs. The click chemistry we use for site-specific conjugation may also minimize damage to the critical immunogenic epitopes on the protein carrier and the polysaccharides through milder and shorter reactions, while other PCVs use conventional chemistries that involve harsher and longer reaction conditions.

Figure 11.



Furthermore, VAX-24 nearly doubles the serotype spectrum of coverage of PCV13, yet contains a similar aggregate amount of protein carrier. We believe the resulting decreased carrier burden per conjugate of VAX-24 is critical for minimizing carrier suppression and producing broader-spectrum pneumococcal vaccines without sacrificing immunogenicity.

Where appropriate, we capitalize on the efficiencies of well-established clinical, manufacturing and regulatory precedents by leveraging conventional methods for the development of VAX-24. For example, our polysaccharide antigens are primarily made using conventional fermentation and purification techniques and activated through conventional methods. They are also labeled through conventional amination methods prior to being conjugated to eCRM. In addition, we use the same critical quality attribute assays for molecular weight and free polysaccharide that have served as the physicochemical measures of conjugates and also serve as predictors of their immunogenicity in vivo. We also use conventional IgG and OPA serological assays to gauge the immunogenicity of our conjugates, which have served as surrogate immunological endpoints in clinical studies that enabled the approval of PCV13, PCV20 and PCV15.

We leveraged the same animal models that were utilized in the development of approved PCVs. In particular, our preclinical studies utilized a recognized rabbit model that Pfizer used in its development of Prevnar, PCV13 and PCV20, that Merck used in its development of PCV15 and that GSK used in its development of Synflorix. We believe the demonstration of conjugate-like immune responses in rabbits that results in killing of bacteria via OPA and induction of IgG antibody responses are key development milestones and are critical readouts for the development of PCVs. In our preclinical studies, the rabbit model showed consistent immunological responsiveness across all strains for which we tested our conjugates and differentiated conjugated versus

unconjugated polysaccharide responses (i.e., T-cell dependent versus T-cell independent responses). The rabbit model also provided evidence regarding VAX-24's potential to generate a booster response.

We are pursuing what to date has been a well-characterized clinical development path for VAX-24, consistent with other PCV developers. We anticipate that we will be able to conduct smaller and shorter clinical trials that target immune endpoints (e.g., OPA and IgG responses) previously recognized by regulatory authorities. Pfizer applied this approach to the development of PCV13 and PCV20 and Merck applied it to the development of PCV15. Based on this standard to date, as a prerequisite for regulatory approval, we believe that any investigational PCV will have to be compared to the standard of care at the time a clinical trial is initiated. Currently, the standard of care is either PCV20 alone or PCV15 followed by PPSV23 in adults and PCV13 or PCV15 in infants.

Preclinical Data

To obtain preclinical proof of concept on our way to the clinic, we evaluated VAX-24 compared to the then standard of care, PCV13, and assessed the comparative immune responses of VAX-24 using the same rabbit model utilized by other PCV developers. We dosed rabbits in our preclinical studies with 0.11mcg, as measured by the amount of polysaccharide in each conjugate, for each of the 24 conjugates in VAX-24, as well as 0.11mcg for the thirteen conjugates in PCV13 (except serotype 6B at 0.22mcg) and compared both PCVs immunogenically to each other and to PPSV23, where each of the 23 polysaccharides were dosed at 1.1mcg. The doses are representative of body weight differences in humans versus rabbits and roughly correspond to the dose differential between PCVs and polysaccharide-only vaccines. In humans, PCV13 is dosed at 2.2mcg per conjugate (except serotype 6B at 4.4mcg) or approximately one-tenth the dose of PPSV23, where each polysaccharide is dosed at 25mcg. The species of rabbits used were approximately five percent of the average weight of humans in North America, thus 0.11mcg approximates to the 2.2mcg dose for PCVs and the 1.1mcg dose approximates to the 25mcg dose for PPSV23.

We completed multiple preclinical proof-of-concept studies of VAX-24 compared to PCV13 and PPSV23 in rabbits. The endpoints of the studies were to measure, on a serotype-specific basis, IgG antibody responses, the surrogate endpoint for pediatrics, and OPA responses, the surrogate endpoint for adults. Initial proof of concept was obtained with research-grade raw materials and conjugates made at Vaxcyte prior to initiating technology transfer to Lonza and production scale-up. For subsequent preclinical studies, conjugates were made at Vaxcyte at small-scale using optimized processes and procedures using Lonza-produced raw materials, including our proprietary eCRM carrier and all 24 polysaccharides that had already been tech transferred and scaled up. In anticipation of clinical evaluation and potential commercial launch, we further scaled our manufacturing, completing a technology transfer of the optimized processes and procedures for the production of each of the 24 conjugates in VAX-24. The conjugates were then produced at Lonza at an over fifteen-fold scale increase to the prior scale at Vaxcyte. At each stage, all 24 of the conjugates in VAX-24 met the critical quality attributes and the combination vaccine was administered in the rabbit model.

In each of our preclinical studies, VAX-24 showed comparable or superior OPA responses at 1/10th the dose of PPSV23 and comparable OPA responses to an equivalent dose of PCV13 on a serotype-by-serotype basis. Additionally, VAX-24 showed superior IgG antibody responses at 1/10th the dose of PPSV23 and comparable IgG responses to an equivalent dose of PCV13 on a serotype-by-serotype basis.

VAX-24 Clinical Development Plan

To accelerate our time to market, we are pursuing clinical development first in the United States for adults and then in the pediatric population. We achieved clinical proof of concept in October 2022 when we announced positive topline results from a Phase 1/2 study evaluating the safety, tolerability and immunogenicity of VAX-24 in healthy adults aged 18-64, and we continue to advance our adult clinical development program. For adults, the FDA has granted VAX-24 Fast Track and Breakthrough Therapy designations which are designed to facilitate the development and expedite the review of drugs, including vaccines, that treat or prevent serious conditions and fill an unmet medical need. For the pediatric population, we announced in late February 2023 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.

Adult Indication

We are using OPA titers as the primary immunogenicity endpoint for the VAX-24 program in adults. OPA is believed to be the primary protective mechanism against pneumococcal disease. In addition, we are measuring IgG responses as a secondary endpoint, as such responses may serve as supportive evidence of immunogenicity for comparison. We currently believe that these endpoints, if met in a Phase 3 trial, will be sufficient to obtain regulatory approval of VAX-24 and do not anticipate the need for a clinical field efficacy trial. However, we have not yet obtained feedback from the FDA regarding our pivotal Phase 3 clinical development plans or the acceptability of our approach.

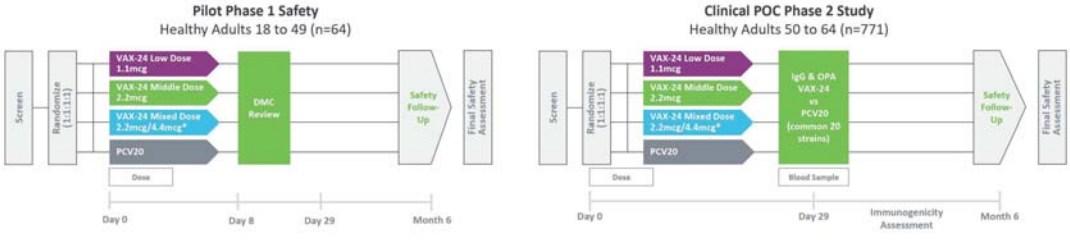
The FDA has previously approved pneumococcal vaccines upon the establishment of non-inferiority based on a head-to-head comparison using established surrogate immune endpoints in the target population. For adults, PCV13 was approved based on the establishment of non-inferiority of OPA responses relative to PPSV23, on a strain-by-strain basis, where non-inferiority was defined as greater than or equal to 0.50 of the lower limit of the two-sided 95% confidence interval of the OPA geometric mean titer ratio. PCV20 and PCV15 were approved based on the same non-inferiority criterion but compared with PCV13 and PPSV23.

Phase 1/2 Clinical Proof-of-Concept Study in Adults Aged 18 to 64

Our first-in-human study was a randomized, observer-blind, dose-finding, controlled Phase 1/2 clinical proof-of-concept study designed to evaluate the safety, tolerability and immunogenicity of VAX-24 in healthy adults. 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 aged 18 to 49. Participants were randomized equally in four separate arms and were evaluated for safety 8 and 29 days after dosing. 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 PCV20 in 771 healthy adults 50 to 64 years of age. Participants were randomized equally in four separate arms and approximately 28 days after participants were dosed, samples were collected to assess immunogenicity. The immunogenicity objectives of the Phase 2 portion of the study included an assessment of the induction of antibody responses, using OPA and IgG, at each of the three VAX-24 doses and compared to PCV20, and for the additional four serotypes contained in VAX-24 (and PPSV23), but not in PCV20, the percentage of subjects that experienced a four-fold rise in antibody titers. Participants in the study are evaluated for safety through six months after vaccination.

Figure 12 is a schematic of the overall study design of our Phase 1/2 study:

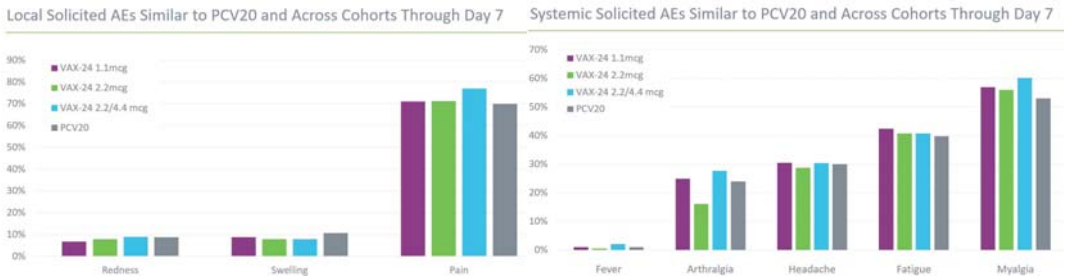
Figure 12.



On October 24, 2022, we announced positive topline results from both the Phase 1 and Phase 2 portions of the study.

In this study, VAX-24 met the primary safety and tolerability objectives, demonstrating a safety profile similar to PCV20 for all doses studied. Frequently reported local and systemic reactions were generally mild-to-moderate, resolving within several days of vaccination, with no difference observed across the cohorts. No serious adverse events or new onset chronic illnesses were considered to be related to study vaccines.

Figure 13.



In this study, VAX-24 demonstrated robust OPA and IgG immune responses for all 24 serotypes at all doses studied (1.1mcg, 2.2mcg, 2.2mcg/4.4mcg). At the conventional 2.2mcg dose, which we intend to move forward into a Phase 3 program, VAX-24 met or exceeded the established regulatory immunogenicity standards for all 24 serotypes. At this dose, VAX-24 met the standard OPA response non-inferiority criteria for all 20 serotypes common with PCV20, of which 16 serotypes (3, 4, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 23F and 33F) achieved higher immune responses and four serotypes (9V, 18C, 19F and 33F) reached statistical significance. Additionally, at all three doses, VAX-24 met the standard superiority criteria for all four serotypes (2, 9N, 17F and 20B) 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.

Figure 14.

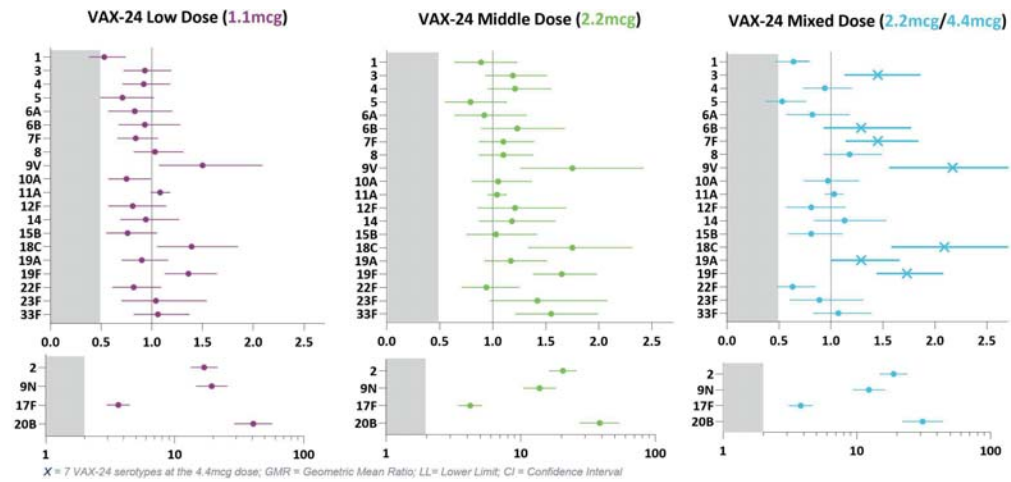
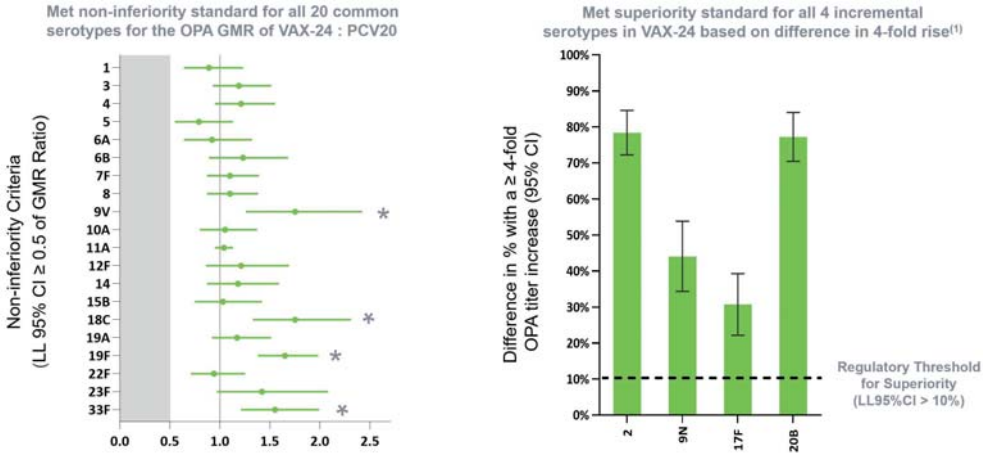


Figure 15.

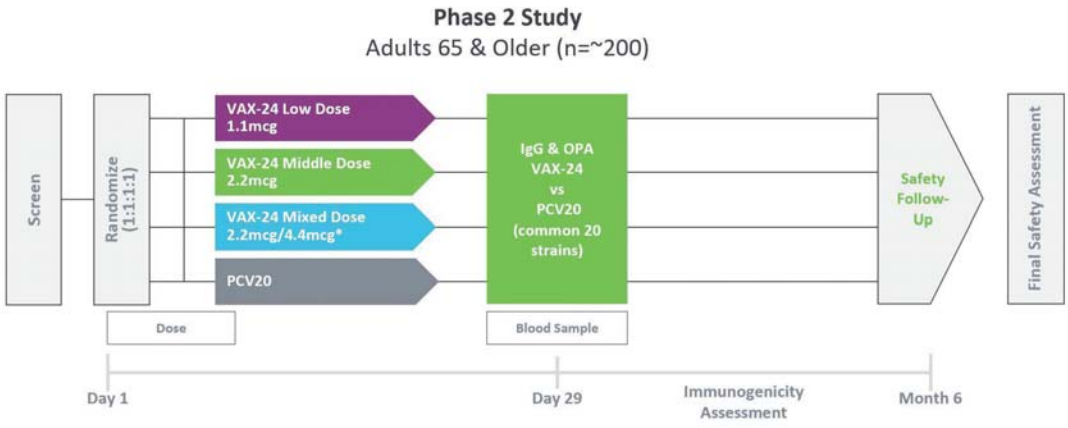


Based on the results of this study, the FDA granted Breakthrough Therapy designation for VAX-24 in adults. The FDA's Breakthrough Therapy process is designed to expedite the development and review of drugs that are intended to treat a serious or life-threatening condition. The designation is based upon preliminary clinical evidence indicating that the drug or vaccine may demonstrate substantial improvement over available therapies on one or more clinically significant endpoints. With Breakthrough Therapy designation, we will have access to all of the elements of the FDA's Fast Track program, as well as the ability to receive guidance and support from the FDA on an efficient drug development program and an organizational commitment from senior managers within the FDA.

Phase 2 Clinical Study in Adults 65 and Older

To add to the body of data in adults, we are conducting a separate Phase 2 study for which we have completed enrollment. This study is a randomized, observer-blind, dose-finding, controlled Phase 2 study designed to evaluate the safety, tolerability and immunogenicity of a single injection of VAX-24 at the same three dose levels evaluated in the Phase 1/2 study, 1.1mcg, 2.2mcg and 2.2mcg/4.4mcg, in approximately 200 healthy adults aged 65 and older. Participants were randomized equally in four separate arms and approximately 28 days after participants were dosed, samples were collected to assess immunogenicity. The immunogenicity objectives of the study include an assessment of the induction of antibody responses, using OPA and IgG, at each of the three VAX-24 doses and compared to PCV20, and for the additional four serotypes contained in VAX-24 (and PPSV23), but not in PCV20, the percentage of subjects that experience a four-fold rise in antibody titers. This study was designed to inform the powering of a Phase 3 study and was not powered to demonstrate non-inferiority. We anticipate announcing topline safety, tolerability and immunogenicity results from this study in the second quarter of 2023. Participants in the study also are evaluated for safety through six months after vaccination.

Figure 16.



Adult Program Next Steps

We anticipate final results with the six-month safety data from both Phase 2 adult studies in the first half of 2023 and to hold regulatory interactions with the FDA to inform the Phase 3 program in the second half of 2023. The purposes of the VAX-24 Phase 3 program in the adult population will be to demonstrate non-inferiority to PCV20 for immunogenicity, generate a sufficient safety database in adults and establish consistency of manufacturing through a lot-to-lot consistency study. The Phase 3 non-inferiority results would then be used to seek approval of VAX-24 in the adult population. This approach is similar to the approaches utilized by Pfizer to develop PCV20 and Merck to develop PCV15, where the immunogenicity of the investigational PCVs was compared to PCV13, which was the standard of care at that time. We expect topline safety, tolerability and immunogenicity data from the Phase 3 non-inferiority study of VAX-24 in adults in 2025.

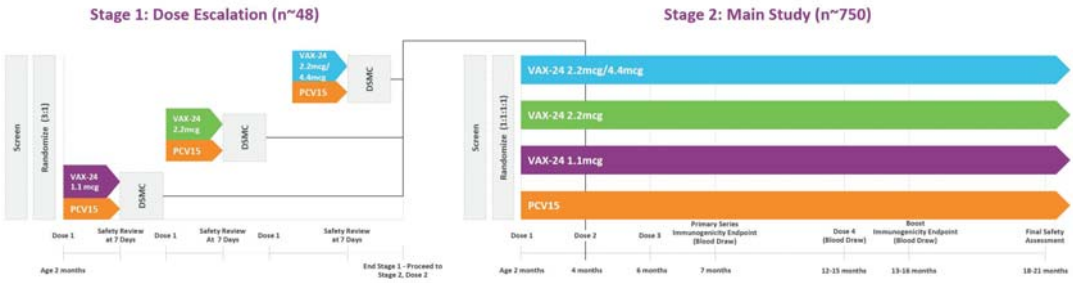
Based on Pfizer's experience with PCV13, we believe that VAX-24, if approved, would have the potential to serve as a "catch-up" or booster for those who have previously received PPSV23 or a lower-valent PCV. We believe a study exploring serial vaccination with PCV20 and/or PPSV23 followed by VAX-24 at different intervals could generate valuable data supporting a recommendation for VAX-24 vaccination in previously vaccinated adults.

Pediatric Indication

We are also developing VAX-24 as a pediatric vaccine. In August 2022, we announced successful completion of a pre-IND meeting with the FDA regarding our pediatric clinical program for VAX-24. We received positive written feedback from the FDA supporting the initiation of a pediatric study that proceeds directly into infants contingent on satisfactory topline safety, tolerability and immunogenicity results from the VAX-24 Phase 1/2 clinical proof-of-concept study in adults 18 to 64 years of age, which we have since demonstrated. This approach provides us with an accelerated clinical path to deliver a potentially best-in-class PCV, VAX-24, to the pediatric population, which represents the largest portion of the pneumococcal vaccine market in the United States. We announced in late February 2023 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.

The Phase 2, randomized, observer-blind, dose-finding two-stage clinical study will evaluate the safety, tolerability and immunogenicity of VAX-24 at three dose levels (low dose/1.1mcg, middle dose/2.2mcg, mixed dose/2.2mcg or 4.4mcg) and compared to PCV15 in healthy infants. The Stage 1 portion of the study will evaluate the safety and tolerability of a single injection of VAX-24 at three dose levels compared to PCV15 in approximately 48 infants in a dose-escalation approach. The Stage 2 portion will evaluate the safety, tolerability and immunogenicity of VAX-24 at three dose levels and compared to PCV15 in approximately 750 infants. In line with recommendations from the ACIP, the study design includes a primary immunization series consisting of three doses given at two months, four months and six months of age, followed by a subsequent booster dose at 12-15 months of age. The key prespecified immunogenicity study endpoints include an assessment of immune responses for all three VAX-24 doses and compared to PCV15 on the shared serotypes measured at 30 days post-dose three, or PD3, and post-dose four, or PD4. Immune responses will be assessed based on anti-pneumococcal polysaccharide serotype-specific IgG responses (proportion of participants achieving the accepted IgG threshold value of ≥0.35mcg/ml) at 30 days PD3 and IgG geometric mean titer ratios at 30 days PD4. All participants in the study will be evaluated for safety through six months following the booster dose. We expect topline safety, tolerability and immunogenicity data following the primary three-dose immunization series expected by 2025.

Figure 17.



If dose-finding is performed in infants, the data would inform on the dose levels for each of the conjugates in the final VAX-24 infant formulation. Consistent with the approval processes for PCV13 and PCV15 in infants, we do not anticipate that a clinical field efficacy trial will be required for VAX-24 in the pediatric population. We expect the clinical development of VAX-24 to follow the same approach utilized for PCV13 and PCV15, where vaccine effectiveness against IPD was inferred from immunologic correlates. In contrast to the adult population, VAX-24 approval in the pediatric population is expected to be based on a non-inferiority comparisons of IgG responses to PCV15, the current standard of care in infants. However, we have not yet obtained feedback from the FDA regarding our clinical development plans or the acceptability of our approach.

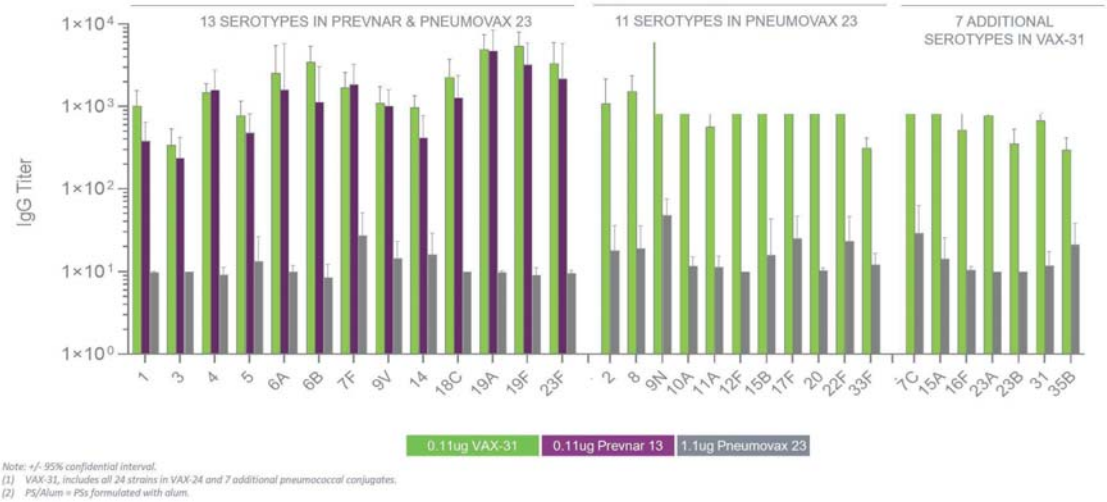
If our Phase 2 trials are completed successfully, we expect to conduct pivotal Phase 3 trials in the pediatric population that focus on evaluating non-inferiority to PCV15 for immunogenicity and seroconversion or antibody concentration threshold; assessing U.S. routine vaccination responses following concomitant administration with VAX-24; and generating a sufficient safety database in infants. The Phase 3 non-inferiority results would then be used to seek approval of VAX-24 in the pediatric population. This approach is similar to the approach utilized to develop PCV13, where the immunogenicity of PCV13 was compared to the original 7-valent Prevnar product, which was the standard of care at the time, as well as PCV15 which was compared to PCV13.

VAX-31 (formerly VAX-XP)

VAX-31 is a franchise extension of VAX-24 that, if approved, would expand strain coverage to 31 strains and demonstrate the scalable and modular nature of conjugate vaccines we can develop. VAX-31 includes all of the strains contained in VAX-24 plus incremental strains that were selected based on the epidemiological evidence demonstrating their role in circulating IPD and is designed to protect against these emerging strains and to help address antibiotic resistance. The serotypes in VAX-31 cover approximately 95% of the circulating IPD in the United States adult population.

We have completed multiple preclinical proof-of-concept studies for VAX-31 in rabbit models compared to PCV13, as well as more than 30 polysaccharides adsorbed onto alum. IgG responses in rabbits were superior to polysaccharide alone plus alum and comparable with PCV13 in the common 13 strains. We completed the process of transferring and scaling the conjugation processes at Lonza for each of the incremental conjugates contained in VAX-31 over and above those contained in VAX-24. The data shown below in Figure 18 was generated using those conjugates produced at larger scale at Lonza and confirm that the eCRM and polysaccharide raw materials and the conjugation processes for each of the conjugates in VAX-31 demonstrate immunogenicity comparable to PCV13 and superior to polysaccharide alone, consistent with prior lots of VAX-31.

Figure 18.



Platform Application Two: Novel Conjugate Vaccine Opportunities

We are also developing novel conjugate vaccine candidates for other diseases for which there are no existing vaccines. By leveraging our platform, we have been able to generate novel protein carriers with site-specific incorporation of nnAAs designed to provide optimal exposure of both B-cell and T-cell epitopes on the carrier. Using these novel protein carriers, we can produce highly stable conjugate vaccine candidates through site-specific conjugation of antigens, including polysaccharides. Functionally, one significant advantage of using carriers may be the additional protective immunity that the protein itself can provide beyond the conjugated antigen itself.

Group A Strep Disease Background and Market Opportunity

Streptococcus pyogenes (*S. pyogenes* or Group A Strep) bacteria cause a wide spectrum of both acute and chronic clinical conditions that lead to considerable disease burden globally. Group A Strep results in 700 million cases of illness each year and is one of the leading infectious disease-related causes of death and disability worldwide. An estimated 500,000 deaths globally result from Group A Strep, which is in line with the impact seen from the Measles, Rotavirus and Pertussis. The annual mortality and loss of productivity costs in the United States attributable to Invasive Group A Strep disease and related acute respiratory infections exceed $6 billion, excluding the impact of significant antibiotic use on individuals and contribution to antimicrobial resistance. Among older adults (≥ 65 years) in the United States, rates of invasive disease and deaths caused by Group A Strep have more than doubled over the last decade. Some of the most serious consequences of Group A Strep include flesh eating disease (necrotizing fasciitis) and invasive diseases such as sepsis and rheumatic heart disease (RHD). Approximately 40 million people are currently affected by RHD worldwide. Importantly, the majority of Group A Strep infections lead to pharyngitis, commonly known as strep throat, which is highly prevalent in school-age children. In the United States, an estimated 17% of outpatient antibiotic prescriptions dispensed to children aged 3 to 9 years are for the treatment of suspected Group A Strep infections. Studies have indicated that antibiotic resistance to Group A Strep has significantly increased over the past decade, leading the CDC to categorize Group A Strep as a

concerning threat. Additionally, the development of vaccines against Group A Strep has become a priority for the WHO amid recognition of the rising disease incidence globally, as well as the need to combat avoidable antibiotic consumption.

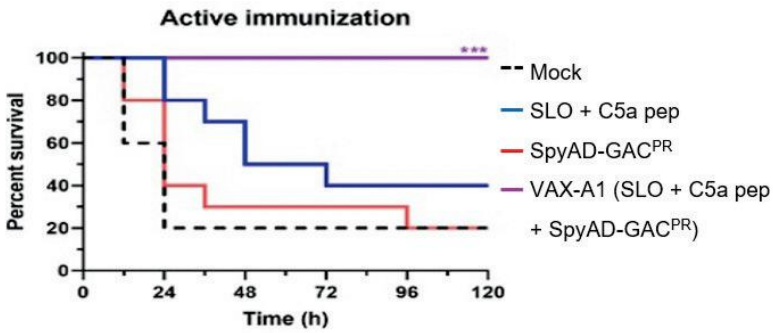
It has been established that the repeated natural infection of children with Group A Strep results in immune responses that are protective against subsequent Group A Strep infection. We believe this observation justifies the development of a rationally designed vaccine for Group A Strep that is focused on conserved antigens expressed by all strains of the bacteria.

VAX-A1

We have developed a conjugate vaccine candidate, VAX-A1, designed to confer broad protection against subtypes of Group A Strep by virtue of polyrhamnose, a conserved polysaccharide, conjugated to Group A Strep specific immunogenic protein carrier using our site-specific conjugation technology. The resulting conjugate is designed to ensure optimal exposure of both the B-cell and T-cell epitopes on the protein carrier to confer robust, boostable and durable protective immune responses. We believe this single conjugate could potentially cover all Group A Strep strains. The vaccine is a combination of this novel protein-polysaccharide conjugate along with two additional conserved surface proteins.

Our initial preclinical proof-of-concept study was published in the journal *Infectious Microbes & Diseases* in December 2020. In the study, a novel protein and polysaccharide conjugate of the Group A Strep polysaccharide was constructed for inclusion in a universal subunit vaccine against infections by the pathogen. The VAX-A1 vaccine candidate, based on SpyAD-conjugated to a modified polyrhamnose backbone (lacking N-acetyl glucosamine) and including SLO and C5a peptidase, demonstrated protection from subcutaneous and systemic challenge in mice, antibody binding and opsonophagocytic killing for multiple Group A Strep M Protein Gene, or emm, types and no evidence of cross-reactivity to human heart and brain tissue antigens (Figure 19), which is a key leading indicator of vaccine safety. The study was carried out in collaboration with researchers at the Division of Host-Microbe Systems and Therapeutics, Department of Pediatrics, University of California School of Medicine and the Skaggs School of Pharmacy and Pharmaceutical Sciences at the University of California, San Diego.

Figure 19.



Our VAX-A1 vaccine development program currently is funded in part by a grant obtained from CARB-X, a global non-profit partnership dedicated to accelerating antibacterial innovation to tackle the rising global threat of drug-resistant bacteria. The award committed initial funding of up to $1.6 million. In July 2020, the initial funding amount was amended from $1.6 million to $2.7 million and, if options to extend are exercised by CARB-X, up to $15.1 million in total funding available upon achievement of development milestones through Phase 1 human clinical trials. In April 2021, we received approval for the next phase of CARB-X development and executed the cost-reimbursement sub-award agreement with the Trustees of Boston University in August 2021. Pursuant to the agreement, the award committed additional funding of $3.2 million for IND-enabling activities and total potential funding of up to $29.7 million (including $6.6 million awarded funding to date) upon the achievement of future VAX-A1 development milestones. In January 2022, CARB-X revised the parameters for the contribution

of CARB-X funding and implemented maximum funding levels for all grant recipients. As a result, our total funding available upon achievement of development milestones through Phase 1 human clinical trials was revised from $29.7 million to $14.6 million.

We nominated the final vaccine candidate for our VAX-A1 program 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 we intend to provide further information about the anticipated timing of an IND application as the program progresses. Upon completion of the preclinical development program and IND-enabling activities for VAX-A1, we intend to conduct a multi-center, randomized, placebo-controlled Phase 1/2 study in adults. The primary objectives of the initial clinical trial will be to evaluate safety and tolerability. Secondary exploratory endpoints will be to measure IgG immune response to the vaccine antigens and to evaluate the ability of the antibodies produced in response to vaccination to inhibit and prevent infections caused by Group A Strep.

Platform Application Three: Protein Vaccine Opportunities

We believe we can also develop novel protein vaccine candidates constructed using "tough-to-make" protein antigens uniquely able to be expressed using the platform. In particular, the lack of a cellular membrane in our platform allows for the exogenous addition of components to manipulate transcription, translation and folding by modification of reaction conditions. Furthermore, removal of the typical restriction to maintain cell viability also creates unique avenues for optimizing and promoting protein production for antigens that might be cytotoxic to a cell-based system or require non-physiological conditions for optimal protein folding. Thus, utilizing these advantages, we believe we can express and purify important protein targets to generate unique candidates that are beyond the scope of traditional production systems. Our therapeutic periodontitis vaccine candidate is the first example of a "tough-to-make" protein-based vaccine.

Periodontitis Disease Background and Market Opportunity

Periodontal disease is a highly complex, chronic oral inflammatory disease that leads to the destruction of the soft and hard tissues supporting the teeth. The subgingival niche (below the gum margin of teeth) is populated by a diverse polymicrobial plaque. It is increasingly understood that the shift from periodontal health to disease is associated with changes in the microbial composition of the subgingival plaque, including activities of bacteria such as Porphyromonas gingivalis (P. gingivalis). The development of precise approaches to control this keystone pathogen, such as a vaccine, could then positively impact the periodontal disease burden.

Those with periodontitis also have an increased risk for heart attack, stroke and other serious cardiovascular events. In addition to gum and tooth disease, periodontal inflammation and infection with P. gingivalis have been linked to atherosclerotic heart disease mediated by P. gingivalis residing in atherosclerotic plaque. While we are focused on the treatment of periodontal disease with this vaccine candidate, if P. gingivalis is found to be causative in other chronic disorders, our vaccine candidate could potentially be a highly effective treatment and allow disease intervention at a much earlier stage of the disease. For example, recent research has suggested the potential for a link between P. gingivalis and Alzheimer's disease.

Neither the natural host immune response nor currently available treatments are curative for periodontal disease. Existing treatment includes highly aggressive and invasive procedures, including scaling and root planing and surgical intervention, coupled with antibiotic use. Despite these types of aggressive treatments, diseased sites frequently progress, leading to tooth loss. Thus, the development of an effective vaccine for periodontitis would be highly desirable.

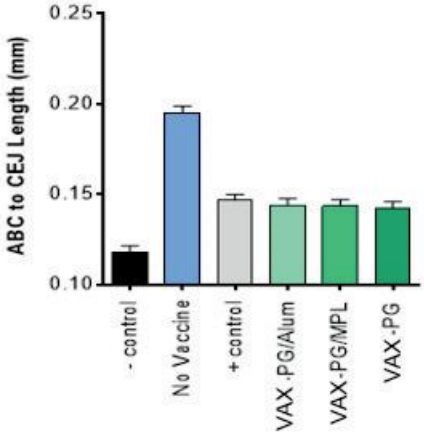
Periodontitis is a highly prevalent disease impacting > 40% of US adults above the age of 30, and with similar rates globally. Periodontal disease caused an estimated loss of $330.6 billion in the United States and Europe in 2018, with the direct costs alone exceeding $6 billion. The indirect costs are multiples of the direct costs as a result of high rates of edentulism (loss of teeth) and increased risk of many other diseases mentioned above.

VAX-PG

We are developing a novel protein vaccine candidate, VAX-PG, targeting *P. gingivalis* that incorporates protein antigens that we believe are uniquely enabled with our technology. 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-PG, which includes cell-free produced P. gingivalis virulence factors, including gingipains, were tested in a preclinical model that mimics periodontal disease. The results, which we believe generally demonstrate preclinical proof of concept for a periodontitis protein vaccine, were published in the *Journal of Clinical Periodontology* in February 2019. The vaccine elicited protein-specific IgG response following immunization and protected mice from P. gingivalis-elicited oral bone loss. Shown in Figure 20 is the objective bone loss of VAX-PG with alum, Monophospholipid A, or no adjuvant. Immunization with all formulations of VAX-PG provided significant protection against oral bone loss compared to the no vaccine oral challenged control group ($p<0.01$, ANOVA with Dunns multiple comparisons).

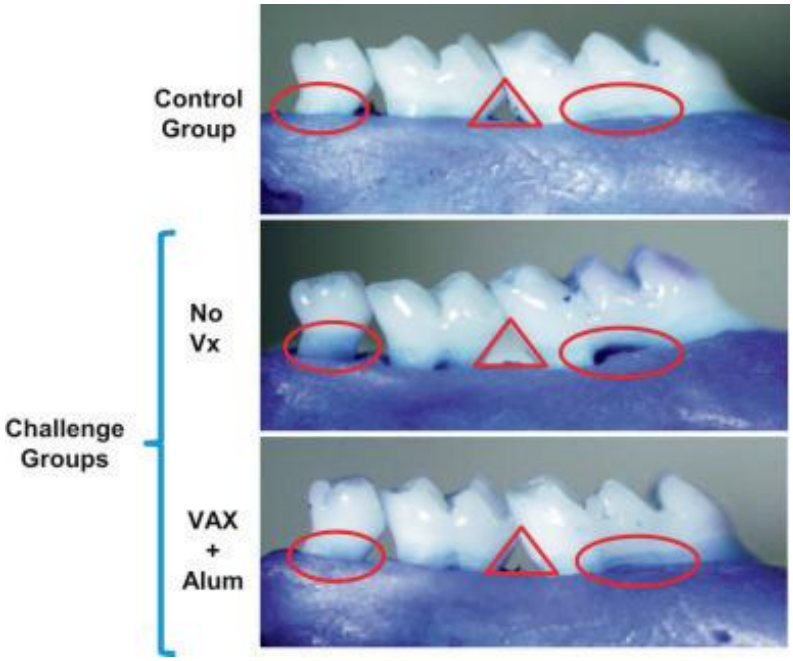
Figure 20.



ABC = alveolar bone crest
CEJ = cement-enamel junction

Shown below in Figure 21 are pictures of representative mouse jaws from the experiment. As can be seen, the vaccinated mice had considerably less bone loss than the unvaccinated and challenged control animals.

Figure 21.



We nominated a final vaccine candidate for our VAX-PG program in the fourth quarter of 2022. Upon completion of the preclinical development program and IND-enabling activities for VAX-PG, we intend to conduct a multi-center, randomized, placebo-controlled Phase 1/2 study in adults with mild to moderate chronic periodontal disease. The primary objectives of the initial clinical trial will be to evaluate safety and tolerability. Secondary exploratory endpoints will be to measure IgG immune response to the vaccine antigens and to evaluate the ability of the antibodies produced in response to vaccination to inhibit the formation of the poly-microbial biofilm, which is characteristic of periodontal disease.

VAX-GI

We announced that we have added VAX-GI, designed to prevent Shigellosis, to our pipeline. Shigella is a bacterial illness that causes dysentery with symptoms including bloody diarrhea, fever, and stomach cramps. Currently there are no prophylactics and treatment is primarily oral rehydration therapy, with antibiotics (mainly ciprofloxacin and azithromycin) used to shorten the duration of infection. However, the growing incidence of antibiotic resistance has complicated this approach with an increasing rate of extensively drug resistant (XDR). Shigella 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. Further, in young children Shigella can cause to malnutrition and induce or exacerbate stunting, leading to a long-term impact on both physical and cognitive development. This has resulted in the WHO including Shigella vaccine development as a priority goal.

Manufacturing and Supply

We have designed and developed a proprietary, scalable and portable manufacturing process for VAX-24 and VAX-31 that we believe can scale to address clinical and commercial vaccine supply needed to serve both adult and pediatric populations.

VAX-24 and VAX-31 Process

The manufacturing process for our VAX-24 and VAX-31 vaccine candidates consists of four key components: (i) our proprietary eCRM protein carrier; (ii) the 24 or 31 pneumococcal polysaccharides; (iii) the 24 or 31 conjugate drug substances and (iv) the mixture of these 24 or 31 drug substances into the final drug product.

eCRM

Our proprietary eCRM protein carrier is produced using our cell-free protein synthesis platform, which is exclusively licensed from Sutro Biopharma for the Vaccine Field (as defined in the Sutro Biopharma License Agreement (as defined below)). eCRM, contains multiple copies of non-native para azido-methyl-phenylalanine, or pAMF, amino acid. The pAMF amino acids have a specific structure that enables eCRM to participate in the site-specific click chemistry conjugation reaction with activated pneumococcal polysaccharides.

The cell-free reaction is performed in a manner analogous to traditional fermentation but without the cells. The first step in the production of eCRM is the manufacture of critical raw materials, namely E. coli extracts and lysates that contain the cellular machinery required for in vitro DNA transcription and translation. The eCRM protein is then manufactured by combining these E. coli extracts and lysates with classic media components such as amino acids, minerals and salts, with the in vitro reaction driven by the addition of plasmid DNA coding for the eCRM protein's amino acid sequence. This cell-free reaction takes place in a standard fermenter, followed by standard protein purification chromatographic and filtration processes. The manufacturing process has consistently yielded a product of the desired quality.

Pneumococcal Polysaccharides

Each of the 24 or 31 pneumococcal polysaccharides is individually isolated from S. pneumoniae bacterial strains. Each individual S. pneumoniae strain is cultured in a bioreactor using an improved single standardized fed-batch bioreactor process and a single standardized downstream purification process. Overall, this standardized upstream and downstream process is simple and streamlined, thereby reducing manufacturing cost of goods and providing an efficient path of progression for the program from process characterization and validation through to commercialization, if our vaccine candidates are approved.

Conjugate Drug Substances

Each of the 24 or 31 conjugate drug substances is manufactured individually, as monovalent conjugates, by conjugating each of the 24 or 31 activated pneumococcal polysaccharide strains, one at a time, to the eCRM carrier protein.

Click chemistry provides for a conjugation reaction that is quick, consistent and high-yielding, and which we optimized to be largely standardized across the various polysaccharides. Through statistical design of experiment, or DoE, studies, we have gained a significant understanding of which variables to adjust to maximize product quality and, accordingly, immunogenicity in rabbit models.

Drug Product

All 24 or 31 conjugate drug substances are mixed, formulated with appropriate excipients and adsorbed onto alum. Clinical doses are filled in vials and stored refrigerated.

Key Achievements and Status

For VAX-24, we have completed the manufacturing, testing and release of all 24 drug substance conjugates and the final drug product for the Phase 1/2 and Phase 2 studies in adults and the Phase 2 study in infants. We are now progressing to Phase 3 clinical manufacturing and commercial supply activities.

For VAX-31, we have completed the manufacturing, testing and release of all 31 drug substance conjugates for the Phase 1/2 and Phase 2 studies in adults, and must complete the manufacturing, testing and release of the final drug product prior to initiation of these studies and contingent on the submission and acceptance of an IND filing.

We currently do not own or operate any manufacturing facilities, but our strategic partnerships with Lonza and other contract manufacturing organizations, or CMOs, provide us with access to substantial resources to facilitate an independent supply path to the market. We have entered into agreements with Lonza, a leading global contract manufacturer with deep domain expertise and experience in large and small-scale production of clinical, as well as commercial-stage products, to secure capacity, technical expertise and resources to support the production of eCRM, polysaccharides and drug substance for our VAX-24 Phase 3 program and VAX-31 Phase 1/2 and Phase 2 studies in adults. We believe we can satisfy the expected initial eCRM, polysaccharide and drug substance supply requirements following a potential launch of VAX-24 in adults using the existing facilities at Lonza; however, we would need to secure additional capacity at a new facility or facilities to satisfy the expected eCRM, polysaccharide and drug substance production requirements to support expected increased commercial quantities upon the potential approval and launch of VAX-24 in infants and to expand into other markets outside of the United States. We have relationships with other leading CMOs for the production of the final drug product for VAX-24 and VAX-31, for the extract and lysates that we use to manufacture eCRM and for certain raw materials. We have an agreement with Sutro Biopharma pursuant to which Sutro Biopharma supplies us with extract and custom reagents for use in manufacturing preclinical and certain clinical supply of vaccine compositions. In December 2019, we exercised our right to require Sutro Biopharma to establish a second supplier for extract and custom reagents to support future clinical and commercial needs. In December 2022, we entered into a separate agreement with Sutro Biopharma pursuant to which we enhanced our rights with the second supplier of extract and acquired an option to access expanded rights to develop and manufacture extract, among other rights.

Lonza Agreements

In October 2016, we entered into a non-exclusive development and manufacturing services agreement, as amended, with Lonza, or the 2016 Lonza DMSA, pursuant to which Lonza is obligated to perform manufacturing process development and the manufacture of components for VAX-24, including the polysaccharide antigens, our proprietary eCRM protein carrier and conjugated drug substances.

In June 2018, we entered into a letter agreement with Lonza, or the Lonza Letter Agreement, pursuant to which we agreed to certain terms for potential future payments in shares of our common stock as partial satisfaction of future obligations to Lonza. The Lonza Letter Agreement states that the initial pre-IND cash payments under the 2016 Lonza DMSA would be subject to a specified dollar cap, or the Initial Cash Cap. After the Initial Cash Cap has been reached, we would have the option to make any further pre-IND payments owed to Lonza in cash, in shares of our common stock at then market prevailing prices, or a combination of both, at our election. In April 2021, we reached the Initial Cash Cap and notified Lonza that we would be exercising our option to issue approximately $10.0 million in shares of our common stock as payment for a portion of pre-IND payments due April 30, 2021. In June 2021, we issued 399,680 shares of our common stock to Lonza at a price of $25.02 per share to pay for $10.0 million of the pre-IND payments due April 30, 2021.

In October 2018, we entered into a second non-exclusive development and manufacturing services agreement with Lonza, or the 2018 Lonza DMSA, pursuant to which Lonza is obligated to perform services including manufacturing process development and the manufacture and supply of VAX-24 finished drug product.

In April 2022, we entered into a third non-exclusive development and manufacturing services agreement with Lonza, as amended, or the 2022 Lonza DMSA, effective as of March 22, 2022. Pursuant to the 2022 Lonza DMSA, Lonza will perform manufacturing process development and clinical manufacture and supply of our proprietary PCV.

Under each of the 2016 Lonza DMSA, 2018 Lonza DMSA and 2022 Lonza DMSA, collectively the Lonza Agreements, we will pay Lonza agreed-upon fees for its performance of development and manufacturing services and pass through expenses incurred by Lonza for raw materials, as well as customary procurement and handling fees. Under each Lonza Agreement, we will own all right, title and interest in and to any and all New Customer Intellectual Property (as defined in each Lonza Agreement), and Lonza shall own all right, title and interest in New General Application Intellectual Property (as defined in each Lonza Agreement). Subject to the terms and conditions set forth in the Lonza Agreements, Lonza granted us a non-exclusive, world-wide, fully paid-up, irrevocable, transferable license, including the right to grant sublicenses, under the New General Application Intellectual Property (as defined in each Lonza Agreement), to research, develop, make, have made, use, sell and import the Product (as defined in each Lonza Agreement) manufactured under each Lonza Agreement.

Unless earlier terminated, each Lonza Agreement will remain in place for a period of five years and includes customary conditions for termination prior to that period. The 2016 Lonza DMSA has been amended to extend its term until March 31, 2023.

Sutro Biopharma Agreements

Sutro Biopharma is a clinical stage, publicly traded drug discovery, development and manufacturing company using precise protein engineering and rational design (enabled by Sutro Biopharma's proprietary XpressCF platform technology) to advance next-generation oncology therapeutics. Following our corporate formation, we acquired an exclusive license to Sutro Biopharma's proprietary cell-free protein synthesis platform, XpressCF, for the discovery, development and sale of vaccines for the treatment or prevention of infectious diseases, excluding cancer vaccines. Under a related supply agreement with Sutro Biopharma, we have an exclusive relationship in our field to buy extract and certain custom reagents for use in manufacturing the vaccine compositions covered by the exclusive license, which we use to produce our protein carriers and certain of our antigens. Under a separate agreement with Sutro Biopharma, we enhanced our rights with respect to access to a second supplier of extract and acquired an option to access expanded rights to develop and manufacture extract, among other rights.

Amended and Restated License Agreement with Sutro Biopharma

We are party to a license agreement with Sutro Biopharma, or the Sutro Biopharma License Agreement, on August 1, 2014. The Sutro Biopharma License Agreement was amended on October 12, 2015 and again on May 9, 2018 and May 29, 2018. Under the Sutro Biopharma License Agreement, we received an exclusive, worldwide, royalty-bearing, sublicensable license under Sutro Biopharma's patents and know-how relating to cell-free expression of proteins to (i) research, develop, use, sell, offer for sale, export, import and otherwise exploit specified vaccine compositions, such rights being sublicensable, for the treatment or prophylaxis of infectious diseases, excluding cancer vaccines, and (ii) manufacture, or have manufactured by an approved contract manufacturing organization, such vaccine compositions from extracts supplied by Sutro Biopharma pursuant to the Sutro Biopharma Supply Agreement (as described below). We are obligated to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize the vaccine compositions. In consideration of the rights granted under the Sutro Biopharma License Agreement, we are obligated to pay Sutro Biopharma a 4% royalty on worldwide aggregate annual net sales of our vaccine products for human health and a 2% royalty on such net sales of vaccine products for animal health. Such royalty rates are subject to specified reductions, including standard reductions for third-party payments and for expiration of relevant patent claims. We are also obligated to pay Sutro Biopharma any royalties due to Stanford University (the upstream licensor of Sutro Biopharma), to the extent the royalties payable by Sutro Biopharma to Stanford University are greater than the royalties payable by us to Sutro

Biopharma. Royalties are payable on a vaccine composition-by-vaccine composition and country-by-country basis until the later of expiration of the last valid claim in the licensed patents covering such vaccine composition in such country and ten years after the first commercial sale of such vaccine composition. The latest expiration date of a licensed Sutro Biopharma patent application, if issued, would be 2036, subject to any adjustment or extension of patent term that may be available in a particular country. In addition, we are obligated to pay Sutro Biopharma a percentage of net sublicensing revenue received in the low teen percentages. In addition, in the event we sublicense our non-manufacturing rights under the Sutro Biopharma License Agreement before a specified date, we are obligated to pay Sutro Biopharma a percentage, in the low double-digits, of the sublicensing revenue we receive under such agreement.

The Sutro Biopharma License Agreement will remain in effect until terminated. The agreement may be terminated by either party for the other party's material breach uncured within 60 days' notice, by us at will with 60 days' notice, or by Sutro Biopharma if we challenge Sutro Biopharma's patents or if we undergo a change of control with a specified competitor of Sutro Biopharma.

Supply Agreement with Sutro Biopharma

In May 2018, we entered into a supply agreement, or the Sutro Biopharma Supply Agreement, with Sutro Biopharma pursuant to which we purchase from Sutro Biopharma extract and custom reagents for use in manufacturing non-clinical and certain clinical supply of vaccine compositions utilizing the technology licensed under the Sutro Biopharma License at prices not to exceed a specified percentage above Sutro Biopharma's fully burdened manufacturing cost. If any extracts or custom reagents do not meet the specifications and warranties provided, then we will not have an obligation to pay for the non-conforming product, and Sutro Biopharma will be obligated to replace the non-conforming product within the shortest possible time with conforming product at our cost. The term of the Sutro Biopharma Supply Agreement is from execution until the later of July 31, 2022 and the date the parties enter into and commence activities under the supply agreement unless extended through a subsequent supply agreement for the supply of extract and custom reagents for vaccine compositions for Phase 3 and commercial uses as contemplated in the Sutro Biopharma Supply Agreement.

The Sutro Biopharma Supply Agreement may be terminated by either party for the other party's material breach uncured within 60 days' notice, by us at will with 60 days' notice, or by mutual agreement of the parties. In December 2019, we exercised our right to require Sutro Biopharma to establish a second supplier for extract and custom reagents to support our anticipated clinical and commercial needs.

Option Agreement with Sutro Biopharma

In December 2022, we entered into an option grant agreement with Sutro Biopharma, or the Option Agreement. Pursuant to the Option Agreement, we acquired from Sutro Biopharma (i) authorization to enter into an agreement with an independent alternate CMO to directly source Sutro Biopharma's cell-free extract, allowing us to have direct oversight over financial and operational aspects of the relationship with the CMO; and (ii) a right, but not an obligation, to obtain certain exclusive rights to internally manufacture and/or source extract from certain CMOs and the right to independently develop and make improvements to extract (including the right to make improvements to the extract manufacturing process as well as cell lines) for use in connection with the exploitation of certain vaccine compositions, or the Option. We and Sutro Biopharma have agreed to negotiate the terms and conditions of a form definitive agreement to be entered into in the event we exercise the Option, which shall include the terms and conditions set forth in an executed term sheet between us, or the Term Sheet, and such terms that are necessary to give effect to each of the terms and conditions set forth in the Term Sheet, or the Form Definitive Agreement. The Option period is five years from the date of the Option Agreement, subject to potential acceleration in the event we undergo a change of control.

As consideration for the Option and other rights and authorizations granted to us under the Option Agreement, we agreed to pay Sutro Biopharma upfront consideration of $22.5 million, consisting of (i) $10.0

million in cash and $7.5 million worth of shares of our common stock (the number of shares to be calculated based on the arithmetic average of the daily volume weighted average price of our common stock as traded on Nasdaq in the three consecutive trading days immediately prior to the issuance thereof), and (ii) $5.0 million payable within five business days after we and Sutro Biopharma mutually agree in writing upon the Form Definitive Agreement. The 167,780 shares of common stock issued was recorded at fair value of $8.0 million on the date of settlement, December 22, 2022. In the event that we elect to exercise the Option, we would pay Sutro Biopharma an aggregate Option exercise price of $75.0 million in cash in two installments and, upon the occurrence of certain regulatory milestones, certain additional milestone payments totaling up to $60.0 million in cash. In the event that we undergo a change of control, certain rights and payments may be accelerated.

University of California, San Diego License Agreement

We are party to a license agreement with the University of California, San Diego, or the UCSD License, dated February 2019 whereby we are the exclusive licensee of an issued U.S. patent and pending U.S. patent application related to a non-cross-reactive Group A Strep carbohydrate antigen and methods of producing the antigen. We licensed this technology for the development of our Group A Strep vaccine candidate.

Upon execution of the UCSD License, we made an upfront payment of $10,000, and each year during the term we are obligated to pay an annual license maintenance fee in the single digit thousands. We are also obligated to pay UCSD up to approximately $1 million in development and regulatory milestone payments for each licensed product under the agreement. Additionally, we are obligated to pay UCSD a fixed royalty on net sales of licensed products in the low single digits. Such royalty rate is subject standard reductions for third-party payments. Royalties are payable until expiration of the last licensed patent. Additionally, in the event we sublicense commercial rights under the UCSD License, we are obligated to pay UCSD a percentage of all sublicensing revenue received, excluding any earned royalties or reimbursements of research and development expenses, of 20% up to a maximum of $2.5 million.

We are obligated to use commercially reasonable efforts to diligently develop, manufacture and sell licensed products and to achieve specified research and clinical development milestone events. If we are unable to meet our diligence obligations and do not agree with UCSD to modify such obligations or do not cure such obligations, then UCSD may terminate the license or convert the license to non-exclusive.

The UCSD License will remain in effect until the expiration of the last licensed patent. The UCSD patent and patent application, if issued, would expire in 2032, subject to any adjustment or extension of patent term that may be available in the United States. The UCSD License may be terminated by us at will with 90 days' notice or by UCSD for our breach uncured within 90 days' notice or if we challenge the licensed patents.

Other Partners

In addition to those listed above, we seek to partner with various academic, governmental and public or private research institutions as needed to advance the discovery or development of our vaccine candidates.

Competition

In recent history, the global vaccine market has been highly concentrated among a small number of multinational pharmaceutical companies. Pfizer, Merck, GSK and Sanofi have been responsible for developing and introducing most new vaccines to the world. As a result of the COVID-19 pandemic, there have been a number of new entrants to the vaccines market, including multinational companies such as Johnson & Johnson, and emerging biopharmaceutical companies. Other pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions are also working towards new solutions given the continuing global unmet medical need.

Within the current pneumococcal vaccine market, Pfizer, Merck and GSK have historically dominated, with Pfizer's PCV13 and PCV20, Merck's PPSV23 and PCV15 and GSK's Synflorix totaling a combined $7.4 billion in global pneumococcal vaccine sales in 2022 (approximately 85%, 10% and 5%, of such sales for these three products, respectively). While PCV13 covers fewer pneumococcal strains than PPSV23, it delivers a T-cell dependent immune response leading to a stronger and more durable immune response than PPSV23.

Existing vaccine makers, as well as new entrants, are competing to develop the next generation of pneumococcal vaccines. For use in adults, Pfizer's PCV20 was approved by the FDA in June 2021 and Merck's PCV15 was approved in July 2021. As a result of these approvals, the current standard of care in adults consists of the administration of either PCV20 alone or PCV15 followed by the administration of PPSV23. For use in infants, Merck's PCV15 was approved by the FDA in June 2022. Based on this approval, the current standard of care in infants is PCV13 or PCV15. Pfizer has a PDUFA goal date of April 2023 for PCV20 in infants.

In August 2022, Pfizer announced topline results from its U.S. Phase 3 study in infants evaluating PCV20 for the prevention of IPD, and in January 2023, the FDA accepted for priority review a supplemental Biologics License Application for PCV20 for the prevention of IPD in infants and children. Merck announced in April 2022 that V116, the company's investigational 21-valent PCV for adults, received Breakthrough Therapy designation from the FDA, and later announced that it enrolled the first patient in their Phase 3 clinical trial. In June 2022, Merck presented positive results from its Phase 1/2 study evaluating V116 in pneumococcal vaccine-naïve adults 18-49 years of age (Phase 1) and 50 years of age and older (Phase 2). Also in June 2022, Merck announced that the CDC's ACIP unanimously voted to provisionally recommend use of Merck's PCV15 as an option for pneumococcal vaccination in infants and children and in September 2022, Merck announced it received a positive CHMP Opinion for PCV15 in infants and children. Sanofi and SK Chemicals have partnered to develop a 21-valent PCV, and GSK, which recently acquired Affinivax, is developing an affinity-bound pneumococcal vaccine that includes 24 pneumococcal serotypes. GSK also has a 30-plus valent pneumococcal candidate vaccine in preclinical development. We believe success will ultimately be based on the combination of immunogenicity, boostability and the broadest coverage of serotypes, as well as safety and tolerability. Convenience and pricing may also be factors. Other vaccines in development may obtain FDA approval and commercially launch before VAX-24. However, if approved, we believe VAX-24 may obtain an ACIP preferred recommendation and potentially replace both incumbents for pneumococcal disease prevention in both adult and pediatric populations because of its broader coverage should compare favorably to these PCV candidates as a 24-valent alternative, based on our unique site-specific conjugation and carrier-sparing technology. We also believe VAX-31 has the potential to compete favorably in the PCV market based on its further expanded spectrum.

The competitive landscape for vaccine development for Group A Strep was dormant for more than three decades. However, the FDA lifted a 30-year ban on Group A Strep vaccine clinical trials in 2005, and research has slowly started to resurface in academic institutions. However, we are not aware of other Group A Strep vaccines in clinical development that would cover all strains of the bacteria. Additionally, we are not aware of any other vaccines under clinical development to treat periodontitis. We believe the success of our vaccine candidates in these areas will be based on potential efficacy, safety, tolerability, convenience and pricing. We are aware of some companies developing treatments for other diseases that target the same underlying pathogens that cause Group A Strep and periodontitis.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize vaccines that are safer, more effective, more convenient, less expensive or with a more favorable label than VAX-24, VAX-31 or any other vaccine we may develop. Many of the companies against which we

compete have significantly greater financial resources, and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do.

Intellectual Property

We have developed, and are continuing to develop, a comprehensive intellectual property portfolio related to vaccine applications, including manufacturing, formulation and process applications as well as protection for our specific vaccine candidates.

Our success depends in part on our ability to obtain and maintain proprietary protection for our vaccine candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements and vaccine candidates that are important to the development and implementation of our business. Our patent portfolio is intended to cover our vaccine candidates and components thereof, their methods of use and processes for their manufacture and any other inventions that are commercially important to our business. We may also rely on trademarks, trade secrets and know-how to develop and maintain our proprietary position.

Generally, issued patents are granted a term of 20 years from the earliest claimed non-provisional filing date. In certain instances, patent term can be adjusted to recapture a portion of delay by the U.S. Patent and Trademark Office, or USPTO, in examining the patent application or extended to account for term effectively lost as a result of the FDA regulatory review period, or both. In addition, we cannot provide any assurance that any patents will be issued from our pending or future applications or that any issued patents will adequately protect our vaccine candidates.

Our patent portfolio as of February 27, 2023 contains one issued U.S. patent, one issued Japanese patent, one issued Mexican patent, seven pending U.S. patent applications and three pending patent cooperation treaty applications that are solely owned by us, as well as certain foreign counterparts of a subset of these patent applications in foreign countries, including Australia, Brazil, Canada, China, India, Israel, Japan, South Korea, Taiwan, Mexico, New Zealand, the Philippines, Singapore, South Africa and countries within the European Patent Convention and the Eurasian Patent Organization. For our pneumococcal vaccines, these applications are directed to vaccine formulations, protein-antigen conjugates, methods of making protein-antigen conjugates and other processes related to vaccine production, and the promotion of immunogenicity using the protein-antigen conjugates and vaccines. For our Group A Strep vaccine, these patent applications are directed to vaccine formulations, protein-antigen conjugates, vaccines and components thereof, as well as processes for their manufacture. For our periodontitis vaccine, the patent and applications relate to vaccine formulations, protein antigens, and methods of using the vaccine. If issued, the 20-year term expiration dates of our patents will expire between 2037 and 2042, not including any extension of the patent term that may be available in certain jurisdictions. We continue to seek to maximize the scope of our patent protection for all our programs.

In addition to patents, we also rely upon trademarks, trade secrets, know-how and continuing technological innovation to develop and maintain our competitive position. We maintain and are seeking both registered and common law trademarks. Common law trademark protection typically continues where and for as long as the mark is used. Registered trademarks continue in each country for as long as the trademark is registered. We believe that we have certain know-how and trade secrets relating to our technology and vaccine candidates. We rely on trade secrets to protect certain aspects of our technology related to our current and future vaccine candidates. However, trade secrets can be difficult to protect. We seek to protect our proprietary information, including trade secrets, in part, by using confidentiality agreements with our commercial partners, collaborators, employees and consultants, and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our commercial partners and selected consultants. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining the physical security of our premises and physical and

electronic security of our information technology systems. To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Obtaining patents does not guarantee our right to practice the patented technology or commercialize the patented product. Third parties may have or obtain rights to patents that could be used to prevent or attempt to prevent us from commercializing our vaccine candidates. If third parties prepare and file patent applications in the United States or other jurisdictions that also claim technology to which we have rights, we may have to participate in interference or derivation proceedings in the USPTO or similar proceedings in other jurisdictions to determine the priority of invention.

Coverage and Reimbursement

Sales of our products in the United States will depend, in part, on the extent to which the costs of the products are covered by third-party payors, such as government health programs, commercial insurance and managed health care organizations. The process for determining whether a third-party payor will provide coverage for a pharmaceutical or biological product is typically separate from the process for setting the price of such a product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. As a result, a third-party payor's decision to provide coverage for a pharmaceutical or biological product does not imply that the reimbursement rate will be adequate. Certain Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, ACA, marketplace and other private payor plans are required to include coverage for certain preventative services, including vaccinations recommended by the ACIP without cost share obligations (i.e., co-payments, deductibles or co-insurance) for plan members. Children through 18 years of age without other health insurance coverage may be eligible to receive such vaccinations free-of-charge through the CDC's Vaccines for Children program, or VCF. For Medicare beneficiaries, vaccines may be covered under either the Part B program or Part D depending on several criteria, including the type of vaccine and the beneficiary's coverage eligibility. If our vaccine candidates, once approved, are covered only under the Part D program, physicians may be less willing to use our products because of the claims adjudication costs and time related to the claims adjudication process and collection of co-payments associated with the Part D program.

Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. As such, one third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service or will provide coverage at an adequate reimbursement rate. Further, coverage policies and third party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products that receives regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, safety, effectiveness, manufacture, quality control, approval, post-approval monitoring and reporting, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new biological product must be licensed by the FDA through the approval of a BLA, before it may be legally marketed in the United States.

In the United States, pharmaceutical products are regulated by the FDA under the Federal Food, Drug and Cosmetic Act and other laws, including, in the case of biologics, the Public Health Service Act, or PHS Act.

Failure to comply with FDA requirements, both before and after product approval, may subject us or our partners, contract manufacturers and suppliers to administrative or judicial sanctions, including FDA refusal to

approve applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, fines and/or criminal prosecution.

The steps required before a biologic may be approved for marketing of an indication in the United States generally include:

- completion of preclinical laboratory tests, animal studies, formulation studies conducted in accordance with good laboratory practices and other applicable regulations;
- submission to the FDA of an IND application, which must be active before human clinical trial commencement;
- approval by an institutional review board, or IRB, or ethics committee at each clinical site before a clinical trial is commenced;
- completion of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish that the biological product is "safe, pure and potent," which is analogous to the safety and efficacy approval standard for a chemical drug product for its intended use;
- preparation and submission to the FDA of a BLA for marketing approval that includes substantive evidence of safety, purity and potency from results of nonclinical testing and clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with applicable current good manufacturing practices, or cGMPs, to assure that the facilities, methods and controls are adequate to preserve the products identify, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the BLA; and
- FDA review of the BLA and issuance of a biologics license, which is the approval necessary to market a vaccine.

Before conducting studies in humans, laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and efficacy of the biologic candidate, must be conducted. Preclinical toxicology studies in animals must be conducted in compliance with FDA regulations.

The results of the preclinical tests, together with manufacturing information, known as CMC, and analytical data, are submitted to the FDA as part of an IND application. Some preclinical testing may continue even after the IND application is submitted. In addition to including the results of the preclinical testing, the IND application will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase or phases of the clinical trial lend themselves to an efficacy determination. The IND application will automatically become effective 30 days after receipt by the FDA unless the FDA within the 30-day time period places the IND application on clinical hold because of safety concerns about the vaccine candidate or the conduct of the trial described in the clinical protocol included in the IND application. The IND application sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. Submission of an IND application therefore may or may not result in FDA authorization to begin a clinical trial.

All clinical trials for new drugs and biologics must be conducted under the supervision of one or more qualified principal investigators in accordance with GCPs, which include the requirement that all research subjects

provide their informed consent for their participation in any clinical trial. They must be conducted under protocols detailing, among other things, the objectives of the applicable phase of the trial, dosing procedures, research subject selection, exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND application, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors must also report to the FDA within specified timeframes, serious and unexpected adverse reactions, any clinically significant increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator's brochure or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the vaccine candidate. An IRB at each institution participating in the clinical trial must review and approve the protocol before a clinical trial commences at that institution, approve the information regarding the trial and the consent form that must be provided to each research subject or the subject's legal representative and monitor the trial until completed.

Clinical trials are typically conducted in three sequential phases, but the phases may overlap, and different trials may be initiated with the same vaccine candidate within the same phase of development in similar or differing patient populations.

- *Phase 1:* Clinical trials may be conducted in a limited number of patients or healthy volunteers, as appropriate. The vaccine candidate is initially tested for safety and immunogenicity.

- *Phase 2*: The vaccine candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.

- *Phase 3*: Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may also be made a condition to approval of the BLA. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND application safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects or any clinically relevant increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND application safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product has been associated with unexpected serious harm to patients.

Assuming successful completion of all required testing in accordance with applicable regulatory requirements, the results of the preclinical studies and clinical trials, together with other detailed information, including information on the manufacture and composition of the vaccine candidate, are submitted to the FDA as part of a BLA requesting approval to market the vaccine candidate for a proposed indication or indications. The BLA must include all relevant data available from preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's CMC and proposed

labeling, among other things. Under the Prescription Drug User Fee Act, the fees payable to the FDA for reviewing a BLA, as well as annual program user fees for approved products, can be substantial but are subject to certain limited deferrals, waivers and reductions that may be available. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication. Each BLA submitted to the FDA for approval is reviewed for administrative completeness and reviewability within 60 days following receipt by the FDA of the application. If the BLA is found complete, the FDA will file the BLA, triggering a full review of the application. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission. The FDA's established goal is to review 90% of priority BLAs within six months after the application is accepted for filing and 90% of standard BLAs within 10 months of the acceptance date, whereupon a review decision is to be made. Priority review will direct overall attention and resources to the evaluation of applications for products that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis or prevention of serious conditions. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may also convene an advisory committee to provide clinical insight on application review questions. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions regarding approval.

Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response Letter without first conducting required inspections, testing submitted product lots and/or reviewing proposed labeling. In issuing the Complete Response Letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor the safety or efficacy of a product.

If a product is approved, the approval may impose limitations on the uses for which the product may be marketed, may require that warning statements be included in the product labeling, may require that additional studies be conducted following approval as a condition of the approval and may impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a Risk Evaluation and Mitigation Strategy, or REMS, or otherwise limit the scope of any approval. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. In most cases, the FDA must approve a BLA supplement or a new BLA before a product may be marketed for other uses or before specific manufacturing or other changes may be made to the approved product. As a condition of approval, the FDA may also require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies. Also, product approvals may be withdrawn if compliance with regulatory standards is not maintained or if safety or manufacturing problems

occur following initial marketing. In addition, new government requirements may be established that could delay or prevent regulatory approval of our vaccine candidates under development.

Both before and after the FDA approves a product, the manufacturer and the holder or holders of the BLA for the product are subject to comprehensive regulatory oversight. For example, quality control and manufacturing procedures must conform, on an ongoing basis, to cGMP requirements, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to spend time, money and effort to maintain cGMP compliance.

Post-Approval Requirements

Any drug products manufactured or distributed by us or our partners pursuant to FDA approvals will be subject to pervasive and continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, distribution requirements, complying with individual electronic records and signature requirements and complying with FDA promotion and advertising requirements. Once approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. After approval, most changes to the approved product, such as adding new indications, specific manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Biologic manufacturers, their subcontractors and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP regulations and other laws and regulations. Changes to the manufacturing process are strictly regulated and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

Discovery of previously unknown problems, including adverse events of unanticipated severity or frequency, or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal or suspension of an approval or license, clinical holds, warning or untitled letters, product recalls, product seizures, safety alerts, Dear Healthcare Provider letters, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, consent decrees or civil or criminal penalties.

The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market and imposes requirements and restrictions on drug manufacturers, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or inpatient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities and promotional activities involving the internet. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict the manufacturer's communications on the subject of off-label use of their products.

Additional Controls for Biologics

To help reduce the increased risk of the introduction of adventitious agents, the PHS Act emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHS Act also provides authority to the FDA to immediately suspend licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases in the United States and between states.

After a BLA is approved, the product will also be subject to official lot release as a condition of approval. As part of the manufacturing process, the manufacturer is required to perform specific tests on each lot of the product before it is released for distribution. If the product is subject to an official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of the manufacture of the lot and the results of all the manufacturer's tests performed on the lot. The FDA may also perform specific confirmatory tests on lots of some products, such as vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency and effectiveness of biological products. As with drugs, after approval of biologics, manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing and are subject to periodic inspection after approval.

Expedited Development and Review Programs

A sponsor may seek approval of its vaccine candidate under programs designed to accelerate the FDA's review and approval of new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. For a fast track product, the FDA may consider sections of the BLA for review on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable and the sponsor pays any required user fees upon submission of the first section of the application. A fast track designated vaccine candidate may also qualify for priority review, under which the FDA sets the target date for FDA action on the BLA at six months after the FDA accepts the application for filing. Priority review is granted when there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious disease or condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of 10 months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve a BLA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the biologic's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. FDA may withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product.

In addition, a sponsor may seek FDA designation of its vaccine candidate as a breakthrough therapy if the vaccine candidate is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If the FDA designates a product as a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout

the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and considering alternative clinical trial designs when scientifically appropriate, which may result in smaller trials or more efficient trials that require less time to complete and may minimize the number of patients exposed to a potentially less efficacious treatment. Breakthrough therapy designation comes with all of the benefits of fast track designation.

Even if a drug or biologic qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will be shortened.

Biosimilars and Exclusivity

The ACA includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

United States Healthcare Reform

In the United States, there has been and continues to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of vaccine candidates, restrict or regulate post-approval activities and affect the profitable sale of vaccine candidates.

Among policymakers and payors in the United States, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things: (1) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations; (2) created a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that

are inhaled, infused, instilled, implanted or injected; (3) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in specific government healthcare programs; (4) expanded the eligibility criteria for Medicaid programs; (5) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; (6) created a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and (7) established a Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drugs.

There have been judicial and political challenges to certain aspects of the ACA. By way of example, the Tax Cuts and Jobs Act of 2017, or the Tax Act, was signed into law and included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on specific individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." The Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Prior to the U.S. Supreme Court ruling on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is unclear how any additional healthcare reform measures of the Biden administration will impact the ACA and our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. For example, on August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, resulted in aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the Infrastructure Investment and Jobs Act, will remain in effect through 2031, with the exception of a temporary suspension and reduction from May 1, 2020 through June 30, 2022, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries, presidential executive orders and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drug products. At the federal level in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the Department of Health and Human Services, or HHS, released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. The IRA will also, among other things, (i) allow HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics under Medicare Part B and Medicare Part D, and subject drug manufacturers to civil monetary penalties and a potential excise tax if they do not offer Medicare a price that is

equal to or less than the negotiated "maximum fair price" under the law, and (ii) impose rebates for certain drugs and biologics sold under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. Unless an exception applies, single-source vaccines can qualify for Medicare price negotiations 11 years after their BLA is approved and become subject to the IRA's negotiated maximum fair price ceiling two years after that. However, certain vaccines, including pneumococcal virus vaccines, are excluded from the Medicare Part B inflation rebate. Additionally, CMS has stated in guidance released on February 9, 2023, that it will not impose Medicare Part D inflation rebates at this time on vaccines and other drugs and biologics that are not "covered outpatient drugs" under Medicaid or otherwise do not have an obligation to report drug pricing data to Medicaid. Further, as of January 1, 2023, the IRA eliminates patient cost sharing for FDA-approved adult vaccines that are recommended by the ACIP, and covered under Medicare Part D and mandates that all state Medicaid programs cover FDA-approved adult vaccines that are recommended by the ACIP and their administration without cost sharing starting October 1, 2023. However, the IRA does not change either VFC or the related provisions added in 2010 under the ACA. VFC was established to give first-dollar coverage to children up to 18 years of age whose families could not pay for vaccinations while the ACA guaranteed coverage of vaccines without cost sharing for Americans who are either privately insured or newly covered in states that expanded Medicaid. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be effectuated but is likely to have a significant impact on the pharmaceutical industry. The Biden administration also released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to regulate pharmaceutical product pricing, including price or reimbursement constraints, discounts, restrictions on specific product access, marketing cost disclosure and transparency measures and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. Further, it is possible that additional government action is taken in response to the COVID-19 pandemic.

United States Healthcare Fraud and Abuse Laws and Compliance Requirements

Federal and state healthcare laws and regulations restrict certain business practices in the biopharmaceutical industry, including anti-kickback and false claims laws and regulations, data privacy and security laws and regulations and transparency laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, individuals or entities from knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in-kind to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation.

The federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, prohibit, among other things, any individual or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. Private individuals, commonly known as "whistleblowers," can bring civil False Claims Act qui tam actions, on behalf of the government and such individuals and may share in amounts paid by the entity to the government in recovery or settlement. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal civil and criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, imposes specific requirements relating to the privacy, security and transmission of

protected health information on HIPAA covered entities, which include certain healthcare providers, health plans and healthcare clearinghouses and their business associates and covered subcontractors who conduct certain activities for or on their behalf involving protected health information on their behalf.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members. Similar state, local and foreign healthcare laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information or which require tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state and local laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure compliance with applicable healthcare laws and regulations can involve substantial costs. Violations of healthcare laws can result in significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other U.S. healthcare programs, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and curtailment or restructuring of operations.

Foreign Regulation

In addition to regulations in the United States, we expect to be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our vaccine candidates. Whether or not we obtain FDA approval for a vaccine candidate, we must obtain approval from the comparable regulatory authorities of foreign countries or economic areas, such as the European Union, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Certain countries outside of the United States have a process that requires the submission of a clinical trial application, much like an IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application, or CTA, must be submitted to the competent national health authority and to independent ethics committees in each country in which a company intends to conduct clinical trials. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed in that country. In all cases, the clinical trials must be conducted in accordance with GCPs and other applicable regulatory requirements.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure is compulsory for medicinal products produced by biotechnology or those medicinal products containing new active substances for specific

indications such as the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and designated orphan medicines, and optional for other medicines which are highly innovative. Under the centralized procedure, a marketing application is submitted to the European Medicines Agency, or EMA, where it will be evaluated by the Committee for Medicinal Products for Human Use, and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all European Union member states within 67 days of receipt of the opinion. The initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period.

To market a medicinal product in the European Economic Area, or EEA, (which is comprised of the 28 Member States of the EU plus Norway, Iceland and Liechtenstein), we must obtain a Marketing Authorization, or MA. There are two types of marketing authorizations:

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the EMA, and which is valid throughout the entire territory of the European Economic Area, or EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced therapy products and medicinal products containing a new active substance indicated for the treatment certain diseases, such as AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU; and

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in the various Member States through the Decentralized Procedure.

Under the above-described procedures, before granting the MA, the EMA, or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Additional Regulation

We are also subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other present and potential federal, state or local regulations. These and other laws govern our use, handling and disposal of various biological and chemical substances used in, and waste generated by our operations. Our research and development involve the controlled use of hazardous materials, chemicals, bacteria and viruses. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, we could be held liable for any damages that result and any such liability could exceed our resources.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biological products, government control and other changes to the healthcare system of the United States. It is uncertain what legislative proposals will be adopted or what actions federal, state or private payors for medical goods and services may take in response to any healthcare reform proposals or legislation. We

cannot predict the effect medical or healthcare reforms may have on our business, and no assurance can be given that any such reforms will not have a material adverse effect.

Privacy and Data Protection Laws

We are, or may become subject to numerous data privacy and security obligations, including federal, state, local, and foreign laws, regulations, guidance, and industry standards related to data privacy, security, and the protection of health-related and other personal data. Such obligations may include, without limitation, the Federal Trade Commission Act, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020, or the CPRA, and collectively, the CCPA, the European Union's General Data Protection Regulation 2016/679, or EU GDPR, and the EU GDPR as it forms part of United Kingdom, or UK, law by virtue of section 3 of the European Union (Withdrawal) Act 2018, or the UK GDPR, and the ePrivacy Directive. In addition, several states within the United States have enacted or proposed data privacy laws. For example, Virginia passed the Consumer Data Protection Act, and Colorado passed the Colorado Privacy Act.

These privacy and security laws (including the EU GDPR and UK GDPR) may impose significant and complex compliance obligations on entities that are subject to those laws. For example, the EU GDPR applies to any company established in the European Economic Area, or the EEA, and to companies established outside the EEA that process personal data in connection with the offering of goods or services to data subjects in the EEA or the monitoring of the behavior of data subjects in the EEA. Failure to comply with the requirements of GDPR and the applicable national data protection laws of the EU member states may result in fines of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties;; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

See the section titled "Risks Related to Government Regulation" for additional information about the laws and regulations to which we are or may become subject to and about the risks to our business associated with such laws and regulations.

Employees & Human Capital

As of December 31, 2022, we had 158 full-time employees, 30 of whom have Ph.D. degrees. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees and directors through the granting of stock-based compensation awards.

Corporate and Other Information

We are headquartered in San Carlos, California. We were incorporated in the state of Delaware on November 27, 2013 as Sutrovax, Inc. and we changed our name to Vaxcyte, Inc. in May 2020. Our website is located at https://www.vaxcyte.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K including their exhibits, proxy and information statements, and amendments to those reports filed or furnished pursuant to Section 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available through the "Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein or therein by reference. In addition, our filings with the SEC may be accessed through the SEC's website at http://www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Item 1A. Risk Factors.

RISK FACTORS

Our business involves significant risks, some of which are described below. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10-K, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements and the related notes. Many of the following risks and uncertainties are, and will be, exacerbated by the COVID-19 pandemic and any worsening of the global business and economic environment as a result. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Annual Report on Form 10-K.

Risks Related to Our Financial Position and Capital Needs

We are in the clinical or preclinical stages of vaccine development and have a very limited operating history and no products approved for commercial sale, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

To date, we have devoted substantially all of our resources to performing research and development, undertaking preclinical studies, clinical trials and manufacturing activities in support of our product development efforts, acquiring and developing our technology and vaccine candidates, organizing and staffing our company, performing business planning, establishing our intellectual property portfolio and raising capital to support and expand such activities. As an organization, we have not yet demonstrated an ability to successfully complete clinical development, obtain regulatory approvals, manufacture a commercial-scale product or conduct sales and marketing activities necessary for successful commercialization or arrange for a third party to conduct these activities on our behalf. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Our current vaccine candidate pipeline includes five preclinical programs. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives, including with respect to our vaccine candidates. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We have incurred significant net losses since inception and anticipate that we will continue to incur substantial net losses for the foreseeable future. We currently have no source of product revenue and may never achieve profitability. Our stock is a highly speculative investment.

We are a clinical-stage biotechnology vaccine company. Investment in clinical-stage companies and vaccine development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential vaccine candidate will not gain regulatory approval or become commercially viable. We do not have any products approved for sale and have not generated any revenue from product sales. As a result, we are not profitable and have incurred losses in each year since inception. Our net losses were $223.5 million and $100.1 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $522.1 million.

We expect to continue to spend significant resources to fund research and development of, and seek regulatory approvals for, our vaccine candidates. We expect to incur substantial and increasing operating losses over the next several years as our research, development, manufacturing, preclinical testing and clinical trial activities increase. As a result, our accumulated deficit will also increase significantly. We may encounter unforeseen

expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. However, we do not expect to generate any revenue from commercial product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our vaccine candidates, which we expect will take a number of years. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Even if we eventually generate revenue, we may never be profitable and, if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We will require substantial additional funding to finance our operations, which may not be available to us on acceptable terms, or at all. If we are unable to raise additional capital when needed, we could be forced to delay, reduce or terminate certain of our development programs or other operations.

As of December 31, 2022, we had cash, cash equivalents and investments of $957.9 million. We believe our existing cash, cash equivalents and investments will fund our current operating plans through at least 12 months from the filing date of this Annual Report on Form 10-K. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. We have raised substantial capital, however, we will need to raise substantial additional capital to complete the development and commercialization of our drug candidates. We expect to finance our cash needs through public or private equity or debt financings, third-party (including government) funding and marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements or any combination of these approaches. In July 2021, we entered into an Open Market Sales Agreement℠, or the ATM Sales Agreement with Jefferies LLC, or Jefferies, which provides that, upon the terms and subject to the conditions and limitations set forth in the ATM Sales Agreement, we may elect to issue and sell, from time to time, shares of our common stock having an aggregate offering price of up to $150.0 million through Jefferies acting as our sales agent or principal. As of December 31, 2022, we have sold 4,488,573 shares of our common stock under the ATM Sales Agreement at an average price of $25.56 per share for aggregate gross proceeds of $114.7 million ($111.2 million net of commissions and offering expenses). Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions, including higher inflation rates and changes in interest rates and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide, including the trading price of common stock, resulting from the ongoing COVID-19 pandemic and civil and political unrest in certain countries and regions. Our future capital requirements will depend on many factors, including:

- the timing, scope, progress, results and costs of research and development, testing, screening, manufacturing, preclinical development and clinical trials;
- the costs of future commercialization activities, including product manufacturing, marketing, sales, royalties and distribution, for any of our vaccine candidates for which we receive marketing approval;
- our exercise of the Option (as described below) with Sutro Biopharma, Inc., or Sutro Biopharma;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the U.S. Food and Drug Administration, or FDA, and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform field efficacy studies for our pneumococcal conjugate vaccine, or PCV, candidates, require more studies than those that we currently expect or change their requirements regarding the data required to support a marketing application;
- the costs of establishing additional manufacturing capacity to meet potential incremental supply requirements following the initial commercial launch of VAX-24;
- the costs of building a sales force in anticipation of any product commercialization;
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- any product liability or other lawsuits related to our products;

- the revenue, if any, received from commercial sales, or sales to foreign governments, of our vaccine candidates for which we may receive marketing approval;
- the costs to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing our patents or other intellectual property rights;
- expenses needed to attract, hire and retain skilled personnel;
- the costs of operating as a public company; and
- the impact of the COVID-19 pandemic, which may exacerbate the magnitude of the factors discussed above.

Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our vaccine candidates or other research and development initiatives. Our license agreements may also be terminated if we are unable to meet the payment obligations or milestones under the agreements. We could be required to seek collaborators for our vaccine candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available, or relinquish or license on unfavorable terms our rights to our vaccine candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

Due to the significant resources required for the development of our vaccine candidates, and depending on our ability to access capital, we must prioritize development of certain vaccine candidates. Moreover, we may expend our limited resources on vaccine candidates that do not yield a successful vaccine and fail to capitalize on vaccine candidates that may be more profitable or for which there is a greater likelihood of success.

Due to the significant resources required for the development of our vaccine candidates, we must decide which vaccine candidates to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, management and financial resources toward particular vaccine candidates may not lead to the development of any viable commercial vaccines and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate, license or collaborate with third parties in respect of certain vaccine candidates may subsequently also prove to be less than optimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our vaccine candidates or misread trends in the biopharmaceutical industry, in particular for vaccines, our business could be seriously harmed. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other vaccine candidates that may later prove to have greater commercial potential than those we choose to pursue or relinquish valuable rights to such vaccine candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

Risks Related to Our Business and Industry

Our approach to the discovery and development of our vaccine candidates is based on novel technologies that are unproven, which may expose us to unforeseen risks, require us to modify processes, and make it difficult to predict the time and cost of vaccine candidate development and the timing to apply for and obtain regulatory approvals.

We are developing a pipeline of vaccine candidates utilizing our cell-free protein synthesis platform, which is comprised of the XpressCF platform exclusively licensed from Sutro Biopharma, and our proprietary know-how for vaccine applications against infectious disease, and our future success depends on the successful application of this approach to vaccine development. We are in the clinical or preclinical stages of developing our vaccine candidates and there can be no assurance that any development problems we experience in the future will not cause significant delays or unanticipated costs, or that such development problems can be overcome. For

example, although we have achieved proof-of-concept for our carrier-sparing approach with VAX-24, our approach may not be validated for our other vaccine candidates or subsequent trials of VAX-24. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to manufacturing partners, which may prevent us from completing our clinical trials or commercializing our products on a timely or profitable basis, if at all. In addition, since we have not yet completed clinical development, we do not know the specific doses that may be effective in the clinic or, if approved, commercially. Finding a suitable dose may delay our anticipated clinical development timelines.

Furthermore, our expectations with regard to our scalability and costs of manufacturing may vary significantly as we develop our vaccine candidates and understand these critical factors. Conjugate vaccine development is highly complex, and development of broad-valency PCVs is further complicated by the number of components, analytical assays and potential for adjustments, including but not limited to changes in raw materials, composition, formulation, manufacturing methods and dosing, which could result in drug substances and/or drug product that may vary between preclinical and clinical studies over time. Over the course of the development and manufacturing of VAX-24, we have encountered process-related matters that have required us to make adjustments to our processes. We encountered such process-related matters during our drug substance manufacturing campaign for VAX-24 at Lonza, Ltd., or Lonza. The cumulative impact of the time required to make adjustments to our processes led to a delay of our drug substance manufacturing campaign due to scheduling conflicts and capacity constraints at Lonza. There can be no assurance that we or Lonza will be able to successfully manufacture drug substances in a timely manner in the future, or at all. Such process changes and manufacturing delays have caused a change in our Investigational New Drug, or IND, application timelines in the past and future changes or delays could impact future timelines for VAX-24 or for our other product candidates.

In addition, the preclinical and clinical trial requirements of the FDA, European Medicines Agency, or EMA, and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a vaccine candidate are determined according to the type, complexity, novelty and intended use and market of the potential products. Approvals by the FDA and EMA for existing pneumococcal vaccines, such as PCV13, PPSV23, PCV20 and PCV15 may not be indicative of what these regulators may require for approval of our vaccine candidates. For example, we have used opsonophagocytic activity, or OPA, titers as the primary immunogenicity surrogate endpoint for the VAX-24 program in adults because PCV13 and PCV20 were approved based on the establishment of non-inferiority of serotype-specific OPA responses relative to PPSV23 and PCV13 respectively; however, there can be no assurance that this streamlined non-inferiority approach will be sufficient for regulatory approval or that regulators will not require field efficacy trials. Furthermore, while there have been approvals granted for both PCVs and meningococcal conjugate vaccines based on surrogate immune endpoints rather than field efficacy studies, we will not be able to confirm this approach's applicability for our vaccines until we complete our Phase 2 clinical development program. Additionally, novel aspects of our vaccine candidates and manufacturing processes may create further challenges in obtaining regulatory approval. The regulatory approval process for our novel vaccine candidates can be more complex and consequently more expensive and take longer than for other, better known or extensively studied pharmaceutical or other vaccine candidates. More generally, approvals by any regulatory agency may not be indicative of what any other regulatory agency may require for approval or what such regulatory agencies may require for approval in connection with new vaccine candidates. Moreover, our vaccine candidates may not perform successfully in clinical trials.

Our vaccine candidates are in clinical or preclinical stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability. If we are unable to complete development of or commercialize our vaccine candidates or experience significant delays in doing so, our business would be materially harmed.

None of our vaccine candidates have been the subject of late-stage or pivotal clinical trials. On October 24, 2022, we announced positive topline results from our Phase 1/2 clinical proof-of-concept study of VAX-24 in adults ages 18 to 64. We also announced in July 2022 the initiation of a separate Phase 2 study of VAX-24 in healthy adults aged 65 and older and expect to announce topline safety, tolerability and immunogenicity results from this study in the second half of 2023. Final results with the six-month safety data of the Phase 2 adult studies are anticipated in the first half of 2023. Regulatory interactions to inform the Phase 3 program are anticipated in the second half of 2023 following the receipt of the final safety reports from the two adult Phase 2 studies, and topline safety, tolerability and immunogenicity data from the pivotal Phase 3 non-inferiority study in adults are expected in

2025. With regard to our VAX-24 pediatric program, in late February 2023, we announced that the FDA cleared the IND application for the prevention of IPD in infants. We plan to initiate an 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. We anticipate submitting an IND application to the FDA for VAX-31 (formerly VAX-XP) in the second half of 2023. Topline safety, tolerability and immunogenicity data from a Phase 1/2 study in adults are expected in 2024. In addition to our PCV franchise, our pipeline includes VAX-A1, a novel conjugate vaccine candidate designed to prevent disease caused by Group A Strep; VAX-PG, a novel protein vaccine candidate targeting the keystone pathogen responsible for periodontitis; VAX-GI, a vaccine designed to prevent Shigellosis; and other discovery-stage programs. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals for and successfully commercializing our vaccine candidates, either alone or with third parties, and we cannot guarantee that we will ever obtain regulatory approval for any of our vaccine candidates. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. Before obtaining regulatory approval for the commercial distribution of our vaccine candidates, we must conduct extensive preclinical studies and clinical trials to demonstrate the safety and efficacy of our vaccine candidates.

We may not have the financial resources to continue development of, or to enter into new collaborations for, a vaccine candidate if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, vaccine candidates, including:

- negative or inconclusive results from our preclinical or clinical trials, leading to a decision or requirement to conduct additional preclinical studies or clinical trials or abandon a program;
- product-related adverse effects experienced by volunteers in our clinical trials;
- difficulty achieving successful development of our manufacturing processes, including process development and scale-up activities to supply products for preclinical studies, clinical trials and commercial sale, if approved;
- timely completion of our preclinical studies and clinical trials, including any field efficacy studies that may be required, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- inability of us or any third-party contract manufacturer to scale up manufacturing of our vaccine candidates to supply the needs of preclinical studies, clinical trials and commercial sales, and to manufacture such products in conformity with regulatory requirements;
- delays in submitting IND applications or compatible foreign applications or delays or failures in obtaining necessary approvals from regulators to commence a clinical trial, or suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or similar foreign authorities regarding the scope or design of our clinical trials, including any requirements to perform field efficacy studies;
- delays in enrolling subjects in our clinical trials;
- inadequate supply or quality of vaccine candidate components or materials or other supplies necessary for conducting clinical trials;
- inability to obtain alternative sources of supply for which we have a single source for vaccine candidate components;
- the availability of coverage and adequate reimbursement and pricing from third-party payors, including government authorities, pertaining to the vaccine candidate, once approved, and patients' willingness to pay out-of-pocket if third-party payor reimbursement is limited or not available;
- greater than anticipated costs of our clinical trials, including chemistry, manufacturing and controls, or CMC, activities related to our clinical trials;
- harmful side effects or inability of our vaccine candidates to meet efficacy endpoints;

- unfavorable FDA or other regulatory agency inspection and review of one or more of our clinical trial sites or our contract manufacturers' facilities;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology or vaccine candidates in particular; or
- varying interpretations of our data by the FDA and comparable foreign regulatory authorities.

In particular, while we believe our PCVs could receive regulatory approval based on well-defined surrogate immune endpoints, consistent with how other PCVs have obtained regulatory approval in the past, rather than requiring clinical field efficacy studies, there can be no assurance that the FDA or comparable foreign regulatory authorities will provide approvals on such basis. In addition, changes to the standard of care or the approval of new vaccines could change the threshold for achievement of non-inferiority using the established surrogate immune endpoints that our PCVs will need to meet in our clinical trials.

Our inability to complete development of or commercialize our vaccine candidates, or significant delays in doing so due to one or more of these factors, could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authorities may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authorities, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our vaccine candidates.

Our business is highly dependent on the success of VAX-24, which is in clinical development. If we are unable to obtain approval for VAX-24 and effectively commercialize VAX-24, our business would be significantly harmed.

Our business and future success depends on our ability to obtain regulatory approval of, and then successfully commercialize, our most advanced vaccine candidate, VAX-24. Although VAX-24 has produced positive topline results in a Phase 1/2 clinical study, it may not demonstrate the same results in future pivotal studies. VAX-24 will require additional clinical and non-clinical development, regulatory review and approval in multiple jurisdictions, substantial investment, access to sufficient clinical and commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. We cannot provide any assurance that we will be able to successfully advance VAX-24 through the development process.
The clinical and commercial success of VAX-24 and future vaccine candidates will depend on a number of factors, including the following:

- our ability to raise any additional required capital on acceptable terms, or at all;
- our ability to complete IND-enabling studies and successfully submit IND or comparable applications;
- the ability of third parties with whom we contract to manufacture adequate clinical study and commercial supplies of our lead vaccine candidates or any future vaccine candidates, remain in good standing with regulatory agencies and develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices, or cGMP, and do so in a timely manner;
- timely completion of our preclinical studies and clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;

- whether we are required by the FDA or similar foreign regulatory agencies to conduct additional clinical trials, including field efficacy studies, or other studies beyond those planned to support the approval and commercialization of our vaccine candidates or any future vaccine candidates;
- acceptance of our proposed indications and primary surrogate endpoint assessments for our PCV candidates by the FDA and similar foreign regulatory authorities;
- any changes to the required threshold for the achievement of non-inferiority using established surrogate immune endpoints that our PCVs will need to meet in our clinical trials;
- our ability to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities the safety, efficacy and acceptable risk to benefit profile of VAX-24 or any future vaccine candidates;
- the pace and prevalence of serotype replacement following the introduction of VAX-24 or VAX-31 or other vaccines targeting pneumococcal disease;
- any vaccine-vaccine interference studies that may be required, particularly with the standard of care pediatric vaccine regimen;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our vaccine candidates or future approved products, if any;
- the timely receipt of necessary marketing approvals from the FDA or comparable foreign regulatory authorities;
- achieving, maintaining and, where applicable, ensuring that our third-party contractors achieve and maintain compliance with our contractual obligations and with all regulatory requirements applicable to our lead vaccine candidates or any future vaccine candidates or approved products, if any;
- obtaining and maintaining an Advisory Committee on Immunization Practices, or ACIP, preferred recommendation or comparable foreign regulatory authority's recommendation of our vaccine candidates and the willingness of physicians, operators of clinics and patients to utilize or adopt any of our future vaccine candidates to prevent or treat age-associated diseases;
- our ability to successfully develop a commercial strategy and thereafter commercialize our vaccine candidates or any future vaccine candidates in the United States and internationally, if approved for marketing, reimbursement, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- the convenience of our treatment or dosing regimen;
- acceptance by physicians, payors and patients of the benefits, safety and efficacy of our vaccine candidates or any future vaccine candidates, if approved, including relative to alternative and competing treatments;
- patient demand for our vaccine candidates, if approved;
- our ability to establish and enforce intellectual property rights in and to our vaccine candidates or any future vaccine candidates;
- our ability to avoid third-party patent interference, intellectual property challenges or intellectual property infringement claims; and
- the impact of the COVID-19 pandemic, which may exacerbate the magnitude of the factors discussed above.

These factors, many of which are beyond our control, could cause us to experience significant delays or an inability to obtain regulatory approvals or commercialize our vaccine candidates. Even if regulatory approvals are obtained, we may never be able to successfully commercialize any of our vaccine candidates. Accordingly, we cannot provide assurances that we will be able to generate sufficient revenue through the sale of our vaccine candidates or any future vaccine candidates to continue our business or achieve profitability.

Our primary competitors have significantly greater resources and experience than we do, which may make it difficult for us to successfully develop our vaccine candidates, or may result in others discovering, developing or commercializing products before or more successfully than us.

The vaccine market is intensely competitive and is dominated by a small number of multinational, globally established pharmaceutical corporations with significant resources; in recent history, Pfizer Inc, or Pfizer, Merck & Co., Inc., or Merck, GSK plc, or GSK and Sanofi have been responsible for developing and introducing most new vaccines to the world. We may also face competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions.

Vaccine candidates that we successfully develop and commercialize may compete with existing vaccines and new vaccines that may become available in the future. Many of our competitors have substantially greater financial, lobbying, technical, human and other resources than we do and may be better equipped to develop, manufacture and market technologically superior vaccines, including the potential that our competitors may develop chemical processes or utilize novel technologies for developing vaccines that may be superior to those we employ. In addition, many of these competitors have significantly greater experience than we have in undertaking preclinical studies and clinical trials of new products and in obtaining regulatory approvals, including for many vaccine franchises. Accordingly, our competitors may succeed in obtaining FDA approval or a preferred recommendation for their products. For example, PCV13 obtained FDA approval for the prevention of invasive pneumococcal disease, or IPD, in infants based on non-inferior IgG antibody responses relative to Prevnar, using the surrogate immune endpoints established by the prior Prevnar field efficacy study. Pfizer implemented a similar approach to development of its 20-valent PCV vaccine candidate, PCV20, which was approved by the FDA in June 2021 for use in adults. In August 2022, Pfizer announced topline results from its U.S. Phase 3 study in infants evaluating PCV20 for the prevention of IPD and in January 2023, the FDA accepted for priority review a supplemental Biologics License Application for PCV20 for the prevention of IPD in infants and children. Merck received approval for PCV15, its 15-valent PCV, in July 2021 for use in adults and in June 2022 for use in infants. Merck announced in April 2022 that V116, the company's investigational 21-valent PCV for adults, received Breakthrough Therapy designation from the FDA, and later announced that it enrolled the first patient in their Phase 3 clinical trial. In June 2022, Merck announced positive results from its Phase 1/2 study evaluating the safety, tolerability and immunogenicity of V116 in pneumococcal vaccine-naïve adults 18-49 years of age (Phase 1) and 50 years of age and older (Phase 2). In addition, Sanofi and SK Chemicals have partnered to develop a PCV, and GSK, which recently acquired Affinivax, is developing a 24-valent affinity-bound pneumococcal vaccine. Affinivax also has a 30-plus valent pneumococcal candidate vaccine in preclinical development.

Many of our competitors have established distribution channels for the commercialization of their vaccine products, whereas we have no such established channels or capabilities. In addition, many competitors have greater name recognition, more extensive collaborative relationships or the ability to leverage a broader vaccine portfolio. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize vaccines that are safer, more effective, more convenient, less expensive or with a more favorable label than any vaccine candidates that we may develop.

As a result of these factors, our competitors may obtain regulatory approval of their products before we are able to, which may limit our ability to develop or commercialize our vaccine candidates, or achieve a competitive position in the market. This would adversely affect our ability to generate revenue. Our competitors may also develop vaccines that are safer, more effective, more widely accepted or less expensive than ours, and may also be more successful than we are in manufacturing and marketing their products. These advantages could render our vaccine candidates obsolete or non-competitive before we can recover the costs of such vaccine candidates' development and commercialization.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and subject enrollment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We and our contract manufacturers may face difficulty satisfying chemistry, manufacturing and controls requirements imposed by the FDA and comparable foreign regulatory authorities. To date, no product developed using a cell-free manufacturing platform has received approval from the FDA or been commercialized.

While we are designing and developing a manufacturing process that we believe can scale to address clinical and commercial vaccine supply, we do not own or operate any manufacturing facilities. We rely on contract manufacturing organizations, or CMOs, including our strategic partnership with our contract manufacturer, Lonza, to access resources to facilitate the development and, if approved, commercialization of VAX-24 and our other vaccine candidates. Advancing our vaccine candidates may create significant challenges, including:

- manufacturing our vaccine candidates to our specifications, including process development, analytical development and quality control testing, and in a timely manner to support our preclinical and clinical trials and, if approved, commercialization;
- sourcing the raw materials used to manufacture our vaccine candidates for preclinical, clinical and, if approved, commercial supplies; and
- establishing sales and marketing capabilities upon obtaining any regulatory approval to gain market acceptance of our vaccines.

Before we can initiate a clinical trial or commercialize any of our vaccine candidates, we must demonstrate to the FDA that the CMC for our vaccine candidates meet applicable requirements, and prior to authorization in the European Union, or EU, a manufacturing authorization must be obtained from the appropriate EU regulatory authorities. Because no product manufactured on a cell-free manufacturing platform has been approved in the United States, there is no manufacturing facility that has demonstrated the ability to comply with FDA requirements, and, therefore, the timeframe for demonstrating compliance to the FDA's satisfaction is uncertain. Delays in establishing that our manufacturing process and the facilities we utilize for manufacturing comply with cGMP or disruptions in our manufacturing processes, implementation of novel technologies or scale-up activities, may delay or disrupt our development efforts.

Even if we obtain regulatory approval of our vaccine candidates, the products may not gain market acceptance among regulators, advisory boards, physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Even if any of our vaccine candidates receive marketing approval, they may fail to receive recommendations for use by regulators or advisory boards that recommend vaccines, or gain market acceptance by physicians, patients, third-party payors and others in the medical community. If such vaccine candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of any vaccine candidate, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- receiving Centers for Disease Control and Prevention, or CDC, and ACIP recommendations for use, as well as recommendations of comparable foreign regulatory and advisory bodies;
- prevalence and severity of the disease targets for which our vaccine candidates are approved;
- physicians, hospitals, third-party payors and patients considering our vaccine candidates as safe and effective;
- the potential and perceived advantages of our vaccine candidates over existing vaccines, including with respect to spectrum of coverage or immunogenicity;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or comparable foreign regulatory and advisory bodies;
- limitations or warnings contained in the labeling approved by the FDA or comparable foreign regulatory and advisory bodies;

- the timing of market introduction of our vaccine candidates as well as competitive products;
- the cost in relation to alternatives;
- the availability of coverage and adequate reimbursement and pricing by third-party payors, including government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage and adequate reimbursement by third-party payors, including government authorities;
- relative convenience and ease of administration, including as compared to competitive vaccines and alternative treatments; and
- the effectiveness of our sales and marketing efforts.

In the United States, the CDC and ACIP develop vaccine recommendations for both children and adults, as do similar agencies around the world. To develop its recommendations, ACIP forms working groups that gather, analyze and prepare scientific information. The ACIP also considers many of the factors above, as well as myriad additional factors such as the value of vaccination for the target population regarding the outcomes, health economic data and implementation issues. ACIP recommendations are also made within categories, such as in an age group or a specified risk group. For example, the ACIP may determine that a preferred recommendation in a smaller child population may be more economical than recommending vaccinations for a larger adult population, which could adversely impact our market opportunity.

New pediatric vaccines that receive an ACIP preferred recommendation are almost universally adopted, and adult vaccines that receive a preferred recommendation are widely adopted. For example, in 2014, the ACIP voted to recommend PCV13 for routine use to help protect adults aged 65 years and older against pneumococcal disease, which caused PCV13 to become the standard of care along with continued use of PPSV23. ACIP can also modify its preferred recommendation. For instance, in June 2019, the ACIP voted to revise the pneumococcal vaccination guidelines and recommend PCV13 for adults 65 and older based on the shared clinical decision making of the provider and patient, rather than a preferred use recommendation, which means the decision to vaccinate should be made at the individual level between health care providers and their patients. In October 2021, the ACIP voted to recommend the use of either Pfizer's PCV20, or Merck's PCV15 with PPSV23, for routine use in adults aged 65 years and older as well as for those between the ages of 19 and 64 years with certain underlying medical conditions or other risk factors. In June 2022, ACIP voted to recommend that Merck's PCV15 may be used as an option to the currently available PCV13 for children aged under 19 years according to currently recommended PCV13 dosing and schedules.

If our vaccine candidates are approved but fail to receive CDC and ACIP recommendations, or recommendations of other comparable foreign regulatory and advisory bodies, or achieve market acceptance among physicians, healthcare providers, patients, third-party payors or others in the medical community, we will not be able to generate significant revenue. Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete.

We may not be successful in our efforts to use our cell-free protein synthesis platform to expand our pipeline of vaccine candidates and develop marketable products.

The success of our business depends in large part upon our ability to identify, develop and commercialize products based on our cell-free protein synthesis platform. We intend to pursue clinical development of additional vaccine candidates beyond VAX-24, including VAX-31 for PCV, VAX-A1 for Group A Strep, VAX-PG for periodontitis and VAX-GI for Shigellosis. Our research programs may fail to identify potential vaccine candidates for clinical development for a number of reasons or we may focus our efforts and resources on potential programs or vaccine candidates that ultimately prove to be unsuccessful. In addition, we cannot provide any assurance that we will be able to successfully advance any of our existing or future vaccine candidates through the development process.

Our potential vaccine candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. If any of these events occur, we may be forced to abandon our development efforts for a program or for multiple programs, which would materially harm our business and could potentially cause us to cease operations.

Even if we receive FDA approval to market additional vaccine candidates, we cannot provide assurance that any such vaccine candidates will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. In addition, current PCVs do not address the majority of circulating strains causing pneumococcal disease. There has been a decrease in the incidence of disease attributable to the strains covered by existing vaccines but an increase in incidence attributable to non-covered strains that now cause most residual disease. Such change is driven by the void created when strains are taken out of circulation after widespread vaccination, which is a phenomenon known as serotype replacement. As a result of such change, broader spectrum PCVs are required to maintain protection against historically pathogenic strains while expanding coverage to current circulating and emerging strains. There can be no assurance that we will be able to develop higher-valent vaccines to address serotype replacement.

In addition, because VAX-24 is our most advanced vaccine candidate, and because our other vaccine candidates are also based on our cell-free protein synthesis platform, if VAX-24 encounters safety or efficacy problems, manufacturing problems, developmental delays, regulatory issues or other problems, our development plans and business would be significantly harmed.

We currently rely on third-party manufacturing and supply partners, including Lonza and Sutro Biopharma, to supply raw materials and components for, and manufacture of, our preclinical and clinical supplies as well as our vaccine candidates. Our inability to procure necessary raw materials or to have sufficient quantities of preclinical and clinical supplies or the inability to have our vaccine candidates manufactured, including delays or interruptions at our third-party manufacturers, or our failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, would materially and adversely affect our business.

Efficient and scalable manufacturing and supply is a vital component of our business strategy. We currently do not own or operate any manufacturing facilities. We are designing and developing a manufacturing process that we believe can scale to address clinical and commercial vaccine supply. However, our assumptions as to our ability and our CMOs' ability to produce vaccines at the scale needed for clinical development and commercial demand, in particular for our PCVs, may prove to be wrong. If we encounter substantial problems in our manufacturing processes or in our ability to scale to address commercial vaccine supply, our business would be materially adversely affected. Examples of potential issues related to our manufacturing processes or our ability to scale include difficulties with production costs, yields and quality control, including stability of the drug substance or drug product.

We rely on third-party contract manufacturers to manufacture preclinical and clinical trial product materials and supplies for our needs. There can be no assurance that our preclinical and clinical development product supplies will not be limited or interrupted or be of satisfactory quality or continue to be available on acceptable terms. Over the course of the development and manufacturing of VAX-24, we have encountered process-related matters that have required us to make adjustments to our processes. We encountered such process-related matters during our drug substance manufacturing campaign for VAX-24 at Lonza. The cumulative impact of the time required to make adjustments to our processes led to a delay of our drug substance manufacturing campaign due to scheduling conflicts and capacity constraints at Lonza. There can be no assurance that we or Lonza will be able to successfully manufacture drug substances in a timely manner in the future, or at all. Such process changes and manufacturing delays have caused a change in our IND timelines in the past and future changes or delays could impact future timelines for VAX-24 or for our other product candidates. As a third-party manufacturer, we are also subject to Lonza's scheduling commitments for its other clients. Scheduling conflicts with Lonza's other clients have contributed to manufacturing delays in the past, and there is no guarantee that future scheduling conflicts or related capacity constraints will not affect our manufacturing campaigns and related timelines. In addition, certain aspects of our manufacturing process for our clinical trial product materials and supplies were adversely affected by the COVID-19 pandemic, and could be adversely affected by the ongoing COVID-19 pandemic, earthquakes and other natural or man-made disasters, equipment failures, labor shortages, power failures and numerous other factors

in the future. Please see the risk factor titled "*Health epidemics, including the effects of the ongoing COVID-19 pandemic, have impacted and could continue to impact our business, including in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of potential clinical trial sites or other business operations.*"

The manufacturing process for a vaccine candidate is subject to FDA or comparable foreign regulatory authority review. Our suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMPs.

If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or comparable foreign regulatory authorities, we may not be able to rely on their manufacturing facilities for the manufacture of elements of our vaccine candidates. Moreover, we do not control the manufacturing process at our contract manufacturers and are completely dependent on them for compliance with current regulatory requirements. In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills, raw materials or technology required to manufacture our vaccine candidates may be unique or proprietary to the original manufacturer or supplier, and we may have difficulty applying such skills or technology or sourcing such raw materials ourselves, or in transferring such skills, technology or raw materials to another third party, or such transfer may be subject to certain consent obligations and payment terms to Lonza. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to enable us, or to have another third party, manufacture our vaccine candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines, and we may be required to repeat some of the development program. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop vaccine candidates in a timely manner or within budget.

We expect to continue to rely on third-party manufacturers and suppliers, including Lonza, if we receive regulatory approval for any PCV or any other vaccine candidates. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. In December 2019, we exercised our right to require Sutro Biopharma to establish a second supplier for extract and custom reagents to support our anticipated clinical and commercial needs. In December 2022, we entered into an option agreement with Sutro Biopharma, or the Option Agreement, pursuant to which we acquired, among other thing, authorization to enter into an agreement with an independent alternate CMO to directly source Sutro Biopharma's cell-free extract, allowing us to have direct oversight over financial and operational aspects of the relationship with the CMO. If we are unable to obtain or maintain third-party manufacturing for vaccine candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our vaccine candidates successfully. Our or a third party's failure to execute on our manufacturing requirements and comply with cGMPs could adversely affect our business in a number of ways, including:

- an inability to initiate or complete clinical trials of vaccine candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for our vaccine candidates;
- subjecting third-party manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our vaccine candidates; and
- in the event of approval to market and commercialize a vaccine candidate, an inability to meet commercial demands for our products.

In addition, because VAX-24 is our most advanced vaccine candidate, and because our other vaccine candidates are also based on our cell-free protein synthesis platform, if VAX-24 encounters safety or efficacy problems, manufacturing problems, developmental delays, regulatory issues or other problems, our development plans and business would be significantly harmed.

Additionally, we and our contract manufacturers may experience manufacturing difficulties due to limited vaccine manufacturing experience, resource constraints or as a result of labor disputes or unstable political environments. If we or our contract manufacturers were to encounter any of these difficulties, our ability to manufacture sufficient vaccine supply for our preclinical studies and clinical trials, or to provide product for patients once approved, would be jeopardized.

Our vaccine candidates may cause undesirable side effects or have other properties, including interactions with existing vaccine regimens, that could halt their clinical development, prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.

Adverse effects or other undesirable or unacceptable side effects caused by our vaccine candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. In such an event, our clinical trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our vaccine candidates. Such side effects could also affect trial recruitment or the ability of enrolled subjects to complete the clinical trial or result in potential product liability claims. A data safety monitoring board may also suspend or terminate a clinical trial at any time on various grounds, including a finding that the research volunteers are being exposed to an unacceptable health risk. Vaccine-related side effects could also affect recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. In addition, any vaccine to be approved in pediatric populations may need to undergo extensive vaccine-vaccine interference studies with the standard of care pediatric vaccine regimen. Further, to the extent field efficacy studies are required, prophylactic vaccines typically require clinical testing in thousands to tens of thousands of healthy volunteers to define an approvable benefit-risk profile. The need to show a high degree of safety and tolerability when dosing healthy individuals could result in rare and even spurious safety findings, negatively impacting a program prior to or after commercial launch. Any of these occurrences may harm our business, financial condition and prospects significantly.

Negative developments and negative public opinion of new technologies on which we rely may damage public perception of our vaccine candidates or adversely affect our ability to conduct our business or obtain regulatory approvals for our vaccine candidates.

Negative developments and negative public opinion of new or existing technologies on which we rely may damage public perception of our vaccine candidates or adversely affect our ability to conduct our business or obtain regulatory approvals for our vaccine candidates. Public perception may be influenced by claims that vaccines are unsafe, and products incorporating new vaccine technology may not gain the acceptance of the public or the medical community. Adverse public attitudes may negatively impact our ability to enroll subjects in clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, our vaccine candidates in lieu of, or in addition to, existing, more familiar vaccines for which greater clinical data may be available. Any increase in negative perceptions of the technologies that we rely on may result in fewer physicians prescribing our products or may reduce the willingness of patients to utilize our products or participate in clinical trials for our vaccine candidates.

We may not be able to file IND applications to commence clinical trials on the timelines we expect, and even if we are able to, the FDA may not permit us to proceed.

Our timing of submitting the IND applications for our product candidates is dependent on preclinical and manufacturing success, and if we experience additional delays, we may fail to meet our anticipated timelines. In addition, we cannot be sure that submission of an IND application or IND application amendment will result in the FDA allowing testing and clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate

such clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND or clinical trial application, we cannot guarantee that such regulatory authorities will not change their requirements in the future.

We may encounter substantial delays in our clinical trials or may not be able to conduct our trials on the timelines we expect.

Clinical testing is expensive, time consuming and subject to uncertainty. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. Even if these trials begin as planned, issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical studies can occur at any stage of testing, and our future clinical studies may not be successful. Events that may prevent successful or timely completion of clinical development include:

- inability to generate sufficient preclinical, toxicology or other in vivo or in vitro data to support the initiation of clinical trials;
- delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for advanced clinical trials;
- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical study sites;
- delays in obtaining required institutional review board, or IRB, approval at each clinical study site;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND application or amendment, or equivalent application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; a negative finding from an inspection of our clinical study operations or study sites; developments on trials conducted by competitors for related technology that raise FDA concerns about risk to patients of the technology broadly; or if the FDA finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned clinical trials;
- delays in adding a sufficient number of trial sites and recruiting volunteers to participate in our clinical trials;
- failure by our CROs, other third parties or us, to adhere to clinical study requirements;
- failure to perform in accordance with the FDA's good clinical practice, or GCP, requirements or applicable regulatory guidelines in other jurisdictions;
- transfer of manufacturing processes to any new CMO or our own manufacturing facilities or any other development or commercialization partner for the manufacture of vaccine candidates;
- delays in having subjects complete participation in a study or return for post-injection follow-up;
- subjects dropping out of a study;
- occurrence of side effects associated with our vaccine candidates that are viewed to outweigh their potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of our vaccine candidates being greater than we anticipate;

- clinical studies of our vaccine candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical studies or abandon product development programs;
- delays or failure to secure supply agreements with suitable raw material suppliers, or any failures by suppliers to meet our quantity or quality requirements for necessary raw materials; and
- delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our vaccine candidates for use in clinical studies or the inability to do any of the foregoing.

For example, based on the positive topline results from the VAX-24 Phase 1/2 proof-of-concept study, which evaluated the safety, tolerability and immunogenicity of VAX-24 in adults 18-64 years of age, the FDA supported the initiation of a pediatric study in infants. This study could uncover risks in this study population that could have potentially been discovered during a child and/or toddler study, which could then delay completion of clinical development. Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our vaccine candidates, we may be required to or we may elect to conduct additional studies to bridge our modified vaccine candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our vaccine candidates and may harm our business and results of operations.

If we encounter difficulties enrolling subjects in any clinical trials we may conduct, including any field efficacy trials that may be required, our clinical development activities could be delayed or otherwise adversely affected.

We may experience difficulties in enrolling subjects in any clinical trials we may conduct for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of subjects who remain in the study until its conclusion. The enrollment of subjects depends on many factors, including:

- the eligibility and exclusion criteria defined in the protocol;
- the size of the population required for analysis of the trial's primary endpoints;
- the proximity of volunteers to study sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain subject consents;
- the ability to monitor volunteers adequately during and after injection;
- the risk that volunteers enrolled in clinical trials will drop out of the trials before the injection of our vaccine candidates or trial completion; and
- the risks and disruptions caused by the COVID-19 pandemic related to patient and physician investigator recruitment and retention and study site initiation and clinical trial activities.

To the extent we are required to conduct any field efficacy studies, enrollment of a sufficient number of subjects may require additional time and resources given widespread vaccination rates in the United States, particularly in the pediatric population. As a result, we may be required to conduct any such trials outside the United States, which could cause additional complexity and delay. Delays in enrollment may result in increased costs or may affect the timing or outcome of any clinical trials we may conduct, which could prevent completion of these trials and adversely affect our ability to advance the development of our vaccine candidates.

Interim topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim topline or preliminary data from our preclinical or clinical trials. For instance, on October 24, 2022, we announced positive topline results from the Phase 1/2 clinical proof-of-concept study evaluating the safety, tolerability and immunogenicity of VAX-24 in healthy adults aged 18-64. Interim topline data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as more patient data become available. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data when we publish such data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results once additional data have been received and fully evaluated. Preliminary or topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we may publish. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular vaccine candidate and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular vaccine candidate or our business. If the topline data that we report differ from final results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, vaccine candidates may be harmed, which could significantly harm our business prospects.

We may seek Breakthrough Therapy designation or Fast Track designation by the FDA for one or more of our vaccine candidates, but we may not receive such designation, and even if we do, such designation may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our vaccine candidates will receive marketing approval.

We may seek Breakthrough Therapy or Fast Track designation for some of our vaccine candidates. For instance, in August 2022 we announced that the FDA granted Fast Track designation to VAX-24 in adults ages 18 and older and, in January 2023, we announced that the FDA granted Breakthrough Therapy designation for VAX-24 for the prevention of IPD in adults. A sponsor may seek FDA designation of its vaccine candidate as a Breakthrough Therapy if the vaccine candidate is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For vaccines that have been designated as Breakthrough Therapies, the FDA may take actions to expedite the development and review of the application, and interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

A vaccine designated as a Breakthrough Therapy by the FDA may also be eligible for expedited review and approval. If a vaccine candidate is intended for the treatment of a serious or life-threatening condition and clinical or preclinical data demonstrate the potential to address unmet medical needs for this condition, the sponsor may apply for Fast Track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular vaccine candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it.

Even if we obtain Fast Track designation for one or more of our vaccine candidates, we may not experience a faster development process, review or approval compared to non-expedited FDA review procedures. For instance, although the FDA has granted Fast Track designation to VAX-24 in adults, we may not experience a faster development, review or approval process compared to the conventional process. In addition, the FDA may withdraw Fast Track designation from VAX-24, or from any other of our vaccine candidates that may receive the

designation in the future, if it believes that the designation is no longer supported. Fast Track designation alone does not guarantee qualification for the FDA's Priority Review procedures.

Whether to grant Breakthrough Therapy or Fast Track designations are within the discretion of the FDA. Accordingly, even if we believe one of our vaccine candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of either of these designations for a vaccine candidate may not result in a faster development process, review or approval compared to vaccine candidates considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our vaccine candidates qualify for either of these designations, the FDA may later decide that the vaccine candidate no longer meets the conditions for qualification and rescind the designations.

We currently have no marketing and sales organization, and as an organization have no experience in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our vaccine candidates, we may not be able to generate product revenue.

We currently have no sales, marketing or distribution capabilities and as an organization have no experience in marketing products. If we develop an in-house marketing organization and sales force, we will require significant capital expenditures, management resources and time, and we will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel.

If we are unable or decide not to establish internal sales, marketing and distribution capabilities, we will pursue collaborative arrangements regarding the sales and marketing of our products; however, there can be no assurance that we will be able to establish or maintain such collaborative arrangements, or if we are able to do so, that they will have effective sales forces. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized our vaccine candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our vaccine candidates.

There can be no assurance that we will be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product that receives regulatory approval in the United States or overseas. If we are unable to develop in-house sales and distribution capabilities or enter into relationships with third-party collaborators on acceptable terms or at all, we may not be able to successfully commercialize our products. If we are not successful in commercializing our products or any future products, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would incur significant additional losses.

A variety of risks associated with potentially conducting research and clinical trials abroad and marketing our vaccine candidates internationally could materially adversely affect our business.

As we pursue approval and commercialization for our vaccine candidates overseas and conduct CMC and other operations overseas, we will be subject to additional risks related to operating in foreign countries, including:

- differing regulatory requirements in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- increased difficulties in managing the logistics and transportation of storing and shipping vaccine candidates abroad;
- import and export requirements and restrictions;
- differing and changing data protection and privacy regimes and requirements;

- economic weakness, including inflation and interest rates, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- differing payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;
- potential liability under the U.S. Foreign Corrupt Practices Act of 1977, as amended, or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism.

These and other risks associated with our international operations and our collaborations with Lonza, based in Switzerland, may materially adversely affect our ability to attain or maintain profitable operations.

We are highly dependent on our key personnel, and if we are not able to retain these members of our management team or recruit and retain highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, including our Chief Executive Officer, our President and Chief Financial Officer, our Vice President of Research and our Executive Vice President and Chief Operating Officer. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and our inability to find suitable replacements, could result in delays in product development and harm our business.

We conduct substantially all of our operations at our facilities in the San Francisco Bay Area. This region is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options and restricted stock units, or RSUs, that vest over time. The value to employees of stock options and RSUs that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management and scientific and development teams may terminate their employment with us on short notice. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain “key person” insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

We have grown rapidly and will need to continue to grow the size of our organization, and we may experience difficulties in managing this growth.

As our discovery, development and commercialization plans and strategies develop, we have rapidly expanded our employee base and expect to continue to add managerial, operational, sales, research and development, marketing, financial and other personnel. Current and future growth imposes significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our vaccine candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our vaccine candidates will depend, in part, on our ability to effectively manage our growth. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize our vaccine candidates and, accordingly, may not achieve our research, development and commercialization goals.

Obtaining and maintaining regulatory approval of our vaccine candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our vaccine candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our vaccine candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval of a vaccine candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the vaccine candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a vaccine candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of vaccine candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our vaccine candidates will be harmed.

We may form or seek strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such alliances or licensing arrangements.

We may form or seek strategic alliances, create joint ventures or collaborations or enter into additional licensing arrangements with third parties that we believe will complement or augment our discovery, development and commercialization efforts with respect to our vaccine candidates and any future vaccine candidates that we may seek to develop. Any of these relationships may require us to incur non-recurring and other charges, increase our

near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our vaccine candidates because they may be deemed to be at too early of a stage of development for collaborative effort, and third parties may not view our vaccine candidates as having the requisite potential to demonstrate safety and efficacy. Any delays in entering into new strategic partnership agreements related to our vaccine candidates could delay the development and commercialization of our vaccine candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

If we license products or businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. We cannot be certain that, following a strategic transaction or license, we will achieve the results, revenue or specific net income that justifies such transaction.

Revenue from any "catch up" opportunity may decline over time as more of the patient population is vaccinated.

We intend to initially seek approval of our VAX-24 vaccine candidate in adults. If approved, we believe it may have the potential to serve as a "catch up" or booster to those adults who have previously received PPSV23 or a lower-valent PCV. Previous vaccines with a "catch up" opportunity have seen a high initial capture rate, but sales may decline over time as the number of individuals who remain unvaccinated with the new vaccine, and eligible for "catch up" opportunities, declines. Such decline could adversely affect our revenue over time.

If our security measures, or those maintained on our behalf by CROs, service providers or other third parties, are compromised now, or in the future, or the security, confidentiality, integrity or availability of our information technology, software, services, networks, communications or data is compromised, limited or fails, this could result in significant fines or other liability, interrupt our development programs, harm our reputation, or otherwise adversely affect our business.

In the ordinary course of our business, we collect, use, retain, safeguard, disclose, share, transfer or otherwise process proprietary, confidential and sensitive information, including personal data (including, key-coded data, health information, data we collect about trial participants in connection with clinical trials and other special categories of personal data), intellectual property, trade secrets, and proprietary business information owned or controlled by ourselves or other parties, and other sensitive third-party data (collectively, "Sensitive Information").

We may use third-party service providers and subprocessors, including our CROs, to help us operate our business and engage in processing on our behalf in a variety of contexts, . including, without limitation, cloud-based infrastructure, data center facilities, encryption and authentication technology, employee email and other functions. We may also share Sensitive Information with our partners or other third parties in connection with our business. Our ability to monitor these third parties' cybersecurity practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award.

Cyberattacks, malicious internet-based activity and online and offline fraud are prevalent and continue to increase. In addition to traditional computer "hackers"; threat actors; software bugs; malicious code (such as viruses and worms); employee error, theft or misuse; denial-of-service attacks (such as credential stuffing); advanced persistent threat intrusions; natural disasters; terrorism; war; telecommunication and electrical failures; and ransomware attacks, sophisticated nation-state and nation-state supported actors are threats to our information technology assets and data. Ransomware attacks, including those perpetrated by organized criminal threat actors, nation-states, and nation-state-supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, loss of data and income, reputational harm and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. We may also be the subject of server malfunction, software or hardware failures, supply-chain cyberattacks, loss of data or other

computer assets and other similar issues. Remote and hybrid work has become more common and has increased risks to our information technology systems and data, as more of our employees utilize network connections, computers and devices outside our premises or network, including working at home, while in transit and in public locations. Any of the previously identified or similar threats could cause a security incident or other interruption. A security incident or other interruption could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to data and could disrupt our ability (and that of third parties upon whom we rely) to provide our products or operate our business.

While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. While we take steps to detect and remediate vulnerabilities, we may be unable in the future to detect vulnerabilities in our information technology systems because such threats and techniques change frequently, are often sophisticated in nature and may not be detected until after a security incident has occurred. Despite our efforts to identify and remediate vulnerabilities, if any, in our information technology systems, our efforts may not be successful. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities. These vulnerabilities pose material risks to our business.

We may be required to expend significant resources, fundamentally change our business activities and practices, or modify our operations, including our clinical trial activities, or information technology in an effort to protect against security breaches and to mitigate, detect and remediate actual or potential vulnerabilities. Certain data privacy and security obligations may require us to implement and maintain specific security measures or industry-standard or reasonable security measures to protect our information technology systems and Sensitive Information. While we have not experienced any such material system failure or security breach to date, if we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences, including interruptions in our operations, which could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our vaccine candidates could be delayed. Furthermore, consequences from an actual or perceived security breach may include: government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing data (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may cause customers to stop using our platform/products/services, deter new customers from using our products, and negatively impact our ability to grow and operate our business.

Additionally, applicable data protection requirements, including, without limitation, laws, regulations, guidance as well as our internal and external policies and our contractual obligations, may require us to notify relevant stakeholders of security breaches, including affected individuals, partners, collaborators, regulators, law enforcement agencies, credit reporting agencies and others. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to litigation or other liability, fines, harm to our reputation, significant costs, or other materially adverse effects. There can be no assurance that any limitations or exclusions of liability in our contracts would be enforceable or adequate or protect us from liability or damages.

We cannot be sure that our insurance coverage, if any, will be adequate or otherwise protect us from or adequately mitigate liabilities or damages with respect to claims, costs, expenses, litigation, fines, penalties, business loss, data loss, regulatory actions or other materially adverse impacts arising out of our processing activities, privacy and security practices, or security breaches we may experience. The successful assertion of one or more large claims against use that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large excess or deductible or co-insurance requirements), could result in substantial cost increase or prevent us from obtaining insurance on acceptable terms. Additionally, our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our CMOs, CROs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The impact of climate change may increase these risks due to changes in weather patterns, such as increases in storm intensity, sea-level rise, melting of permafrost and temperature extremes on facilities or operations. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Our ability to manufacture our vaccine candidates could be disrupted if our operations or those of our suppliers are affected by a man-made or natural disaster or other business interruption, including the COVID-19 pandemic. Our corporate headquarters are located in California near major earthquake faults and fire zones. The ultimate impact on us, our significant suppliers and our general infrastructure of being located near major earthquake faults and fire zones and being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural disaster.

Health epidemics, including the effects of the ongoing COVID-19 pandemic, have impacted and could continue to impact our business, including in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of potential clinical trial sites or other business operations.

Health epidemics could adversely impact our business, including in regions where we have concentrations of potential clinical trial sites or other business operations, and cause significant disruption in the operations of our contract manufacturer and other third parties upon whom we rely. For example, the COVID-19 pandemic has presented a substantial public health and economic challenge around the world and has affected and could continue to affect employees, patients, communities and business operations, as well as the U.S. economy and financial markets. Our headquarters is located in the San Francisco Bay Area, and our contract manufacturer, Lonza, is located in Switzerland. Many geographic regions imposed and in the future may impose, "shelter-in-place" orders, quarantines or similar orders or restrictions to control the spread of COVID-19. The effects of these orders and our work-from-home policies may negatively impact productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. In connection with these measures, we may be subject to claims based upon, arising out of or related to COVID-19 and our actions and responses thereto, including any determinations that we may make to continue to operate or to re-open our facilities where permitted by applicable law. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, financial condition, results of operations and growth prospects.

Moreover, we rely on third parties to supply raw materials and manufacture our preclinical and clinical product supplies of our vaccine candidates, and we cannot guarantee that they will continue to perform their contractual duties in a timely and satisfactory manner as a result of the COVID-19 pandemic. In addition, public health guidelines could impact personnel at third-party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which would disrupt our supply chain. For example, the COVID-19 pandemic slowed raw material supply chains and travel restrictions delayed the qualification of key analytical equipment used in manufacturing and curtailed in-person CMO oversight of manufacturing.

Some of our suppliers of certain materials used in the production of our vaccine candidates are located in Europe. Any manufacturing supply interruption at Lonza's facilities in Switzerland could adversely affect our ability to produce our vaccine candidates for use in the conduct of our preclinical studies or clinical trials. In any event, if the COVID-19 pandemic continues and persists for an extended period of time or more acutely impacts geographies with particular impact on our business, we could experience significant disruptions to our preclinical and clinical development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects.

In addition, our planned clinical trials may be affected by the COVID-19 pandemic. Site initiation and subject enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic. Some subjects may not be able to comply with clinical trial protocols if quarantines impede their movement or interrupt healthcare services. Similarly, our ability to recruit and retain subjects and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, may adversely impact our planned clinical trial operations. Additionally, our clinical trial vendors, including testing labs, may experience short interruptions, delays or reductions in capacity as a result of staff exposure to COVID-19, which could adversely affect our timelines for planned clinical operations.

Furthermore, while the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, the pandemic resulted in significant and prolonged disruption of global financial markets, which may reduce our ability to access capital, which could in the future negatively affect our liquidity.

While the ultimate impact of the COVID-19 pandemic on our business is highly uncertain, any negative impacts that materialize could materially adversely affect our clinical development and operations, financial performance and stock price. In addition, to the extent the evolving effects of the COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described elsewhere in this "Risk Factors" section.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our vaccine candidates.

We face an inherent risk of product liability as a result of the clinical testing of our vaccine candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if our vaccine candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our vaccine candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our vaccine candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any vaccine candidate; and
- a decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with corporate collaborators. Our insurance policies may also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. Assuming we obtain clinical trial insurance for our clinical

trials, we may have to pay amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures, reckless and/or negligent conduct or unauthorized activities that violate (i) the laws and regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities, (ii) manufacturing standards, (iii) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the United States and abroad and (iv) laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government-funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations, any of which could have a negative impact on our business, financial condition, results of operations and prospects.

Changes in tax laws or tax rulings could affect our financial position.

In December 2017, the Tax Cuts and Jobs Act, or Tax Act, was signed into law. The Tax Act, among other things, contains significant changes to corporate taxation, including (i) changes to the expensing of research and development expenses for tax years beginning after December 31, 2021, (ii) reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, (iii) limitation of the tax deduction for interest expense to 30% of adjusted earnings (with certain exceptions, including for certain small businesses), (iv) limitation of the deduction for post-2017 net operating losses, or NOLs, to 80% of current-year taxable income and elimination of net operating loss carrybacks for post-2017 NOLs, (v) immediate deductions for certain new investments instead of deductions for depreciation expense over time and (vi) modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as “orphan drugs”). Effective January 1, 2022, we are also subject to mandatory capitalization of Section 174 research and development expenditures. The capitalized expenses are subject to amortization over five and fifteen years for expenses incurred within the U.S. and outside of U.S., respectively.

In March 2020, the Coronavirus Aid, Relief, and Economic Security, or CARES, Act was signed into law. The CARES Act changed certain provisions of the Tax Act. Under the CARES Act, NOLs arising in taxable years beginning after December 31, 2017 and before January 1, 2021 may be carried back to each of the five taxable years preceding the tax year of such loss, but NOLs arising in taxable years beginning after December 31, 2020 may not be carried back. In addition, the CARES Act eliminated the limitation on the deduction of NOLs to 80% of current year taxable income for taxable years beginning before January 1, 2021, and increased the amount of interest

expense that may be deducted to 50% of adjusted taxable income for taxable years beginning in 2019 or 2020. Notwithstanding the reduction in the corporate income tax, these benefits do not impact our current tax provision.

On December 21, 2020, the President of the United States signed into law the "Consolidated Appropriations Act, 2021," which includes further COVID-19 economic relief and extension of certain expiring tax provisions. The relief package includes a tax provision clarifying that businesses with forgiven Paycheck Protection Program, or PPP, loans can deduct regular business expenses that are paid for with the loan proceeds. Additional pandemic relief tax measures include an expansion of the employee retention credit, enhanced charitable contribution deductions and a temporary full deduction for business expenses for food and beverages provided by a restaurant for tax years 2021 and 2022.

The Infrastructure Investment and Jobs Act was signed on November 15, 2021, and it contained several tax provisions including changes to the Employee Retention Tax Credit and changes to excise taxes. These provisions do not have a material impactful to our current tax provision.

In accordance with the 2017 Tax Act, research and experimental (R&E) expenses under Internal Revenue Code Section 174 are required to be capitalized beginning in 2022. R&E expenses are required to be amortized over a period of five years for domestic expenses and 15 years for foreign expenses. We have capitalized research and experimental expenditures in our current tax provision as a result.

The Inflation Reduction Act of 2022 specifically introduces the topic of corporate alternative minimum tax ("CAMT") on adjusted financial statement income on applicable corporations for taxable years beginning after December 31, 2022. There is no impact to our current tax provision.

The American Rescue Plan Act was signed on March 11, 2021. One of the provisions of the Act included expanding the definition of covered employees subject to IRC 162(m) to include an additional top five highest compensated officers beyond the CEO, CFO, and three highest paid employees currently covered under IRC 162(m). This expanded provision is applicable for tax years beginning after Dec 31, 2026. The Company does not believe that this update to IRC 162(m) would have a material impact on its income tax provision currently and will continue to monitor this.

We are unable to predict what tax changes may be enacted in the future or what effect such changes would have on our business, but such changes could affect our effective tax rate and could have an adverse effect on our overall tax position in the future, along with increasing the complexity, burden, and cost of tax compliance.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses since inception and do not expect to become profitable in the near future, if ever. As of December 31, 2022, we had federal and state NOL carryforwards of $340.2 million and $453.1 million, respectively. The federal and state loss carryforwards, except the federal loss carryforward arising in tax years beginning after December 31, 2017, begin to expire in 2034 unless previously utilized. Federal NOLs arising in tax years beginning after December 31, 2017 have an indefinite carryforward period and do not expire. As of December 31, 2022, we also had federal and state research credit carryforwards of $4.4 million and $2.8 million, respectively. The federal research and development tax credit carryforwards expire beginning in 2039 unless previously utilized, and the state research and development tax credits can be carried forward indefinitely. In general, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change" (generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a rolling three-year period) is subject to limitations on its ability to utilize its pre-change NOLs to offset future taxable income. We have experienced ownership changes in the past. There were no ownership changes identified in 2022, as such we have determined that no federal research credits will expire unutilized or are excluded from our research carryforwards as of December 31, 2022. We do not expect any ownership changes during the year ended December 31, 2022 to result in a limitation that would materially reduce the total amount of net operating loss carryforwards and credits that can be utilized. Subsequent ownership changes may affect the limitation in future years. As a result, if, and to the extent that we earn net taxable income, our ability to use our pre-change NOLs to offset such taxable income may be subject to limitations.

Our insurance policies may be inadequate and potentially expose us to unrecoverable risks.

Although we intend to maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any vaccine candidate. Insurance availability, coverage terms and pricing continue to vary with market conditions. We endeavor to obtain appropriate insurance coverage for insurable risks that we identify; however, we may fail to correctly anticipate or quantify insurable risks, we may not be able to obtain appropriate insurance coverage and insurers may not respond as we intend to cover insurable events that may occur. Conditions in the insurance markets relating to nearly all areas of traditional corporate insurance change rapidly and may result in higher premium costs, higher policy deductibles and lower coverage limits. For some risks, we may not have or maintain insurance coverage because of cost or availability.

Risks Related to Our Reliance on Third Parties

We rely and will continue to rely on third parties to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our vaccine candidates.

We currently do not have the ability to independently conduct preclinical or clinical studies that comply with the regulatory requirements known as good laboratory practices and GCP. The FDA and regulatory authorities in other jurisdictions require us to comply with GCP requirements for conducting, monitoring, recording and reporting the results of clinical trials, in order to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. We rely on independent investigators and collaborators, such as universities, medical institutions, CROs and strategic partners, to conduct our preclinical and clinical trials under agreements with us.

We will need to negotiate budgets and contracts with CROs and study sites, which may result in delays to our development timelines and increased costs. We will rely heavily on these third parties over the course of our clinical trials, and we control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with applicable protocol and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for vaccine candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP regulations. In addition, our clinical trials must be conducted with biologic product produced under cGMPs and will require a large number of test subjects. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of subjects may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our preclinical studies and clinical trials will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our vaccine candidates. As a result, our financial results and the commercial prospects for our vaccine candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with trial sites or any CRO that we may use in the future terminate, we may not be able to enter into arrangements with alternative trial sites or CROs or do so on commercially reasonable terms. Switching or adding third parties to conduct our clinical trials involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines.

We rely on third parties, including Sutro Biopharma and Lonza, to supply raw materials and manufacture our preclinical and clinical product supplies of our vaccine candidates, and expect to rely on third parties to supply raw materials and produce and process our vaccine candidates, if approved. The loss of these suppliers or their failure to comply with applicable regulatory requirements or provide us with sufficient quantities at acceptable quality levels or prices, or at all, would materially and adversely affect our business.

We do not have the infrastructure or capability internally to manufacture supplies for our vaccine candidates or the materials necessary to produce our vaccine candidates for use in the conduct of our preclinical studies or clinical trials, and we lack the internal resources and the capability to manufacture any of our vaccine candidates on a preclinical, clinical or commercial scale. We have entered into an agreement with Sutro Biopharma to supply us with extract and custom reagents for use in manufacturing non-clinical and certain clinical supply of vaccine compositions. Pursuant to the Option Agreement, we also acquired, among other things, a right, but not an obligation, to obtain certain exclusive rights to internally manufacture and/or source extract from certain CMOs and the right to independently develop and make improvements to extract (including the right to make improvements to the extract manufacturing process as well as cell lines) for use in connection with the exploitation of certain vaccine compositions, or the Option. The Option period is five years from the date of the agreement, and we have not yet exercised the Option and we may never exercise the Option. We have engaged Lonza to perform manufacturing process development and clinical manufacture and supply of components for VAX-24, including the manufacture of polysaccharide antigens, our proprietary eCRM protein carrier and conjugated drug substances. We also engaged Lonza to perform manufacturing process development and clinical manufacture and supply of VAX-24 finished drug product. Our agreements with Lonza are denominated in Swiss Francs. Fluctuations in the exchange rate for Swiss Francs may increase our costs and affect our operating results.

Lonza is currently in the process of manufacturing our vaccine candidates on a clinical scale. We have not yet caused our vaccine candidates to be manufactured on a commercial scale and may not be able to achieve commercial scale manufacturing and may be unable to create an inventory of mass-produced product to satisfy demands for any of our vaccine candidates.

We do not yet have sufficient information to reliably estimate the cost of the commercial manufacturing and processing of our vaccine candidates, and the actual cost to manufacture and process our vaccine candidates could materially and adversely affect the commercial viability of our vaccine candidates. As a result, we may never be able to develop a commercially viable product.

In addition, our anticipated reliance on a limited number of third-party suppliers and manufacturers exposes us to the following risks:

- We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA may have questions regarding any replacement contractor. This may require new testing and regulatory interactions. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA questions, if any.
- Our third-party suppliers and manufacturers might be unable to timely formulate and manufacture or supply raw materials for our vaccine candidates or produce the quantity and quality required to meet our clinical and commercial needs, if any.
- Contract manufacturers may not be able to execute our manufacturing procedures appropriately.

- Our future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our products.
- Manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration and corresponding state agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.
- We may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our products.
- Our third-party suppliers and manufacturers could breach or terminate their agreement with us.

Each of these risks could delay our clinical trials, the approval, if any, of our vaccine candidates by the FDA or the commercialization of our vaccine candidates, or result in higher costs or deprive us of potential product revenue. In addition, we will rely on third parties to perform release tests on our vaccine candidates prior to delivery to patients. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm.

If we or our third-party suppliers use hazardous, non-hazardous, biological or other materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials. We and our suppliers are subject to federal, state and local laws and regulations in the United States governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that we and our suppliers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we and our suppliers cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business prospects, financial condition or results of operations.

Risks Related to Government Regulation

The FDA regulatory approval process is lengthy and time-consuming, and we may experience significant delays in the clinical development and regulatory approval of our vaccine candidates.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products, including biologics such as conjugate vaccines, are subject to extensive regulation by the FDA and other regulatory authorities in the United States. We expect that our vaccine candidates will be regulated by the FDA as biologics. We are not permitted to market any biological drug product in the United States until we receive approval of a Biologics License Application, or BLA, from the FDA. We have not previously submitted a BLA to the FDA, or similar approval filings to comparable foreign regulatory authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish the vaccine candidate's safety and effectiveness for each desired indication. Further, because our vaccine candidates that are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure and potent for use in their target indications. The BLA must also include significant information regarding the CMC for the product, including with respect to chain of identity and chain of custody of the product.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies of our vaccine candidates may not be predictive of the results of early-stage or later-stage clinical trials, and results of early clinical trials of our vaccine candidates may not be predictive of the results of later-stage clinical trials. The results

of clinical trials in one set of patients or indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same vaccine candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. Vaccine candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most vaccine candidates that begin clinical trials are never approved by regulatory authorities for commercialization. In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit a BLA or other marketing application.

We may also experience delays in completing planned clinical trials for a variety of reasons, including delays related to:

- obtaining regulatory authorization to begin a trial, if applicable;
- the availability of financial resources to commence and complete the planned trials;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval at each clinical trial site by an independent IRB;
- recruiting suitable volunteers to participate in and complete a trial;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- addressing any safety concerns that arise during the course of a trial;
- adding new clinical trial sites; or
- manufacturing sufficient quantities of qualified materials under cGMPs and applying them for use in clinical trials.

We could also encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our vaccine candidates in lieu of using existing vaccines that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such trials are being conducted or by the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a vaccine candidate, changes in governmental regulations or administrative actions, lack of adequate funding to continue the clinical trial or based on a recommendation by the data safety monitoring board. If we experience termination of, or delays in the completion of, any clinical trial of our vaccine candidates, the commercial prospects for our vaccine candidates will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may ultimately lead to the denial of regulatory approval of our vaccine candidates.

The FDA may disagree with our regulatory plan, and we may fail to obtain regulatory approval of our vaccine candidates.

The general approach for FDA approval of a new biologic or drug is for the sponsor to provide dispositive data from two Phase 3 clinical trials of the relevant biologic or drug in the relevant patient population. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and are time consuming. While

we have not had extensive discussions with the FDA regarding our regulatory plan, as a prerequisite for FDA approval, we believe that any new PCV, such as VAX-24, will have to be compared to the current standard of care, PCV13 and PCV15 in infants and PCV20 in adults. We believe that a successful comparison for an adult study would be based on demonstrating clinical non-inferiority of the immune response to PCV20 for common serotypes. In addition, we expect to use OPA titers as the primary immunogenicity surrogate endpoint for the VAX-24 program in adults because PCV13 was approved based on the establishment of non-inferiority of OPA responses relative to PPSV23, on a strain-by-strain basis. On October 24, 2022, we announced positive topline results from the Phase 1/2 clinical proof-of-concept study evaluating the safety, tolerability and immunogenicity of VAX-24 in healthy adults aged 18-64. In this study, VAX-24 met the primary safety and tolerability objectives, demonstrating a safety profile similar to PCV20for 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 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 believe these topline results support clinical non-inferiority to PCV20, but there can be no assurance that this approach in pivotal studies will be sufficient for regulatory approval or that regulators will not require field efficacy trials.

We may seek Accelerated Approval from the FDA for our vaccine candidates and, if granted, the FDA may require us to perform post-marketing studies as a condition of approval to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint. If the results from such post-marketing studies are not positive or otherwise fail to show the predicted effect, the drug or biologic may be subject to expedited withdrawal procedures by the FDA. In addition, the standard of care may change with the approval of new products in the same disease areas that we are studying. This may result in the FDA or other regulatory agencies requesting additional studies to show that our vaccine candidate is non-inferior or superior to the new products.

Our clinical trial results may also not support approval. In addition, our vaccine candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our vaccine candidates are safe and effective;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that our vaccine candidates' clinical and other benefits outweigh their safety risks;
- any changes to the required threshold for the achievement of non-inferiority using established surrogate immune endpoints that our PCVs will need to meet in our clinical trials;
- any vaccine to be approved in pediatric populations may need to undergo extensive vaccine-vaccine interference studies with the standard of care pediatric vaccine regimen;
- the need to perform superiority or field efficacy trials, which can be larger, longer and more costly, if an existing vaccine is approved for a disease indication;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our vaccine candidates may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of a BLA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;

- the FDA or comparable foreign regulatory authorities will inspect the commercial manufacturing facilities we may utilize and may not approve such facilities; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Even if we receive regulatory approval of our vaccine candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our vaccine candidates.

Any regulatory approvals that we receive for our vaccine candidates may also be subject to limitations on the approved indicated uses for which a product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including post-marketing clinical trials, and surveillance to monitor the safety and efficacy of the vaccine candidate.

In addition, if the FDA or a comparable foreign regulatory authority approves our vaccine candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, conduct of post-marketing studies, storage, sampling, advertising, promotion, import, export and recordkeeping for our vaccine candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration and continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any BLA, other marketing application and previous responses to inspectional observations. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. In addition, the FDA could require us to conduct another study to obtain additional safety or biomarker information. Further, we will be required to comply with FDA promotion and advertising rules, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved uses (known as "off-label use"), limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet and social media. Later discovery of previously unknown problems with our vaccine candidates, including side effects of unanticipated severity or frequency, or with our third-party suppliers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our vaccine candidates, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of regulatory approvals;
- product seizure or detention, or refusal to permit the import or export of our vaccine candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our vaccine candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration took several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance and review and approval of marketing applications. It is difficult to predict how these orders will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority.

If these executive actions impose restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

We expect the vaccine candidates we develop will be regulated as biological products, or biologics, and therefore they may be subject to competition sooner than anticipated.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, ACA, to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until twelve years after the reference product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement the BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of the vaccine candidates we develop that is approved in the United States as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject vaccine candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Our relationships with customers, physicians and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, health information privacy and security laws and other healthcare laws and regulations. If we or our employees, independent contractors, consultants, commercial partners and vendors violate these laws, we could face substantial penalties.

Healthcare providers, including physicians and third-party payors, in the United States and elsewhere will play a primary role in the recommendation and prescription of any vaccine candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors subject us to various federal and state fraud and abuse laws and other healthcare laws.

These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our vaccine candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in

part, under any U.S. federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the U.S. federal civil and criminal false claims laws, including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, and civil monetary penalties laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. Pharmaceutical manufacturers can cause false claims to be presented to the U.S. federal government by engaging in impermissible marketing practices, such as the off-label promotion of a product for an indication for which it has not received FDA approval. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, which also impose certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy and security of individually identifiable health information of covered entities subject to the rule, including health plans, healthcare clearinghouses and certain healthcare providers and their business associates, independent contractors of a covered entity that perform certain services involving the use or disclosure of individually identifiable health information for or on their behalf, as well as their covered subcontractors;
- the Federal Food Drug or Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which require certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as information regarding ownership and investment interests held by the physicians described above and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which require tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts;

- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers; and
- laws governing the privacy and security of certain protected information, such as the EU GDPR, and the CCPA, which impose obligations and restrictions on the collection, use and disclosure of personal data (including health data) relating to individuals located in the European Economic Area, or EEA, and California, respectively.

We may also be subject to other laws, such as the U.S. Foreign Corrupt Practices Act of 1977, as amended, which prohibit, among other things, U.S. companies and their employees and agents from authorizing, promising, offering or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office and foreign political parties or officials thereof, as well as federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Ensuring that our internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, some of whom are compensated in the form of stock options for consulting services provided, may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, injunctions, damages, fines, disgorgement, imprisonment, exclusion from participating in government-funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations.

Even if resolved in our favor, litigation or other legal proceedings relating to healthcare laws and regulations may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, manufacturing, sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have an adverse effect on our ability to compete in the marketplace. In addition, if the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

Coverage and reimbursement may be limited or unavailable in certain market segments for our vaccine candidates, which could make it difficult for us to sell our vaccine candidates, if approved, profitably.

Successful sales of our vaccine candidates, if approved, depend on the availability of coverage and adequate reimbursement from third-party payors including governmental healthcare programs, such as Medicare and Medicaid, managed care organizations and commercial payors, among others. Significant uncertainty exists as to the coverage and reimbursement status of any vaccine candidates for which we obtain regulatory approval.

Patients who receive vaccines generally rely on third-party payors to reimburse all or part of the associated costs. Obtaining coverage and adequate reimbursement from third-party payors is critical to new product acceptance.

Third-party payors decide which drugs and treatments they will cover and the amount of reimbursement. Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;

- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. Even if we obtain coverage for a given product, if the resulting reimbursement rates are insufficient, hospitals may not approve our product for use in their facility or third-party payors may require co-payments that patients find unacceptably high. Patients are unlikely to use our vaccine candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our vaccine candidates. Separate reimbursement for the product itself may or may not be available. Instead, the hospital or administering physician may be reimbursed only for administering the product. Further, from time to time, CMS revises the reimbursement systems used to reimburse health care providers, including the Medicare Physician Fee Schedule and Outpatient Prospective Payment System, which may result in reduced Medicare payments. In some cases, private third-party payors rely on all or portions of Medicare payment systems to determine payment rates. Changes to government healthcare programs that reduce payments under these programs may negatively impact payments from third-party payors and reduce the willingness of physicians to use our vaccine candidates. Certain ACA marketplace and other private payor plans are required to include coverage for certain preventative services, including vaccinations recommended by the ACIP without cost share obligations (i.e., co-payments, deductibles or co-insurance) for plan members. Children through 18 years of age without other health insurance coverage may be eligible to receive such vaccinations free-of-charge through the CDC's Vaccines for Children Program, or VFC. For Medicare beneficiaries, vaccines may be covered under either the Part B program or Part D depending on several criteria, including the type of vaccine and the beneficiary's coverage eligibility. If our vaccine candidates, once approved, are covered only under the Part D program, physicians may be less willing to use our products because of the claims adjudication costs and time related to the claims adjudication process and collection of co-payments associated with the Part D program.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Further, coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

We intend to seek approval to market our vaccine candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our vaccine candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in Europe, the pricing of biologics is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a vaccine candidate. Some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular vaccine candidate to currently available vaccines. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. The downward pressure on health care costs has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any vaccine candidates for which we receive regulatory approval for commercial sale may suffer if government and other third-party payors fail to provide coverage and adequate reimbursement. We expect downward pressure on pharmaceutical pricing to continue. Further, coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare legislative reform measures may have a negative impact on our business, financial condition, results of operations and prospects.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of vaccine candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any vaccine candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both governmental and private payors in the United States. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include:

- an annual, non-deductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs;
- a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a requirement that certain ACA marketplace and other private payor plans include coverage for preventative services, including vaccinations recommended by the ACIP without cost share obligations (i.e., co-payments, deductibles or co-insurance) for plan members;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There have been executive, judicial and Congressional challenges to the ACA. For example, the Tax Act included a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate." On June 17, 2021, the United States Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Moreover, prior to the United States Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others,

reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. On August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how additional healthcare reform measures of the Biden administration will impact the ACA.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and, due to subsequent legislative amendments to the statute, including the BBA and the Infrastructure Investment and Jobs Act, will remain in effect until 2031 unless additional Congressional action is taken. COVID-19 pandemic relief support legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2022. Under the current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several types of providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, which ended the use of the statutory formula for clinician payment and established a quality payment incentive program, also referred to as the Quality Payment Program. This program provides clinicians with two ways to participate, including through the Advanced Alternative Payment Models, or APMs, and the Merit-based Incentive Payment System, or MIPS. In November 2019, CMS issued a final rule finalizing the changes to the Quality Payment Program. At this time, the full impact of the introduction of the Medicare quality payment program on overall physician reimbursement remains unclear. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Further, in the United States there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug and biological product pricing, reduce the cost of prescription drugs and biological products under government payor programs and review the relationship between pricing and manufacturer patient programs. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the Department of Health and Human Services, or HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. Further, the IRA will, among other things, (i) allow HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law, and (ii) impose rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. However, the IRA does not change either the VFC or the provisions added in 2010 under the ACA. VFC was established to give first-dollar coverage to children up to 18 years of age whose families could not pay for vaccinations while the ACA guaranteed coverage of vaccines without cost sharing for Americans who are either privately insured or newly covered in states that expanded Medicaid. The IRA did help with vaccine access by eliminating cost sharing for adult vaccines covered under Medicare Part D and mandating that all state Medicaid programs cover many adult vaccines and their administration without cost sharing. Further, many vaccines are excluded from Medicare Part B rebate requirements. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be effectuated but is likely to have a significant impact on the pharmaceutical industry. The Biden administration also released an additional executive order on

October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. No legislation or administrative actions have been finalized to implement these principles. It is unclear whether these this executive order or similar policy initiatives will be implemented in the future. It is unclear whether these or similar policy initiatives will be implemented in the future. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine which drugs, biological products and suppliers will be included in their healthcare programs. Furthermore, there has been increased interest by third-party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our current or any future vaccine candidates or additional pricing pressures. Further, it is possible that additional governmental action is taken in response to the ongoing COVID-19 pandemic. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing or new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our current or any future vaccine candidates we may develop may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, which could have an adverse effect on demand for our vaccine candidates. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Changes in funding for the FDA and other government agencies could hinder our ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Separately, in response to the global COVID-19 pandemic, the FDA has adopted a risk-based system for the conduct of inspections of manufacturing facilities. Additionally, the FDA is conducting voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites. Regulatory authorities outside the United States have adopted similar restrictions and policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We are subject to increasingly stringent and rapidly changing U.S. and foreign laws, regulations, rules and other obligations related to privacy and data security. The restrictions and costs imposed by these requirements, or our actual or perceived failure to comply with them, could harm our reputation, subject us to significant fines and liability, and adversely affect our business.

In the ordinary course of business, we process personal data and other Sensitive Information. We are subject to or affected by numerous evolving federal, state and foreign laws and regulations, as well as policies, contracts and other obligations governing the collection, use, disclosure, retention, and security of personal data. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future.

For example, HIPAA, as amended by HITECH, imposes requirements relating to the privacy and security of individually identifiable health information on health plans, healthcare clearinghouses and certain healthcare providers, and their respective contractors and their covered subcontractors that perform services for them involving individually identifiable health information. Additionally, certain states have adopted healthcare privacy and security laws and regulations comparable to HIPAA, some of which may be more stringent than HIPAA. In the event we fail to properly maintain the privacy and security of individually identifiable health information governed by HIPAA or comparable state laws, or we are responsible for an unauthorized disclosure or security breach of such information, we could be subject to enforcement action under HIPAA or comparable state laws, and significant civil and criminal penalties, and fines.

Domestic privacy and data security laws beyond HIPAA and other healthcare privacy laws are also changing rapidly and becoming more complex. For example, the CCPA imposes obligations on businesses to which it applies. These obligations include, but are not limited to, providing specific disclosures in privacy notices and affording California residents certain rights related to their personal data. The CCPA allows for administrative fines for noncompliance (up to $7,500 per violation). In addition, the CPRA expanded the CCPA's requirements, including by adding a new right of individuals to correct their personal data and establishing a new California Privacy Protection Agency to implement and enforce the CCPA. Other states have enacted data privacy laws that become operative in 2023, such as Virginia and Colorado, and other local, state, and federal laws are under consideration. While these states, like the CCPA, also exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely. If we become subject to new data privacy laws, at the state level, the risk of enforcement action against us could increase because we may become subject to additional obligations, and the number of individuals or entities that can initiate actions against us may increase (including individuals, via a private right of action, and state actors).

We may also become subject to a growing body of privacy, data security and data protection laws outside of the United States as we expand our business and clinical trial activities. For example, the EU GDPR and the UK GDPR impose strict requirements for processing the personal data of individuals located, respectively within the EEA and the United Kingdom. Under the EU GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines of up to 20 million euros or 4% of annual global revenue, whichever is greater. Further, individuals or consumer protection organizations may initiate litigation related to our processing of their personal data.

In addition, many jurisdictions have enacted data localization laws and cross-border personal data transfer laws. These laws may make it more difficult for us to transfer personal data across jurisdictions, which could impede our business. For example, absent appropriate safeguards or other circumstances, the EU GDPR generally restricts the transfer of personal data to countries outside of the EEA, such as the United States, which the European Commission does not consider to be providing an adequate level of data privacy and security. The European Commission released a set of "Standard Contractual Clauses" that are designed to be a valid mechanism by which entities can transfer personal data out of the EEA to jurisdictions that the European Commission has not

found to provide an adequate level of protection. Currently, these Standard Contractual clauses are a valid mechanism to transfer personal data outside of the EEA, but are subject to legal challenges. Due to these legal challenges, there exists some uncertainty regarding whether the Standard Contractual Clauses will remain a valid mechanism for transfers of personal data out of the EEA. In addition, laws in Switzerland and the UK similarly restrict transfers of personal data outside of those jurisdictions to countries such as the United States that do not provide an adequate level of personal data protection. If we need but cannot implement a valid compliance mechanism for cross-border privacy and security transfers, we may face increased exposure to regulatory actions, substantial fines, and injunctions against processing or transferring personal data from Europe or elsewhere. The inability to import personal data to the United States could significantly and negatively impact our business operations, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere; limiting our ability to collaborate with parties that are subject to European and other data privacy and security laws; or requiring us to increase our personal data processing capabilities in Europe and/or elsewhere at significant expense.

Our obligations related to data privacy and security are quickly changing in an increasingly stringent fashion, creating some uncertainty as to the effective future legal framework. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or in conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources (including, without limitation, financial and time-related resources). These obligations may necessitate changes to our information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. In addition, these obligations may require us to change our business model. Although we endeavor to comply with all applicable data privacy and security obligations, we may at times fail (or be perceived to have failed) to do so. Moreover, despite our efforts, our personnel or third parties upon whom we rely may fail to comply with such obligations, which could negatively impact our business operations and compliance posture. For example, any failure by a third-party processor to comply with applicable law, regulations, or contractual obligations could result in adverse effects, including inability to operate our business and proceedings against us by governmental entities or others. If we fail, or are perceived to have failed, to address or comply with data privacy and security obligations, we could face significant consequences. These consequences may include, but are not limited to, government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-related claims); additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including clinical trials); inability to process personal data or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring of our operations.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trademarks, trade secret protection and confidentiality agreements to protect the intellectual property related to our vaccine development programs and vaccine candidates. Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to VAX-24 and any future vaccine candidates, as well as methods of making our vaccine candidates and components thereof. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our development programs and vaccine candidates. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

The patents and patent applications that we own or in-license may fail to result in issued patents with claims that protect VAX-24 or any future vaccine candidate in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending patent application, or be used to invalidate a patent. Even if patents do successfully issue and even if such patents cover VAX-24 or any future vaccine candidate, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, invalidated or held unenforceable. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any vaccine candidates or

companion diagnostic that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a vaccine candidate under patent protection could be reduced.

If the patent applications we hold or have in-licensed with respect to our development programs and vaccine candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for VAX-24 or any future vaccine candidate, it could dissuade companies from collaborating with us to develop vaccine candidates and threaten our ability to commercialize future vaccines. Any such outcome could have a materially adverse effect on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has been and will continue to be the subject of litigation and new legislation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, many countries restrict the patentability of methods of treatment of the human body. Publications of discoveries in scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result of these and other factors, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or the USPTO, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. The costs of defending our patents or enforcing our proprietary rights in post-issuance administrative proceedings and litigation can be substantial and the outcome can be uncertain. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future vaccine candidates.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Generally, issued patents are granted a term of 20 years from the earliest claimed non-provisional filing date. In certain instances, patent term can be adjusted to recapture a portion of delay by the USPTO in examining the patent application (patent term adjustment) or extended to account for term effectively lost as a result of the FDA regulatory review period (patent term extension), or both. The scope of patent protection may also be limited. Without patent protection for our current or future vaccine candidates, we may be open to competition from generic versions of such products. Given the amount of time required for the development, testing and regulatory review of new vaccine candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we fail to comply with our obligations under any license, collaboration or other agreements, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our vaccine candidates.

We have licensed certain intellectual property rights related to the XpressCF platform, components of our PCV candidates, and methods of making components of VAX-24 from Sutro Biopharma and University of

Georgia Research Foundation, Inc. We also license certain intellectual property rights related to a non-cross-reactive Group A Strep carbohydrate antigen and related methods of production from the Regents of the University of California. If, for any reason, these agreements are terminated or we otherwise lose those rights, it could adversely affect our business. These agreements impose, and any future collaboration agreements or license agreements we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement or other obligations on us. If we breach any material obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor(s) may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and other foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign national or international patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of patent rights include, but are not limited to, failure to timely file national and regional stage patent applications based on our international patent application, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering VAX-24 or any future vaccine candidate, or the XpressCF platform, our competitors might be able to enter the market, which would have an adverse effect on our business.

Third-party claims or litigation alleging infringement of patents or other proprietary rights, or seeking to invalidate our patents or other proprietary rights, may delay or prevent the development and commercialization of VAX-24 and any future vaccine candidate.

Our commercial success depends in part on our avoiding infringement and other violations of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, derivation and administrative law proceedings, inter partes review and post-grant review before the USPTO, as well as oppositions and similar processes in foreign jurisdictions. Numerous U.S. and foreign-issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing vaccine candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our vaccine candidates or other business activities may be subject to claims of infringement of the patent and other proprietary rights of third parties. Third parties may assert that we are infringing their patents or employing their proprietary technology without authorization.

Also, there may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our vaccine candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our vaccine candidates may infringe.

In addition, third parties may obtain patent rights in the future and claim that use of our technologies infringes upon these rights. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our vaccine candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such vaccine candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations,

processes for manufacture or methods of use, including combination therapy, the holders of any such patent may be able to block our ability to develop and commercialize the applicable vaccine candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all. In addition, we may be subject to claims that we are infringing other intellectual property rights, such as trademarks or copyrights, or misappropriating the trade secrets of others, and to the extent that our employees, consultants or contractors use intellectual property or proprietary information owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our vaccine candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful infringement or other intellectual property claim against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our affected products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms.

Furthermore, as the vaccine patent landscape is crowded and highly competitive, even in the absence of litigation we may need to obtain licenses from third parties to advance our research or allow commercialization of our vaccine candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our vaccine candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against vaccine candidates resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties or other forms of compensation to third parties.

We may become involved in lawsuits to protect or enforce our patents, the patents of our licensors or our other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. The initiation of a claim against a third party may also cause the third party to bring counter-claims against us such as claims asserting that our patents are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement, written description, or lack of patentable subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third parties may also raise similar validity claims before the USPTO in post-grant proceedings such as ex parte reexaminations, inter partes review or post-grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. For the patents and patent applications that we have licensed, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future vaccine candidates. Such a loss of patent protection could harm our business.

We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license on commercially reasonable

terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our common shares.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

The United States has enacted and implemented wide-ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions or changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future. For example, the complexity and uncertainty of European patent laws have also increased in recent years. In Europe, a new unitary patent system takes effect June 1, 2023, which will significantly impact European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications will have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court, or the UPC. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC will have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC-based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long-term effects of any potential changes.

Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our vaccine candidates that are approved for marketing from the products of our competitors. We have not yet selected trademarks for our vaccine candidates and have not yet begun the process of applying to register trademarks for our current or any future vaccine candidates. Once we select trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose our trademark applications or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks, and we may not have adequate resources to enforce our trademarks.

In addition, any proprietary name we propose to use with our current or any other vaccine candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

We may not be able to protect our intellectual property rights throughout the world, which could impair our business.

Filing, prosecuting and defending patents covering our current vaccine candidates and any future vaccine candidate throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

The ongoing conflict in Ukraine and related sanctions could significantly devalue our Eurasian patent applications. Recent Russian decrees may also significantly limit our ability to enforce Russian patents. We cannot predict when or how this situation will change.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we expect to rely on third parties to manufacture VAX-24 and any future vaccine candidates, and we expect to collaborate with third parties on the development of VAX-24 and any future vaccine candidates, we must, at times, share trade secrets with them. We also conduct joint research and development that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have an adverse effect on our business and results of operations. Further, disputes may arise under these agreements regarding inventorship or ownership of proprietary information generated during research and development.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. Although we seek to protect our ownership of intellectual property rights by ensuring that our agreements with our employees, collaborators and other third parties with whom we do business include provisions requiring such parties to assign rights in inventions to us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

Risks Related to Ownership of Our Common Stock

The price of our stock may be volatile, and the value of our common stock may decline.

The market price of our common stock may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In particular, the COVID-19 pandemic has further heightened the volatility of the stock market for biopharmaceutical companies. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, these factors include:

- the commencement, enrollment or results of our planned or future preclinical studies or clinical trials of our vaccine candidates and those of our competitors;
- regulatory or legal developments in the United States and abroad;
- the success of competitive vaccines or technologies;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the level of expenses related to our vaccine candidates or preclinical and clinical development programs;
- the results of our efforts to develop additional vaccine candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations or reports by securities analysts;
- the level of expenses and capital investment related to manufacturing our vaccine candidates;
- our inability to obtain or delays in obtaining adequate supply for any approved vaccine candidate;
- significant lawsuits, including patent or stockholder litigation;
- variations in our financial results or those of companies perceived to be similar to us;
- changes in the structure of healthcare payment systems, including coverage and adequate reimbursement for any approved vaccine;
- general economic, political and market conditions, including higher inflation rates, changes in interest rates and the Russia-Ukraine war, and overall fluctuations in the financial markets in the United States and abroad; and
- investors' general perception of us and our business.

In addition, the stock market in general, and the Nasdaq Global Select Market and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, including in connection with the ongoing COVID-19 pandemic, which has resulted in decreased stock prices for many companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. You may not realize any return on your investment in us and may lose some or all of your investment. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, operating results or financial condition.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Our executive officers, directors and principal stockholders beneficially own a significant portion of our common stock. Accordingly, these stockholders have the ability to influence us through this ownership position and significantly affect the outcome of all matters requiring stockholder approval. For example, these stockholders may be able to significantly affect the outcome of elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

As a public company, we are subject to more stringent federal and state law requirements.

As a public company, we are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Stock Market LLC, or Nasdaq, and other applicable securities rules and regulations.

Sarbanes-Oxley as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC has adopted additional rules and regulations in these areas, such as mandatory ‘‘say on pay’’ voting requirements. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Compliance with the various reporting and other requirements applicable to public companies requires considerable time and attention of management. We cannot assure you that we will satisfy our obligations as a public company on a timely basis.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If we are unable to comply with these requirements on a timely basis or if the attention of our management and personnel is diverted from other business concerns, it could have a material adverse effect on our business, financial condition and results of operations. The increased costs will increase our net loss or decrease our net income, and may require us to reduce costs in other areas of our business. In addition, as we expand, it may be more difficult or more costly for us to obtain certain types of insurance, including directors’ and officers’ liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified personnel to serve on our board of directors, our board committees or as executive officers.

We are also subject to more stringent state law requirements. Compliance costs and penalties or other adverse impacts as a result of non-compliance (including reputational impacts) may adversely affect our business.

Expectations relating to environmental, social and governance programs may impose additional costs and expose us to new risks.

There is an increasing focus from certain investors and other key stakeholders concerning corporate responsibility, specifically related to environmental, social and governance, or “ESG,” factors. As a result, there is an increased emphasis on corporate responsibility ratings and a number of third parties provide reports on companies in order to measure and assess corporate responsibility performance. In addition, the ESG factors by which companies’ corporate responsibility practices are assessed may change, which could result in greater expectations of us and cause us to undertake costly initiatives to satisfy such new criteria. Alternatively, if we are unable to satisfy such new criteria, investors may conclude that our policies with respect to corporate responsibility are inadequate. We risk damage to our brand and reputation if our corporate responsibility procedures or standards do not meet the standards set by various constituencies. We may be required to make investments in matters related to ESG, which could be significant and adversely impact our results of operations. Furthermore, if our competitors’

corporate responsibility performance is perceived to be greater than ours, potential or current investors may elect to invest with our competitors instead. In addition, if we communicate certain initiatives and goals regarding ESG matters, we could fail, or be perceived to fail, in our achievement of such initiatives or goals, or we could be criticized for the scope of such initiatives or goals. If we fail to satisfy the expectations of investors and other key stakeholders or our initiatives are not executed as planned, our reputation and financial results could be materially and adversely affected.

Future sales of a substantial number of shares of our common stock, or the perception that such sales could occur, could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the public's perception that such sales could occur, could have an adverse effect on the market price of our common stock.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- prohibit our stockholders from calling a special meeting of our stockholders;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a stockholder rights plan, or so-called "poison pill," that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 66 ⅔% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or DGCL, which prohibits a person who owns 15% or more of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired 15% or more of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case, to the fullest extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for any breach of fiduciary duties as directors, except liability for:

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

Such limitation of liability does not apply to liabilities arising under federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our amended and restated bylaws provide that we are required to indemnify our directors and officers to the fullest extent permitted by Delaware law and may indemnify our other employees and agents. Our amended and restated bylaws also provide that, on satisfaction of certain conditions, we will advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under the provisions of Delaware law. We have entered and expect to continue to enter into agreements to indemnify our directors and executive officers. With certain exceptions, these agreements provide for indemnification for related expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in connection with any action, proceeding or investigation. We believe that these amended and restated certificate of incorporation and amended and restated bylaws provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

While we maintain directors' and officers' liability insurance, such insurance may not be adequate to cover all liabilities that we may incur, which may reduce our available funds to satisfy third-party claims and may adversely impact our cash position.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will, to the fullest extent permitted by applicable law, be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that 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), to the fullest extent permitted by applicable law, is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;
- any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders;
- any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the DGCL, our certificate of incorporation or our bylaws;
- any action or proceeding to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws; and

- any action or proceeding asserting a claim against us by any of our directors, officers or other employees governed by the internal affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act of 1933, as amended, or the Securities Act, creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation provides that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage these types of lawsuits. If a court were to find the exclusive-forum provision 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, which could harm our business.

General Risk Factors

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or vaccine candidates.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements, including through the use of our "at-the-market" facility. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or vaccine candidates, or grant licenses on terms unfavorable to us.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

The global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including as a result worsening global economic conditions, including higher inflation rates and changes in interest rates, and the COVID-19 pandemic and civil and political unrest in certain countries and regions. Such volatility and disruptions have caused and may continue to cause severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, including higher inflation rates and changes in interest rates, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers,

manufacturers and other partners may not survive an economic downturn, which could directly affect our ability to attain our operating goals on schedule and on budget.

An active trading market for our common stock may never develop or be sustained.

Our common stock is currently listed on the Nasdaq Global Select Market under the symbol "PCVX." However, we cannot assure you that an active trading market for our shares will develop or be sustained. You may not be able to sell your shares quickly or at the market price if trading in shares of our common stock is not active. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration.

Our financial condition and results of operations may fluctuate from quarter to quarter and year to year, which makes them difficult to predict.

We expect our financial condition and results of operations to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting, investor relations and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Stockholder activism, the current political environment and the current high level of U.S. government intervention and regulatory reform may also lead to substantial new regulations and disclosure obligations, which may in turn lead to additional compliance costs and impact the manner in which we operate our business in ways we do not currently anticipate. Our management and other personnel will need to devote a substantial amount of time to comply with these requirements. Moreover, these requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by management related to the internal control over financial reporting in our Form 10-K for the year ended December 31, 2022 and we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation. To comply with the Sarbanes-Oxley Act, the requirements of being a reporting company under the Exchange Act and any complex accounting rules in the future, we may need to upgrade our information technology systems, implement additional financial and management controls, reporting systems and procedures, and hire additional accounting and finance staff. We are currently in the process of hiring additional accounting and finance staff as we grow our business. If we are unable to hire the additional accounting and finance staff necessary to comply with these requirements, we may need to retain additional outside consultants. If we or, if required, our auditors, are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting and the trading price of our common stock may decline.

There can be no assurance that there will not be material weaknesses in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public

accounting firm determines that we have a material weakness in our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Our reported financial results may be adversely affected by changes in accounting principles generally accepted in the United States.

Generally accepted accounting principles in the United States are subject to interpretation by the Financial Accounting Standards Board, the SEC and various bodies formed to promulgate and interpret appropriate accounting principles. A change in these principles or interpretations could have a significant effect on our reported financial results, may retroactively affect previously reported results, could cause unexpected financial reporting fluctuations and may require us to make costly changes to our operational processes and accounting systems.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. We do not have control over these analysts. If securities or industry analysts do not publish research or reports about our business, the trading price for our stock would likely be negatively impacted. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters is located at 825 Industrial Road, Suite 300, San Carlos, California 94070, where we lease and occupy 77,734 square feet of laboratory and office space. Our lease for our San Carlos headquarters expires on December 31, 2025. We use our corporate headquarters primarily for corporate research, development, regulatory, manufacturing and quality functions. We believe that our existing facilities are adequate to meet our current needs.

Item 3. Legal Proceedings.

From time to time we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. We are not presently a party to any legal proceedings that in the opinion of our management, if determined unfavorably to us, would have a material adverse effect on our business, financial condition, operating results or cash flows. Regardless of the outcome, litigation can, among other things, be time consuming and expensive to resolve and divert management resources.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information for Our Common Stock

Our common stock commenced trading on the Nasdaq Global Select Market under the symbol "PCVX" on June 12, 2020.

Holders

As of February 23, 2023, there were approximately 14 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

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.

Securities Authorized for Issuance under Equity Compensation Plans

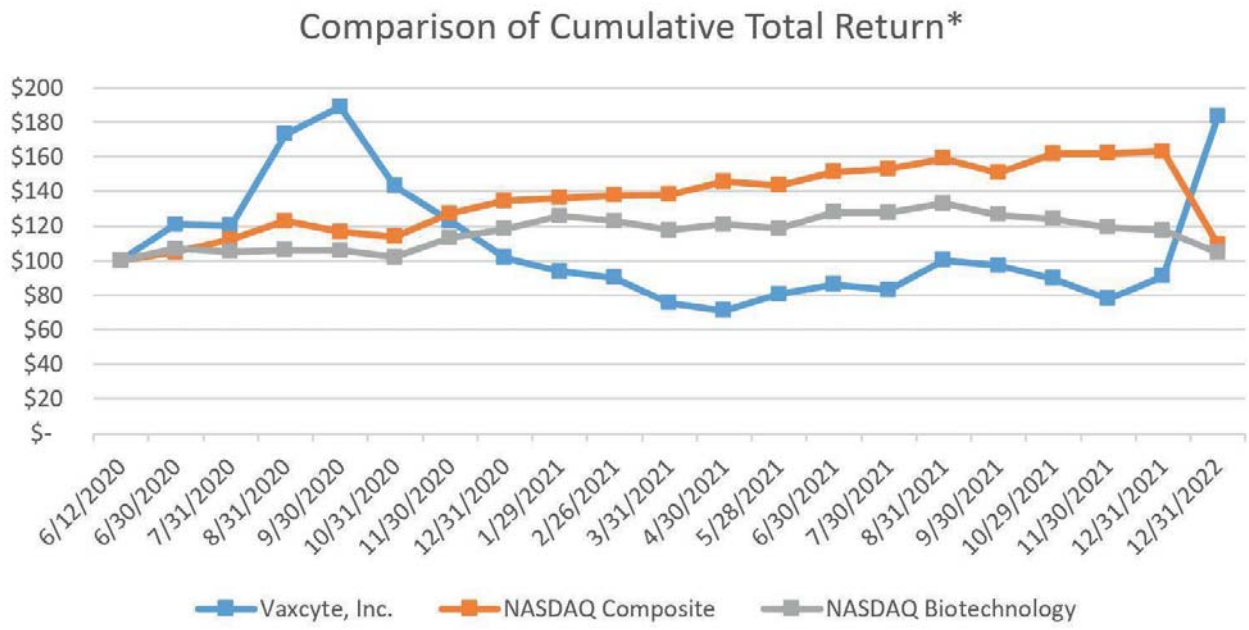
Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Stock Performance Graph

This performance graph shall not be deemed "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, except to the extent that we specifically incorporate this information by reference therein, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

The following stock performance graph compares our cumulative total stock return relative to the cumulative total returns of the Nasdaq Composite Index and the Nasdaq Biotechnology Index for the period from June 12, 2020 (the date our common stock commenced trading on the Nasdaq Global Select Market) through December 31, 2022. The figures below assume an investment of $100 in our common stock at the closing price of $26.15 on June 12, 2020, the date of our IPO, and in each index on the same date and the reinvestment of the full amount of all dividends into shares of common stock; however, no dividends have been declared on our common

stock to date. The stockholder returns shown on the graph below are based on historical results and are not indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.



Unregistered Sales of Equity Securities

On December 19, 2022, we entered into an option grant agreement, or the Option Agreement, with Sutro Biopharma, Inc., or Sutro Biopharma.

As consideration for the Option and other rights and authorizations granted to us under the Option Agreement, we agreed to pay Sutro upfront consideration of $22.5 million, consisting of (i) $10.0 million in cash and $7.5 million in shares of our common stock (the number of shares to be calculated based on the arithmetic average of the daily volume weighted average price of our common stock as traded on Nasdaq (as reported by Bloomberg L.P., or if not reported therein, in another authoritative source mutually selected by the Parties) in the three consecutive trading days immediately prior to the issuance thereof).

On December 22, 2022, we issued 167,780 shares of our common stock to Sutro Biopharma as partial consideration under the Option Agreement, which were not initially registered under the Securities Act of 1933, as amended, or the Securities Act, and were offered pursuant to the exemption provided in Section 4(a)(2) under the Securities Act and Rule 506 of Regulation D thereunder. Pursuant to the Option Agreement, we subsequently filed a resale registration statement on December 22, 2022, covering the shares of our common stock issued.

Use of Proceeds from our Initial Public Offering of Common Stock

In June 2020, we closed our IPO of 17,968,750 shares of our common stock, including shares issued upon the exercise in full of the underwriters' option to purchase 2,343,750 additional shares of common stock, at a public offering price of $16.00 per share. We received gross proceeds to us of $287.5 million. All of the shares issued and sold in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-238630), which was declared effective by the SEC on June 11, 2020. BofA Securities, Inc., Jefferies LLC and Evercore Group L.L.C. acted as joint book-running managers for the offering. Cantor Fitzgerald & Co. and Needham & Company, LLC acted as co-managers for the offering. Shares of our common stock began trading on

the Nasdaq Global Select Market on June 12, 2020 and, following the sale of all the shares upon the closing of the IPO, the offer terminated. The net proceeds to us, after deducting underwriting discounts and commissions of $20.1 million and net offering expenses of $3.4 million, were $264.0 million.

No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

There has been no material change in the planned use of proceeds from our IPO from those disclosed in the prospectus for our IPO dated as of June 11, 2020 and filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on June 15, 2020.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes and other financial information included elsewhere in this Annual Report on Form 10-K. This discussion and analysis contains forward-looking statements based upon our current beliefs, plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and beliefs. Our actual results and the timing of events could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under the section titled "Risk Factors" and elsewhere in this Annual Report on Form 10-K. You should carefully read the "Risk Factors" section of this Annual Report on Form 10-K to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

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.

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: For our VAX-24 pediatric program, in late February 2023, we announced that the FDA cleared the infant investigational new drug, or IND, application for the prevention of IPD in infants. We plan to initiate an infant Phase 2 study in the second quarter of 2023. We expect topline safety, tolerability and immunogenicity data from the infant Phase 2 study primary three-dose immunization series 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 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 we intend to provide further information about the anticipated timing of an IND application will be provided 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 we 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.

Since January 1, 2022, key developments affecting our business include the following:

- ***Dosed First Participants in both the Phase 1 and Phase 2 Portions of VAX-24 Phase 1/2 Clinical Proof-of-Concept Study in Adults:*** In February 2022, we announced that the first participants were dosed in the Phase 1 portion of the VAX-24 Phase 1/2 clinical study. This was followed by an announcement in April 2022 that the first participants had been dosed in the Phase 2 portion of this study. The initiation of the Phase 2 portion occurred after an independent Data

Monitoring Committee completed a prespecified review of initial Phase 1 safety and tolerability data and recommended that the study progress as planned.

  - The VAX-24 Phase 1/2 clinical proof-of-concept study was a randomized, observer-blind, dose-finding, controlled study designed to evaluate the safety, tolerability and immunogenicity of VAX-24 in healthy adults (NCT05266456).
  - The Phase 1 portion of the study evaluated the safety and tolerability of a single injection of VAX-24 at three dose levels and compared to Prevnar 20 in 64 healthy adults 18 to 49 years of age.
  - The Phase 2 portion evaluated the safety, tolerability and immunogenicity of a single injection of VAX-24 at three dose levels and compared to Prevnar 20 in 771 healthy adults 50 to 64 years of age. The prespecified immunogenicity endpoints of the Phase 2 portion of the study included an assessment of the induction of antibody responses, using opsonophagocytic activity, or OPA, and immunoglobulin G, or IgG, at each of the three VAX-24 doses and compared to Prevnar 20™ and, for the additional four serotypes contained in VAX-24 and Pneumovax® 23, but not in Prevnar 20™, the percentage of subjects that experienced a four-fold rise in antibody titers.
  - Participants in the study were evaluated for safety through six months after vaccination.

- ***Completed Successful $115 Million Follow-On Financing:*** In January 2022, we completed an underwritten public offering of 3,250,000 shares of our common stock, which included the full exercise of the underwriters' option to purchase additional shares, and pre-funded warrants to purchase 2,500,000 shares of common stock. The aggregate gross proceeds to us from the offering were $115.0 million, before deducting underwriting discounts and commissions and other estimated offering expenses payable by us, and excluding the exercise of any pre-funded warrants.
- ***Completed Enrollment of Phase 2 Portion of VAX-24 Phase 1/2 Clinical Proof-of-Concept Study in Adults***: In July 2022, we announced the completion of enrollment in the Phase 2 portion of the Phase 1/2 clinical proof-of-concept study.
- ***Initiated Separate VAX-24 Phase 2 Clinical Study in Adults 65 Years and Older:*** In July 2022, we announced that we dosed the first participants in a separate Phase 2 study in adults 65 years of age and older. This study is intended to further build the body of clinical evidence to support the potential of VAX-24 as the broadest-spectrum PCV in adults.
  - This VAX-24 Phase 2 clinical study (VAX-24 Study 102, NCT05297578) is a randomized, observer-blind, dose-finding, controlled study designed to evaluate the safety, tolerability and immunogenicity of VAX-24 in approximately 200 healthy adults 65 years of age and older.
  - The study is evaluating the safety, tolerability and immunogenicity of a single injection of VAX-24 at three dose levels and compared to a single injection of Prevnar 20™. The prespecified immunogenicity endpoints of the study include an assessment of the induction of antibody responses, using OPA and IgG, at each of the three VAX-24 doses and compared to Prevnar 20™ and, for the additional four serotypes contained in VAX-24 and Pneumovax® 23, but not in Prevnar 20™, the percentage of subjects that experience a four-fold rise in antibody titers.
  - Participants in the study are evaluated for safety through six months after vaccination.
- ***Completed Successful Pre-IND Meeting with FDA Regarding VAX-24 Pediatric Development Program:*** In July 2022, we successfully completed a pre-IND meeting with the FDA regarding the pediatric clinical program for VAX-24. We received positive written feedback from the FDA supporting the initiation of a pediatric study that proceeds directly into infants contingent on satisfactory topline safety, tolerability and immunogenicity results from the ongoing VAX-24 Phase 1/2 clinical proof-of-concept study in adults 18 to 64 years of age. This approach provides us with an accelerated clinical path to deliver a potentially best-in-class PCV, VAX-24, to the

pediatric population, which represents the largest portion of the pneumococcal vaccine market in the United States.

- ***Received FDA Fast Track Designation for VAX-24 in Adults:*** In early August 2022, we announced that the FDA granted Fast Track designation to VAX-24 in adults ages 18 and older. The Fast Track designation is an FDA process that has been designed to facilitate the development and expedite the review of drugs, including vaccines, that treat or prevent serious conditions and fill an unmet medical need.
- ***Completed Enrollment of Phase 2 Study Evaluating Safety, Tolerability and Immunogenicity of VAX-24 in Adults 65 Years and Older:*** In September 2022, we announced the completion of enrollment in the Phase 2 portion of the ongoing VAX-24 Phase 1/2 clinical proof-of-concept study in adults 65 years and older.
- ***Announced Positive Topline Results from VAX-24 Phase 1/2 Clinical Proof-of-Concept Study in Adults 18-64 Years of Age:*** In October 2022, we announced positive topline results from the Phase 1/2 clinical proof-of-concept study evaluating the safety, tolerability and immunogenicity of VAX-24 in healthy adults aged 18-64. In this study, VAX-24 met the primary safety and tolerability objectives, demonstrating a safety profile similar to PCV20 for all doses studied. The study also showed 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 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.
- ***Confirmed VAX-31 Serotype Composition:*** In October 2022, we unveiled the serotype composition for VAX-31, the follow-on vaccine in our carrier-sparing PCV franchise, which is designed to contain 31 serotypes that collectively cover approximately 95% of the circulating strains causing IPD in adults in the United States.
- ***Completed Successful $690 Million Follow-On Offering:*** In October 2022, we completed an underwritten public offering of 17,812,500 shares of our common stock, which included the full exercise of the underwriters' option to purchase additional shares, and pre-funded warrants to purchase 3,750,000 shares of common stock. The aggregate gross proceeds to us from the offering were $690.0 million, before deducting underwriting discounts and commissions and other estimated offering expenses payable by us, and excluding the exercise of any pre-funded warrants.
- ***Entered into Option Grant Agreement with Sutro Biopharma for the Development and Manufacturing Rights of Cell-Free Extract:*** In December 2022, we and Sutro Biopharma, Inc., or Sutro Biopharma announced an option grant agreement pursuant to which we acquired from Sutro Biopharma an option to access expanded rights to develop and manufacture cell-free extract, among other rights.
- ***Received FDA Breakthrough Therapy Designation for VAX-24 for the Prevention of IPD in Adults:*** In January 2023, we announced that the FDA granted Breakthrough Therapy designation for VAX-24, for the prevention of IPD in adults. With Breakthrough Therapy designation, Vaxcyte will have access to all of the elements of the FDA's Fast Track program, as well as the ability to receive guidance and support from the FDA on an efficient drug development program and an organizational commitment from senior managers within the FDA. The FDA's decision was based on positive topline results from the Phase 1/2 proof-of-concept study of VAX-24 in adults 18-64 years of age.
- ***FDA Clearance of Investigational New Drug Application for VAX-24 for the Prevention of Invasive Pneumococcal Disease in Infants:*** 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.

- ***Announced new vaccine program VAX-GI:*** In late February 2023, we announced that we added a new vaccine program, VAX-GI, 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.

Since our inception in November 2013, we have devoted substantially all of our resources to performing research and development, undertaking preclinical studies, advancing our vaccine candidates through clinical trials and manufacturing activities in support of our product development efforts, acquiring and developing our technology and vaccine candidates, organizing and staffing our company, establishing our intellectual property portfolio and raising capital to support and expand such activities. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have financed our operations primarily with proceeds from the sales of our common stock, pre-funded warrants to purchase our common stock and, prior to our initial public offering, or IPO, in June 2020, redeemable convertible preferred stock. We will continue to require additional capital to develop and commercialize our vaccine candidates and fund operations for the foreseeable future. Accordingly, until such time as we can generate significant revenue from sales of our vaccine candidates, if ever, we expect to finance our cash needs through public or private equity or debt financings, third-party (including government) funding and marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches.

We have incurred net losses in each year since inception and expect to continue to incur net losses in the foreseeable future. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending in large part on the timing of our preclinical studies, clinical trials and manufacturing activities, and our expenditures on other research and development activities. Our net losses were $223.5 million and $100.1 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $522.1 million and cash, cash equivalents and investments of $957.9 million, We believe our cash, cash equivalents and investments will be sufficient to fund our operating expenses and capital expenditure requirements through at least 12 months from the filing date of this Annual Report on Form 10-K.

We do not expect to generate any revenue from commercial product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our vaccine candidates, which we expect will take a number of years. We expect our expenses will increase substantially in connection with our ongoing activities, as we:

- advance our vaccine candidates through preclinical studies and clinical trials;
- require the scale-up of our manufacturing capabilities, in particular to prepare for our Phase 3 program for VAX-24;
- incur additional costs that may be required for secondary supply sources;
- require the manufacture of supplies for our clinical trials, in particular our clinical trials for our PCV candidates, VAX-24 and VAX-31;
- pursue regulatory approval of our vaccine candidates;
- establish additional manufacturing capacity to meet potential incremental supply requirements following the initial commercial launch of VAX-24;
- hire additional personnel;
- operate as a public company;

- acquire, discover, validate and develop additional vaccine candidates; and

- obtain, maintain, expand and protect our intellectual property portfolio.

We rely and will continue to rely on third parties to conduct our preclinical studies and clinical trials and for manufacturing and supply of our vaccine candidates. We have no internal manufacturing capabilities, and we will continue to rely on third parties, of which the main suppliers are single-source suppliers, for our preclinical and clinical trial materials. Given our stage of development, we do not yet have a marketing or sales organization or commercial infrastructure. Accordingly, if we obtain regulatory approval for any of our vaccine candidates, we also would expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution.

Because of the numerous risks and uncertainties associated with vaccine development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from the sale of our vaccines, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and may be forced to reduce our operations.

Certain Significant Relationships

Lonza

In October 2016, we entered into a non-exclusive development and manufacturing services agreement, as amended, with Lonza, or the 2016 Lonza DMSA, pursuant to which Lonza is obligated to perform manufacturing process development and the manufacture of components for VAX-24, including the polysaccharide antigens, our proprietary eCRM protein carrier and conjugated drug substances.

In June 2018, we entered into a letter agreement with Lonza, or the Lonza Letter Agreement, pursuant to which we agreed to certain terms for potential future payments in shares of our common stock as partial satisfaction of future obligations to Lonza. The Lonza Letter Agreement states that the initial pre-IND cash payments under the 2016 Lonza DMSA would be subject to a specified dollar cap, or the Initial Cash Cap. After the Initial Cash Cap has been reached, we would have the option to make any further pre-IND payments owed to Lonza in cash, in shares of our common stock at then market prevailing prices, or a combination of both, at our election. In April 2021, we reached the Initial Cash Cap and notified Lonza that we would be exercising our option to issue approximately $10.0 million in shares of our common stock as payment for a portion of pre-IND payments due April 30, 2021. In June 2021, we issued 399,680 shares of our common stock to Lonza at a price of $25.02 per share to pay for $10.0 million of the pre-IND payments due April 30, 2021.

In October 2018, we entered into a second non-exclusive development and manufacturing services agreement with Lonza, or the 2018 Lonza DMSA, pursuant to which Lonza is obligated to perform services including manufacturing process development and the manufacture and supply of VAX-24 finished drug product.

In April 2022, we entered into a third non-exclusive development and manufacturing services agreement with Lonza, as amended, or the 2022 Lonza DMSA, effective as of March 22, 2022. Pursuant to the 2022 Lonza DMSA, Lonza will perform manufacturing process development and clinical manufacture and supply of our proprietary PCV.

Under each of the 2016 Lonza DMSA, 2018 Lonza DMSA and 2022 Lonza DMSA, collectively the Lonza Agreements, we will pay Lonza agreed-upon fees for its performance of development and manufacturing services and pass through expenses incurred by Lonza for raw materials, as well as customary procurement and handling fees. Under each Lonza Agreement, we will own all right, title and interest in and to any and all New Customer Intellectual Property (as defined in each Lonza Agreement), and Lonza shall own all right, title and interest in New General Application Intellectual Property (as defined in each Lonza Agreement). Subject to the terms and conditions set forth in the Lonza Agreements, Lonza granted us a non-exclusive, world-wide, fully paid-up, irrevocable, transferable license, including the right to grant sublicenses, under the New General Application

Intellectual Property (as defined in each Lonza Agreement), to research, develop, make, have made, use, sell and import the Product (as defined in each Lonza Agreement) manufactured under each Lonza Agreement.

Unless earlier terminated, each Lonza Agreement will remain in place for a period of five years and includes customary conditions for termination prior to that period. The 2016 Lonza DMSA has been amended to extended its term until March 31, 2023.

For additional details regarding our relationship with Lonza, see Note 6, "Commitments and Contingencies," to our financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Sutro Biopharma

Sutro Biopharma is a clinical stage, publicly traded drug discovery, development and manufacturing company using precise protein engineering and rational design (enabled by Sutro Biopharma's proprietary XpressCF platform technology) to advance next-generation oncology therapeutics. Following our corporate formation, we acquired an exclusive license to Sutro Biopharma's proprietary cell-free protein synthesis platform, XpressCF, for the discovery, development and sale of vaccines for the treatment or prevention of infectious diseases, excluding cancer vaccines. Under a related supply agreement with Sutro Biopharma, we have an exclusive relationship in our field to buy extract and certain custom reagents for use in manufacturing the vaccine compositions covered by the exclusive license, which we use to produce our protein carriers and certain of our antigens. Under a separate agreement with Sutro Biopharma, we enhanced our rights with respect to access to a second supplier of extract and acquired an option to access expanded rights to develop and manufacture extract, among other rights.

Amended and Restated License Agreement with Sutro Biopharma

We are party to a license agreement with Sutro Biopharma, or the Sutro Biopharma License Agreement, on August 1, 2014. The Sutro Biopharma License Agreement was amended on October 12, 2015 and again on May 9, 2018 and May 29, 2018. Under the Sutro Biopharma License Agreement, we received an exclusive, worldwide, royalty-bearing, sublicensable license under Sutro Biopharma's patents and know-how relating to cell-free expression of proteins to (i) research, develop, use, sell, offer for sale, export, import and otherwise exploit specified vaccine compositions, such rights being sublicensable, for the treatment or prophylaxis of infectious diseases, excluding cancer vaccines, and (ii) manufacture, or have manufactured by an approved contract manufacturing organization, such vaccine compositions from extracts supplied by Sutro Biopharma pursuant to the Sutro Biopharma Supply Agreement (as described below). We are obligated to use commercially reasonable efforts to develop, obtain regulatory approval for and commercialize the vaccine compositions. In consideration of the rights granted under the Sutro Biopharma License Agreement, we are obligated to pay Sutro Biopharma a 4% royalty on worldwide aggregate annual net sales of our vaccine products for human health and a 2% royalty on such net sales of vaccine products for animal health. Such royalty rates are subject to specified reductions, including standard reductions for third-party payments and for expiration of relevant patent claims. We are also obligated to pay Sutro Biopharma any royalties due to Stanford University (the upstream licensor of Sutro Biopharma), to the extent the royalties payable by Sutro Biopharma to Stanford University are greater than the royalties payable by us to Sutro Biopharma. Royalties are payable on a vaccine composition-by-vaccine composition and country-by-country basis until the later of expiration of the last valid claim in the licensed patents covering such vaccine composition in such country and ten years after the first commercial sale of such vaccine composition. The latest expiration date of a licensed Sutro Biopharma patent application, if issued, would be 2036, subject to any adjustment or extension of patent term that may be available in a particular country. In addition, we are obligated to pay Sutro Biopharma a percentage of net sublicensing revenue received in the low teen percentages. In addition, in the event we sublicense our non-manufacturing rights under the Sutro Biopharma License Agreement before a specified date, we are obligated to pay Sutro Biopharma a percentage, in the low double-digits, of the sublicensing revenue we receive under such agreement.

The Sutro Biopharma License Agreement will remain in effect until terminated. The agreement may be terminated by either party for the other party's material breach uncured within 60 days' notice, by us at will with 60

days' notice, or by Sutro Biopharma if we challenge Sutro Biopharma's patents or if we undergo a change of control with a specified competitor of Sutro Biopharma.

Supply Agreement with Sutro Biopharma

In May 2018, we entered into a supply agreement, or the Sutro Biopharma Supply Agreement, with Sutro Biopharma pursuant to which we purchase from Sutro Biopharma extract and custom reagents for use in manufacturing non-clinical and certain clinical supply of vaccine compositions utilizing the technology licensed under the Sutro Biopharma License at prices not to exceed a specified percentage above Sutro Biopharma's fully burdened manufacturing cost. If any extracts or custom reagents do not meet the specifications and warranties provided, then we will not have an obligation to pay for the non-conforming product, and Sutro Biopharma will be obligated to replace the non-conforming product within the shortest possible time with conforming product at our cost. The term of the Sutro Biopharma Supply Agreement is from execution until the later of July 31, 2022 and the date the parties enter into and commence activities under the supply agreement unless extended through a subsequent supply agreement for the supply of extract and custom reagents for vaccine compositions for Phase 3 and commercial uses as contemplated in the Sutro Biopharma Supply Agreement. The Sutro Biopharma Supply Agreement may be terminated by either party for the other party's material breach uncured within 60 days' notice, by us at will with 60 days' notice, or by mutual agreement of the parties. In December 2019, we exercised our right to require Sutro Biopharma to establish a second supplier for extract and custom reagents to support our anticipated clinical and commercial needs.

Option Agreement with Sutro Biopharma

In December 2022, we entered into an option grant agreement with Sutro Biopharma, or the Option Agreement. Pursuant to the Option Agreement, we acquired from Sutro Biopharma (i) authorization to enter into an agreement with an independent alternate CMO to directly source Sutro Biopharma's cell-free extract, allowing us to have direct oversight over financial and operational aspects of the relationship with the CMO; and (ii) a right, but not an obligation, to obtain certain exclusive rights to internally manufacture and/or source extract from certain CMOs and the right to independently develop and make improvements to extract (including the right to make improvements to the extract manufacturing process as well as cell lines) for use in connection with the exploitation of certain vaccine compositions, or the Option. We and Sutro Biopharma have agreed to negotiate the terms and conditions of a form definitive agreement to be entered into in the event we exercise the Option, which shall include the terms and conditions set forth in an executed term sheet between us, or the Term Sheet, and such terms that are necessary to give effect to each of the terms and conditions set forth in the Term Sheet, or the Form Definitive Agreement. The Option period is five years from the date of the Option Agreement, subject to potential acceleration in the event we undergo a change of control.

As consideration for the Option and other rights and authorizations granted to us under the Option Agreement, we agreed to pay Sutro Biopharma upfront consideration of $22.5 million, consisting of (i) $10.0 million in cash and $7.5 million worth of shares of our common stock (the number of shares to be calculated based on the arithmetic average of the daily volume weighted average price of our common stock as traded on Nasdaq in the three consecutive trading days immediately prior to the issuance thereof), and (ii) $5.0 million payable within five business days after we and Sutro Biopharma mutually agree in writing upon the Form Definitive Agreement. The 167,780 shares of common stock issued was recorded at fair value of $8.0 million on the date of settlement, December 22, 2022. In the event that we elect to exercise the Option, we would pay Sutro Biopharma an aggregate Option exercise price of $75.0 million in cash in two installments and, upon the occurrence of certain regulatory

milestones, certain additional milestone payments totaling up to $60.0 million in cash. In the event that we undergo a change of control, certain rights and payments may be accelerated.

For additional details regarding our relationship with Sutro Biopharma, see Note 6, "Commitments and Contingencies," and Note 15, "Related Party Transactions," to our financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Impact of COVID-19 and Other Trends

We are continuing to closely monitor the impact of the global COVID-19 pandemic on our business. In particular, the COVID-19 pandemic slowed raw material supply chains and travel restrictions delayed the qualification of key analytical equipment used in manufacturing and curtailed in-person CMO oversight of manufacturing, affecting our manufacturing processes. As the pandemic continues, we could see an additional impact on our ability to advance our programs, obtain supplies from our contract manufacturers or interact with regulators, ethics committees or other important agencies due to limitations in regulatory authority, employee resources or otherwise. In any event, if the COVID-19 pandemic continues and persists for an extended period of time, we could experience significant disruptions to our development timelines, which would adversely affect our business, financial condition, results of operations and growth prospects.

Additionally, the recent trends towards rising inflation may also materially adversely affect our business and corresponding financial position and cash flows. Inflationary factors, such as increases in the cost of our clinical trial materials and supplies, interest rates and overhead costs may adversely affect our operating results. Rising interest and inflation rates also present a recent challenge impacting the U.S. economy and could make it more difficult for us to obtain traditional financing on acceptable terms, if at all, in the future. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, we may experience increases in the near future (especially if inflation rates continue to rise) on our operating costs, including our labor costs and research and development costs, due to supply chain constraints, consequences associated with COVID-19 and the ongoing conflict between Russia and Ukraine, and employee availability and wage increases, which may result in additional stress on our working capital resources.

Components of Results of Operations

Operating Expenses

Research and Development

Research and development expenses represent costs incurred in performing research, development and manufacturing activities in support of our own product development efforts and include personnel-related costs (including salaries, employee benefits and stock-based compensation) for our personnel in research and development functions; costs related to acquiring, developing and manufacturing supplies for preclinical studies, clinical trials and other studies, including fees paid to CMOs; costs and expenses related to agreements with contract research organizations, or CROs, investigative sites and consultants to conduct non-clinical and preclinical studies and clinical trials; professional and consulting services costs; research and development consumables costs; laboratory supplies and equipment costs; and facility and other allocated costs.

Research and development expenses are expensed as incurred. Non-refundable advance payments for services that will be used or rendered for future research and development activities are recorded as prepaid expenses and recognized as expenses as the related services are performed. We do not allocate our costs by vaccine candidates, as our vaccine candidates are at an early stage of development and our research and development expenses include internal costs, such as payroll and other personnel expenses, which are not tracked by vaccine candidate. In particular, with respect to internal costs, several of our departments support multiple vaccine candidate research and development programs.

We expect our research and development expenses to increase substantially in absolute dollars for the foreseeable future as we advance our vaccine candidates into and through preclinical studies and clinical trials, scale up our manufacturing activities, establish additional manufacturing capacity to meet potential incremental supply requirements following the initial commercial launch of VAX-24, pursue regulatory approval of our vaccine candidates and expand our pipeline of vaccine candidates. The process of conducting the necessary preclinical and clinical research and completing the manufacturing requirements to obtain regulatory approval is costly and time-consuming. The actual probability of success for our vaccine candidates may be affected by a variety of factors, including the safety and efficacy or immunogenicity of our vaccine candidates, clinical data, investment in our clinical programs, competition, manufacturing capabilities and commercial viability. We may never succeed in achieving regulatory approval for any of our vaccine candidates. As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our research and development projects or if, when and to what extent we will generate revenue from the commercialization and sale of our vaccine candidates.

We accrue for costs related to research and development activities based on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors, including CMOs and CROs, that conduct research, development and manufacturing activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors exceed the level of services provided and result in a prepayment of the research and development expense. Advance payments for goods and services to be used in future research and development activities are expensed when the activity has been performed or when the goods have been received. We make significant judgments and estimates in determining accrued research and development liabilities as of each reporting period based on the estimated time period over which services will be performed and the level of effort to be expended. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period.

Our research and development costs may vary significantly based on factors such as:

- the costs and timing of our chemistry, manufacturing and controls, or CMC, activities, including fulfilling good manufacturing practice, or GMP, related standards and compliance, and identifying and qualifying second suppliers;
- the costs related to raw materials estimates from our third-party manufacturing and supply partners;
- the cost of clinical trials of our vaccine candidates being greater than we anticipate;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- delays in adding a sufficient number of trial sites and recruiting suitable volunteers to participate in our clinical trials;
- the number of subjects that participate in the trials;
- the number of doses that subjects receive;
- subjects dropping out of a study or lost in follow-up;

- potential additional safety monitoring requested by regulatory agencies;
- the duration of subject participation in the trials and follow-up;
- the cost and timing of manufacturing our vaccine candidates;
- the phase of development of our vaccine candidates;
- the costs of establishing additional manufacturing capacity to meet potential incremental supply requirements following the initial commercial launch of VAX-24;
- the costs that may be required for secondary supply sources; and
- the efficacy and safety profile of our vaccine candidates.

General and Administrative

General and administrative expenses consist primarily of costs and expenses related to personnel (including salaries, employee benefits and stock-based compensation) in our executive, legal, finance and accounting, human resources and other administrative functions; legal services relating to intellectual property and corporate matters; accounting, auditing, consulting and tax services; insurance; and facility and other allocated costs not otherwise included in research and development expenses. We expect our general and administrative expenses to continue to increase in absolute dollars for the foreseeable future as we increase our headcount and expand our services to support our continued research and development activities and grow our business. We expect continued increases in general and administrative expenses related to compliance with the rules and regulations of the SEC and The Nasdaq Stock Market LLC ("Nasdaq"), insurance expenses, investor relations and corporate communications activities and other administrative and professional services.

Other Income (Expense), Net

Other income (expense), net includes interest income earned from our cash and cash equivalents, grant income, foreign currency transaction gains (losses) related to our Swiss Franc and Euro cash and liability balances, loss on disposals of fixed assets and interest expense.

Grant Income

In July 2019, we received a cost-reimbursement research award from Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, a public-private partnership funded under a Cooperative Agreement from Assistant Secretary for Preparedness and Response/Biomedical Advanced Research and Development Authority and by awards from Wellcome Trust, Germany's Federal Ministry of Education and Research, the United Kingdom Global Antimicrobial Resistance Innovation Fund and the Bill & Melinda Gates Foundation. In connection with this funding, we entered into a cost-reimbursement sub-award agreement with the Trustees of Boston University, the administrator of the program, or the CARB-X agreement. CARB-X has awarded us total funding to date of $6.6 million, with potential funding of up to $29.7 million upon the achievement of future VAX-A1 development milestones. In January 2022, CARB-X revised the parameters for the contribution of CARB-X funding and implemented maximum funding levels for all grant recipients. As a result, our total funding available upon achievement of development milestones through Phase 1 human clinical trials was revised from $29.7 million to $14.6 million (inclusive of the $6.6 million awarded to date). Separately, the National Institute of Health, or NIH, awarded us up to $0.5 million in April 2021 to advance the development of a vaccine against Shigella infection. Grant income pursuant to our award agreements is recognized as we incur and pay qualifying expenses over the periods of the awards. We recognized $1.9 million, $1.6 million and $2.5 million in grant income for funding research and development under these awards during the years ended December 31, 2022, 2021 and 2020, respectively. Grant income is included as a component of Other income (expense), net in the statements of operations.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the periods presented:

	Year Ended December 31,		Change	
	2022	2021	$	%
Operating expenses:				
Research and development	$ 169,451	$ 78,411	$ 91,040	116.1%
Acquired manufacturing rights	22,995	-	22,995	100.0%
General and administrative	39,810	25,259	14,551	57.6%
Total operating expenses	232,256	103,670	128,586	124.0%
Loss from operations	(232,256)	(103,670)	(128,586)	124.0%
Other income (expense), net:				
Interest expense	(2)	(7)	5	(71.4)%
Interest income	8,356	344	8,012	*
Grant income	1,931	1,585	346	21.8%
Realized gain on marketable securities	—	2	(2)	(100.0)%
Loss on disposal of fixed assets	(44)	—	(44)	100.0%
Foreign currency transaction gain (loss)	(1,470)	1,669	(3,139)	(188.1)%
Total other income (expense), net	8,771	3,593	5,178	144.1%
Net loss	$ (223,485)	$ (100,077)	$ (123,408)	123.3%

* *not meaningful*

Operating Expenses

Research and Development Expenses

The following table summarizes our research and development expenses for the periods presented:

	Year Ended December 31,		Change	
	2022	2021	$	%
Product and clinical development [(1)]	$ 80,869	$ 37,215	$ 43,654	117.3%
Personnel-related	33,776	17,476	16,300	93.3%
Professional and consulting services	5,811	4,351	1,460	33.6%
Research and development consumables	23,533	6,848	16,685	243.6%
Facility related and other allocated	17,243	8,098	9,145	112.9%
Laboratory supplies and equipment	5,498	3,421	2,077	60.7%
Other [(2)]	2,721	1,002	1,719	171.6%
Total research and development expenses	$ 169,451	$ 78,411	$ 91,040	116.1%

(1) Includes expenses for third-party manufacturing and outsourced contract services, including preclinical studies, clinical trials and outsourced assays.
(2) Includes travel-related expenses and other miscellaneous office expenses.

Research and development expenses increased by $91.0 million, or 116.1%, in 2022 compared to 2021. The increases of $43.7 million in product and clinical development expenses and $2.1 million in laboratory supplies and equipment were primarily due to increased VAX-31 IND readiness activities, increased VAX-24 Phase 3 readiness activities, the initiation of the VAX-24 Phase 1/2 clinical proof-of-concept study in adults 18-64 years of age and the initiation of the VAX-24 Phase 2 clinical study in adults 65 years and older, partially offset by a decrease in VAX-24 IND readiness activities as the IND application for our VAX-24 adult program was submitted

in late 2021. The increase of $16.7 million in research and development consumables was primarily related to costs incurred for extract and reagents for VAX-24 Phase 3 readiness and commercial preparation activities. The increase of $16.3 million in personnel-related expenses was primarily due to growth in the number of employees in our research and development functions and higher compensation costs, including salaries, benefits and stock-based compensation expense. The increase of $9.1 million in facility related and other allocated expenses was primarily due to an increase in lease expense related to our current corporate headquarters.

Acquired Manufacturing Rights

In December 2022, we entered into the Option Agreement with Sutro Biopharma pursuant to which we acquired, among other things, the Option. As consideration for the Option and other rights and authorizations granted to us under the Option Agreement, we paid Sutro Biopharma upfront consideration. As of December 31, 2022, we have determined there is no current alternative future use of the acquired manufacturing rights paid and accrued for the Option as of December 31, 2022. We have classified such costs incurred in entering the Option Agreement as Acquired Manufacturing Rights on the accompanying statement of operations for the year ended December 31, 2022.

General and Administrative Expenses

General and administrative expenses increased by $14.6 million, or 57.6%, in 2022 compared to 2021. The increase was mainly due to increases of $11.5 million in personnel-related costs related to growth in the number of employees in our general and administrative functions and higher compensation costs, including salaries, benefits and stock-based compensation expense and $2.9 million in professional and consulting services.

Other Income (Expense), Net

Other income (expense), net increased by $5.2 million, or 144.1%, in 2022 compared to 2021. The increase was mainly due to an increase of $8.0 million in interest income resulting from higher cash balances generated from our follow-on financings in the first and fourth quarters of 2022 and our ATM program during the year and higher interest rates. This was partially offset by an increase in foreign currency losses due to the appreciation of the U.S dollar against the Swiss Franc and Euro.

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the periods presented:

	Year Ended December 31,		Change	
	2021	2020	$	%
Operating expenses:				
Research and development	$ 78,411	$ 73,564	$ 4,847	6.6%
General and administrative	25,259	16,017	9,242	57.7%
Total operating expenses	103,670	89,581	14,089	15.7%
Loss from operations	(103,670)	(89,581)	(14,089)	15.7%
Other income (expense), net:				
Interest expense	(7)	(7)	—	—
Interest income	344	244	100	41.0%
Grant income	1,585	2,478	(893)	(36.0)%
Realized gain on marketable securities	2	—	2	100.0%
Foreign currency transaction gain (loss)	1,669	(2,351)	4,020	(171.0)%
Total other income (expense), net	3,593	364	3,229	887.1%
Net loss	$ (100,077)	$ (89,217)	$ (10,860)	12.2%

Research and Development Expenses

The following table summarizes our research and development expenses for the periods presented:

	Year Ended December 31,		Change	
	2021	2020	$	%
Product and clinical development [1]	$ 37,215	$ 51,072	$ (13,857)	(27.1)%
Personnel-related	17,476	9,943	7,533	75.8%
Professional and consulting services	4,351	4,184	167	4.0%
Research and development consumables	6,848	2,288	4,560	199.3%
Facility related and other allocated	8,098	2,957	5,141	173.9%
Laboratory supplies and equipment	3,421	2,032	1,389	68.4%
Other [2]	1,002	1,088	(86)	(7.9)%
Total research and development expenses	$ 78,411	$ 73,564	$ 4,847	6.6%

(1) Includes expenses for third-party manufacturing and outsourced contract services, including preclinical studies and outsourced assays.
(2) Includes travel-related expenses, other miscellaneous office expenses and warrant expense.

Research and development expenses increased by $4.8 million, or, 6.6% in 2021 compared to 2020. The increase was primarily attributable to increases in (i) personnel-related expenses of $7.5 million related to the increase in the number of employees to support our research and development activities and higher stock-based compensation expense, (ii) facility related and other allocated expenses of $5.1 million resulting from increases in rent and lease expense as well as expenses allocated to research and development, (iii) research and development consumables of $4.6 million related to higher critical raw materials expenses and (iv) laboratory supplies and equipment expenses of $1.4 million mainly related to our VAX-24 and VAX-A1 programs. These increases were partially offset by a decrease of $13.9 million in product and clinical development expenses, which represented the net impact of a decrease in outsourced manufacturing expenses related to our VAX-24 program and an increase in such expenses related to our VAX-31 program.

General and Administrative Expenses

General and administrative expenses increased by $9.2 million, or, 57.7% in 2021 compared to 2020. The increase was mainly due to increases of $7.0 million in personnel-related costs related to higher stock-based compensation expense resulting from an increase in the number of options granted during the year and growth in the number of employees in our general and administrative functions, $1.3 million in professional and consulting services related primarily to compliance activities under the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, and technology infrastructure enhancements and $1.1 million in directors and officers insurance expense as a result of operating as a public company.

Other Income (Expense), Net

Other income (expense), net increased by $3.2 million, or, 887.1% in 2021 compared to 2020. The increase was mainly due to an increase of $4.0 million in foreign currency gains resulting from the appreciation of the U.S. Dollar against the Swiss Franc in 2021 compared to 2020, partially offset by a decrease of $0.9 million in grant income for the CARB-X program.

Liquidity and Capital Resources

From inception through December 31, 2022, we have incurred losses and negative cash flows from operations and have funded our operations primarily through the issuance of common stock, pre-funded warrants to purchase our common stock and, prior to our IPO, redeemable convertible preferred stock, totaling approximately $1.49 billion in aggregate gross proceeds and $1.42 billion net of underwriting discounts, commissions and offering

expenses. As of December 31, 2022, we had $834.7 million of cash and cash equivalents, $123.2 million in investments and an accumulated deficit of $522.1 million.

On July 2, 2021, we filed a shelf registration statement on Form S-3ASR, or the Shelf Registration Statement, under which we may, from time to time, sell securities in one or more offerings of our common stock, preferred stock, debt securities or warrants. The Shelf Registration Statement became automatically effective upon the filing of the Form S-3ASR on July 2, 2021.

In July 2021, we entered into an Open Market Sales Agreement℠, or the ATM Sales Agreement, with Jefferies LLC, which provides that, upon the terms and subject to the conditions and limitations set forth in the ATM Sales Agreement, we may elect to issue and sell, from time to time, shares of our common stock having an aggregate offering price of up to $150.0 million through Jefferies acting as our sales agent or principal. Under the ATM Sales Agreement, Jefferies may sell the shares of common stock by any method permitted by law deemed to be an "at-the-market offering" as defined under the Securities Act of 1933, as amended, in block transactions or in privately-negotiated transactions with our consent. Jefferies will use commercially reasonable efforts to sell the shares of common stock subject to the ATM Sales Agreement from time to time, based upon our instructions (including any price, time or size limits or other customary parameters or conditions that we may impose). We will pay Jefferies a commission of up to 3.0% of the gross sales proceeds of any common stock sold through Jefferies under the ATM Sales Agreement; however, we are not obligated to make any sales of common stock. As of December 31, 2022, we have sold 4,488,573 shares of our common stock under the ATM Sales Agreement at an average price of $25.56 per share for aggregate gross proceeds of $114.7 million ($111.2 million net of commissions and offering expenses).

In January 2022, we completed an underwritten public offering in which we issued 2,500,000 shares of common stock at a price of $20.00 per share and pre-funded warrants to purchase 2,500,000 shares of our common stock at a price of $19.999 per underlying share. In February 2022, the underwriters exercised their option to purchase an additional 750,000 shares of common stock. In aggregate, we received approximately $107.6 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by us, and excluding the exercise of any pre-funded warrants.

In October 2022, we completed an underwritten public offering of 17,812,500 shares of our common stock, which included the full exercise of the underwriters' option to purchase an additional 2,812,500 shares, at a price of $32.00 per share and pre-funded warrants to purchase 3,750,000 shares of our common stock at a price of $31.999 per underlying share. In aggregate, we received $651.6 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by us, and excluding the exercise of any pre-funded warrants.

Future Funding Requirements

Our primary uses of cash are to fund our operations, which consist primarily of research and development expenditures related to our programs and, to a lesser extent, general and administrative expenditures. We anticipate that we will continue to incur significant expenses for the foreseeable future as we continue to advance our vaccine candidates, expand our corporate infrastructure, including the costs associated with being a public company, further our research and development initiatives for our vaccine candidates and scale our laboratory and manufacturing operations. We are subject to all of the risks typically related to the development of new drug candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We anticipate that we will need substantial additional funding in connection with our continuing operations.

We believe that our existing cash, cash equivalents and investments as of the date of this Annual Report on Form 10-K will be sufficient to fund our operating expenses and capital expenditure requirements through at least 12 months from the filing date of this Annual Report on Form 10-K. We have raised substantial capital, however, we will need to raise substantial additional capital to complete development and commercialization of our drug candidates. Until we can generate sufficient revenue from the commercialization of our vaccine candidates or from collaboration agreements with third parties, if ever, we expect to finance our future cash needs through public or

private equity or debt financings, third-party (including government) funding and marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. The sale of equity, pre-funded warrants or convertible debt securities may result in dilution to our stockholders and, in the case of preferred equity securities or convertible debt, those securities could provide for rights, preferences or privileges senior to those of our common stock. Debt financings may subject us to covenant limitations or restrictions on our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our ability to raise additional funds may be adversely impacted by deteriorating global economic conditions, including higher inflation rates and changes in interest rates, and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide. There can be no assurance that we will be successful in acquiring additional funding at levels sufficient to fund our operations or on terms favorable or acceptable to us. If we are unable to obtain adequate financing when needed or on terms favorable or acceptable to us, we may be forced to delay, reduce the scope of or eliminate one or more of our research and development programs.

Our future capital requirements will depend on many factors, including:

- the timing, scope, progress, results and costs of research and development, testing, screening, manufacturing, preclinical development and clinical trials;
- the costs of establishing additional manufacturing capacity to meet potential incremental supply requirements following the initial commercial launch of VAX-24;
- our exercise of the Option with Sutro Biopharma;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform field efficacy studies for our PCV candidates, require more studies than those that we currently expect or change their requirements regarding the data required to support a marketing application;
- the cost of building a sales force in anticipation of any product commercialization;
- the costs of future commercialization activities, including product manufacturing, marketing, sales, royalties and distribution, for any of our vaccine candidates for which we receive marketing approval;
- our ability to maintain existing, and establish new, strategic collaborations, licensing or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- any product liability or other lawsuits related to our products;
- the revenue, if any, received from commercial sales, or sales to foreign governments, of our vaccine candidates for which we may receive marketing approval;
- the costs to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we

may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing our patents or other intellectual property rights;

- expenses needed to attract, hire and retain skilled personnel;
- the costs of operating as a public company; and
- the impact of the COVID-19 pandemic, which may exacerbate the magnitude of the factors discussed above.

A change in the outcome of any of these or other variables could significantly change the costs and timing associated with the development of our vaccine candidates. Furthermore, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such change.

Cash Flows

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,		
	2022	2021	2020
	(in thousands)		
Net cash used in operating activities	$ (170,597)	$ (121,393)	$ (46,628)
Net cash provided by (used in) investing activities	74,585	(212,308)	(1,105)
Net cash provided by financing activities	861,547	17,796	374,870
Effect of exchange rate changes on cash and cash equivalents	137	(439)	87
Net increase (decrease) in cash and cash equivalents	$ 765,672	$ (316,344)	$ 327,224

Cash Flows from Operating Activities

Net cash used in operating activities for the year ended December 31, 2022 was $170.6 million, which primarily resulted from a net loss of $223.5 million, partially offset by non-cash charges of $40.2 million and a net change in operating assets and liabilities of $12.7 million. Non-cash charges primarily consisted of $23.7 million in stock-based compensation, $8.0 million in non-cash payments for the acquired manufacturing rights, $6.6 million in amortization of right-of-use, or ROU, assets and $2.6 million in depreciation and amortization. The net change in operating assets and liabilities of $12.7 million was primarily due to increases in cash flows from accrued expenses of $7.2 million, accrued payable of $2.9 million and accrued manufacturing expenses of $3.8 million, partially offset by a decrease in cash flows from accrued compensation of $2.3 million.

Net cash used in operating activities for the year ended December 31, 2021 was $121.4 million, which primarily resulted from a net loss of $100.1 million and a net change in operating assets and liabilities of $37.0 million, partially offset by non-cash charges of $15.7 million. The net change in operating assets and liabilities of $37.0 million was primarily due to decreases in cash flows due to operating lease liabilities of $12.9 million resulting from leasehold improvements costs applied against such liabilities upon the commencement of our San Carlos office lease in December 2021; accounts payable of $12.5 million resulting primarily from the payment of deferred Lonza payables in December 2021; accrued manufacturing expenses of $8.6 million resulting from timing of payments; and prepaid and other current assets of $7.4 million related to a receivable for reimbursement of tenant improvement allowance and prepayments on various contracts, including repairs and maintenance, production of critical raw materials, research and clinical trial preparation. These changes were partially offset by increases in cash flows due to accrued expenses of $4.6 million primarily related to costs associated with the manufacture of extract in connection with our relationship with Sutro Biopharma. Non-cash charges consisted of $10.7 million in stock-based compensation expense, $1.8 million in depreciation and amortization, $1.7 million in amortization of operating lease ROU assets and $1.4 million in net amortization of premiums on investments.

Net cash used in operating activities for the year ended December 31, 2020 was $46.6 million, which primarily resulted from a net loss of $89.2 million, partially offset by a net change in operating assets and liabilities of $35.3 million and non-cash charges of $7.3 million. The net change in operating assets and liabilities of $35.3 million was primarily due to increases in accounts payable of $26.1 million resulting from the deferral of completion payments until April 2021 in accordance with our contract with Lonza, accrued manufacturing expenses of $7.2 million related to outsourced manufacturing activities and accrued expenses of $2.2 million related primarily to increases in contract research services related to the VAX-24 program. Non-cash charges primarily consisted of $5.4 million in stock-based compensation expense, $1.4 million in depreciation and amortization and $0.3 million in asset impairment charges.

Cash Flows from Investing Activities

Cash from investing activities for the year ended December 31, 2022 was $74.6 million, which related primarily to $168.7 million in maturities of investments and $14.5 million in sales of investments, partially offset by $102.7 million in purchases of investments and $5.8 million in purchases of lab equipment and furniture and fixtures.

Cash used in investing activities for the year ended December 31, 2021 was $212.3 million, which related primarily to $336.3 million in purchases of investments and $6.6 million in purchases of lab equipment and furniture and fixtures, partially offset by $100.5 million in maturities of investments and $30.1 million in sales of investments.

Cash used in investing activities for the year ended December 31, 2020 was $1.1 million which related primarily to purchases of lab equipment and leasehold improvements.

Cash Flows from Financing Activities

Cash provided by financing activities for the year ended December 31, 2022 was $861.5 million, which primarily consisted of net proceeds from the follow-on offerings in the first and fourth quarters of 2022 of $759.2 million, net proceeds from shares issued under our ATM Sales Agreement of $97.3 million and proceeds from exercises of common stock options of $4.9 million.

Cash provided by financing activities for the year ended December 31, 2021 was $17.8 million, which primarily consisted of net proceeds from shares issued under our ATM Sales Agreement of $13.9 million and proceeds from exercises of common stock options of $3.0 million.

Cash provided by financing activities for the year ended December 31, 2020 was $374.9 million, which primarily consisted of net proceeds of $264.0 million from our IPO and $109.9 million from the issuance of our Series D redeemable convertible preferred stock.

Contractual Obligations and Commitments

Our material cash requirements include the following contractual and other obligations.

Leases

We have operating lease agreements for our office spaces. As of December 31, 2022, we had lease payment obligations totaling $20.6 million, of which $6.7 million is payable within one year.

Option Agreement

Pursuant to the Option Agreement, we and Sutro Biopharma have agreed to negotiate the terms and conditions of the Form Definitive Agreement. Within five business days after we and Sutro Biopharma mutually

agree in writing upon the Form Definitive Agreement, we have agreed to pay Sutro Biopharma $5.0 million. Additionally, in the event that we elect to exercise the Option, we would pay Sutro Biopharma an aggregate Option exercise price of $75.0 million in cash in two installments and, upon the occurrence of certain regulatory milestones, certain additional milestone payments totaling up to $60.0 million in cash. In the event that we undergo a change of control, certain rights and payments may be accelerated.

Purchase Obligations

We have certain payment obligations under various license agreements. Under these agreements, we are required to make milestone payments upon successful completion and achievement of certain intellectual property, clinical, regulatory and sales milestones. The payment obligations under the license agreements are contingent upon future events such as our achievement of specified development, clinical, regulatory and commercial milestones, and we will be required to make development milestone payments and royalty payments in connection with the sale of products developed under these agreements. As the achievement and timing of these future milestone payments are not probable or estimable, such amounts have not been included in our balance sheets as of December 31, 2022 or December 31, 2021.

We enter into agreements in the normal course of business with CMOs and other vendors for manufacturing services and raw materials purchases. We rely on several third-party manufacturers for our manufacturing requirements. As of December 31, 2022, we had the following amounts of non-cancelable purchase commitments related to manufacturing services and raw materials purchased due to our key manufacturing partners. These amounts represent our minimum contractual obligations, including termination fees. If we terminate certain firm orders with our key manufacturing partners, we will be required to pay for the manufacturing services scheduled or raw materials purchased under our arrangements. The actual amounts we pay in the future to the vendors under such agreements may differ from the purchase order amounts.

Years ending December 31,	**(in thousands)**
2023	$ 123,099
2024	2,471
Total non-cancelable purchase commitments due to key manufacturing partners	$ 125,570

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses, stock-based compensation and leases. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in the notes to our financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following critical accounting policies are most important to understanding and evaluating our reported financial results:

Accrued Research and Development Expenses

We have entered into various agreements with CMOs and CROs. As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses, including

accrued manufacturing expenses, as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel and third parties to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We make estimates of our accrued research and development expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments, if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We accrue for costs related to research and development activities based on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors, including CMOs and CROs, that conduct research, development and manufacturing on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. Advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received. We make significant judgments and estimates in determining accrued research and development liabilities as of each reporting period based on the estimated time period over which services will be performed and the level of effort to be expended. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-Based Compensation Expense

Stock-based compensation expense related to awards to employees is measured at the grant date based on the fair value of the award. The fair value of the award that is ultimately expected to vest is recognized as expense on a straight-line basis over the requisite service period, which is generally the vesting period, net of the impact of actual forfeitures recorded in the period in which they occur.

Stock-based compensation expense related to awards to non-employees is recognized based on the then-current fair value at each measurement date over the associated service period of the award, which is generally the vesting term, using the straight-line method. The fair value of non-employee stock options is estimated using the Black-Scholes valuation model with assumptions generally consistent with those used for employee stock options, with the exception of the expected term, which is the remaining contractual life at each measurement date. Refer to Note 2, “Basis of Presentation and Summary of Significant Accounting Policies,” and Note 10, “Equity Incentive Plans,” to our financial statements for more information on assumptions used in estimating stock-based compensation expense.

The Black-Scholes option-pricing model requires the use of subjective assumptions, such as volatility, which determine the fair value of stock-based awards. The assumptions utilized in the Black-Scholes option-pricing model are as follows:

Expected Term

Expected term represents the period that our stock-based awards are expected to be outstanding. The expected term for employee equity instruments is calculated using the simplified method where there is insufficient historical data about exercise patterns and post-vesting employment termination behavior. The simplified method is based on the vesting period and the contractual term for each grant, or for each vesting-tranche for awards with graded vesting. The mid-point between the vesting date and the maximum contractual

expiration date is used as the expected term under this method. For awards with multiple vesting-tranches, the time from grant until the mid-points for each of the tranches may be averaged to provide an overall expected term. The expected term for non-employee stock options is the remaining contractual term.

Expected Volatility

Expected volatility is estimated from the average historical volatilities of publicly traded companies within the life sciences industry that are considered to be comparable to our business over a period approximately equal to the expected term for employees' options and the remaining contractual life for non-employees' options. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

Expected Dividend

We have not paid and do not anticipate paying any dividends in the near future. Accordingly, we have estimated the dividend yield to be zero.

Risk-Free Interest Rate

The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero-coupon notes with remaining terms corresponding with the expected term of the option.

Fair Value of Common Stock

For valuations after the completion of our IPO, the fair value of each share of underlying common stock is based on the closing price of our common stock as reported on the Nasdaq Global Select Market on the date of grant.

Leases

We adopted Accounting Standards Update, or ASU 2016-02, Leases (Topic 842) on January 1, 2021, using the modified retrospective transition approach. There was no cumulative-effect adjustment recorded to retained earnings upon adoption.

Under ASC 842, we assess all arrangements that convey the right to control the use of property, plant and equipment, at inception, to determine if it is, or contains, a lease based on the unique facts and circumstances present in the arrangements. In addition, we determine whether leases meet the classification criteria of a finance or operating lease at the lease commencement date considering: (i) whether the lease transfers ownership of the underlying asset to the lessee at the end of the lease term, (ii) whether the lease contains a bargain purchase option, (iii) whether the lease term is for a major part of the remaining economic life of the underlying asset, (iv) whether the present value of the sum of the lease payments and residual value guaranteed by the lessee equals or exceeds substantially all of the fair value of the underlying asset, and (v) whether the underlying asset is of such a specialized nature that it is expected to have no alternative use to the lessor at the end of the lease term. As of December 31, 2022, our lease population consisted only of operating real estate leases.

Once a lease is identified and its classification determined, we recognize a ROU asset, and a corresponding lease liability. Lease liabilities are recorded based on the present value of lease payments over the expected least term. The corresponding ROU asset is measured from the initial lease liability, adjusted by (i) accrued or prepaid rents, (ii) remaining unamortized initial direct costs and lease incentives, and (iii) any impairments of the ROU asset.

Significant assumptions utilized in recognizing the ROU asset and corresponding lease liabilities included the expected lease term and the incremental borrowing rate. The expected lease term includes both contractual lease periods and, as applicable, extensions of the lease term when we have determined the exercise of the option to extend is reasonably certain to occur. The incremental borrowing rate was utilized to discount lease payments over the expected term given our operating leases do not provide an implicit rate. We estimated the incremental borrowing rate based on an analysis of corporate bond yields with a credit rating similar to us. The determination of our incremental borrowing rate requires management judgment, including development of a synthetic credit rating and cost of debt, as we currently do not carry any debt. We believe that the estimates used in determining the incremental borrowing rate are reasonable based upon current facts and circumstances.

For additional details regarding the impact of adoption and disclosure, see Note 5, "Leases," to our financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Recently Adopted Accounting Pronouncements

See Note 2, "Basis of Presentation and Summary of Significant Accounting Policies," to our financial statements for additional information.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Risk

Our cash and cash equivalents as of December 31, 2022 and December 31, 2021 consisted of readily available checking and money market funds. As of December 31, 2022, we also invested in U.S. Treasury securities, U.S. government agency securities, corporate debt, commercial paper and asset-backed securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the nature of the instruments in our portfolio, a sudden change in market interest rates would not be expected to have a material impact on our financial condition or results of operations. We believe that our exposure to interest rate risks is not significant and that a hypothetical 10% movement in market interest rates would not have a significant impact on the total value of our portfolio or our interest income. In addition, we do not believe that our cash and cash equivalents have significant risk of default or illiquidity.

Foreign Currency Risk

We are exposed to market risk related to changes in foreign currency exchange rates, mainly relating to our contract with Lonza, our CMO in Switzerland. We have also entered into a limited number of contracts with other parties with payments denominated in foreign currencies. Payments under these contracts are made in foreign currencies and are subject to fluctuations in foreign currency rates. We do not currently have a formal program in place to hedge foreign currency risks. However, from time to time, we buy Swiss Francs, or CHF, which is the majority of our foreign currency exposure, at market and are holding CHF in our bank accounts. As of December 31, 2022 and December 31, 2021, we had approximately $21.8 million and $18.8 million of CHF cash and cash equivalents, respectively, held at one financial institution. As of December 31, 2022 and December 31, 2021, we had foreign currency denominated accounts payable and accrued expenses of $13.9 million and $6.9 million, respectively. To date, foreign currency transaction gains and losses have not been material to our financial

statements. The following table shows the impact of a hypothetical 10% increase or decrease in current exchange rates on our net assets as of December 31, 2022 and our net loss for the twelve months ended December 31, 2022:

	Impact on Net Assets as of December 31, 2022	Impact on Net Loss for Twelve Months Ended December 31, 2022
	(in thousands)	
Hypothetical Change in Currency Exchange Rates		
10% increase	$ 789	$ 4,644
10% decrease	$ (789)	$ (4,644)

As our foreign currency risk increases in the future, we will evaluate alternative strategies, including hedging, to mitigate our foreign currency exposure.

Effects of Inflation

Recently, the rate of inflation in the United States has risen to levels not experienced in decades. Inflation generally affects us by increasing our cost of labor and research and development contract costs. The extent of any future impacts from inflation on our business and our results of operations will be dependent upon how long the elevated inflation levels persist and if the rate of inflation were to further increase, neither of which we are able to predict. If elevated levels of inflation were to persist or if the rate of inflation were to accelerate, the purchasing power of our cash and cash equivalents may be eroded, our expenses could increase faster than anticipated and we may utilize our capital resources sooner than expected. We do not believe inflation had a material effect on our results of operations during the periods presented.

Item 8. Financial Statements and Supplementary Data.

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Report of Independent Registered Public Accounting Firm

To the stockholders and the Board of Directors of Vaxcyte, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Vaxcyte, Inc. (the "Company") as of December 31, 2022 and 2021, the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 27, 2023, expressed an unqualified opinion on the Company's internal control over financial reporting.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued Manufacturing Expenses — Refer to Notes 2 and 6 to the financial statements

Critical Audit Matter Description

The Company incurs research and development expenses related to the costs of research and development activities, including those performed by Lonza, a contract manufacturing organization under a development and manufacturing services agreement, to provide research and development services related to preclinical vaccine development. At the end of each period, the Company accrues for costs related to manufacturing expenses based on their estimates of the services received for each phase and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on their behalf. This estimation process involves reviewing open contracts and purchase orders, communicating with Company personnel and third parties to identify services that have been performed on their behalf, and estimating the level of service performed and the associated costs incurred for the services for each phase when the Company has not yet been invoiced or otherwise notified of the actual costs.

We identified the Company's accrued manufacturing expenses as a critical audit matter primarily due to judgments necessary for management to estimate the cost of services provided but not yet invoiced and the significant volume of transactions. The amount of the accrual at period end is based on the terms and conditions per the agreements and is dependent on management's gathering of information from various sources, including Lonza, regarding the progress of the uninvoiced services at the reporting date. Accordingly, this estimate is subjective as it involves management's judgment to analyze the various sources of information. This required extensive audit effort due to the volume and nature of available information from various sources, including Lonza, and required a high degree of auditor judgment when performing audit procedures to audit management's estimates of accrued manufacturing expenses and evaluating the results of those procedures.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the accrued manufacturing expenses included the following, among others:

- We tested the effectiveness of controls over the Company's accrued manufacturing expense process, including controls over the estimation of activities completed to date.

- We met with internal research and development personnel and inspected Board of Directors materials to understand the status of contract manufacturing activities. We then compared this information to the judgment applied in management's estimate of the recorded expenses and corresponding accrual.

- We evaluated the completeness of phases used by the Company by comparing to the tracker obtained from Lonza, as Lonza is the most significant contract manufacturer.

- For a sample of phases, we evaluated the accrued manufacturing expenses by:

    - Sending written confirmations directly to the contract manufacturing organization to confirm the total budgeted amount and percentage of completion incurred as of year-end.

    - Inspecting the development and manufacturing services agreement and related amendments, change orders, statements of work, and agreeing key provisions of the agreements including timeline, budget, and relevant rates, to the Company's analysis of estimated expenses incurred to date.

    - Obtaining invoices, if available, for each selection to substantiate when the transaction should have been recorded.

    - Obtaining cash disbursements to test the accuracy of the accrual.

- Performing a lookback analysis by comparing the estimated accrual balance as of December 31, 2021, to the invoices received after year-end to evaluate the Company’s ability to estimate the accrual.

/s/ Deloitte & Touche LLP

San Francisco, California
February 27, 2023

We have served as the Company's auditor since 2017.

VAXCYTE, INC.
Balance Sheets
(in thousands, except share and per share data)

	December 31,	
	2022	2021
Assets		
Current assets:		
Cash and cash equivalents	$ 834,657	$ 68,985
Short-term investments	96,719	176,985
Prepaid expenses and other current assets	11,179	10,378
Total current assets	942,555	256,348
Property and equipment, net	10,360	7,954
Operating lease right-of-use assets	21,288	27,958
Long-term investments	26,549	27,117
Restricted cash	871	871
Other assets	4,555	4,089
Total noncurrent assets	63,623	67,989
Total assets	$ 1,006,178	$ 324,337
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 9,795	$ 6,758
Accrued compensation	1,180	3,455
Accrued manufacturing expenses	8,265	4,440
Accrued expenses	15,375	8,787
Operating lease liabilities — current	5,910	5,276
Total current liabilities	40,525	28,716
Operating lease liabilities — long-term	12,031	11,507
Other liabilities	9	96
Total liabilities	52,565	40,319
Commitments and contingencies (Note 6)		
Stockholders' Equity		
Preferred stock, $0.001 par value — 10,000,000 authorized at December 31, 2022 and December 31, 2021; no shares issued and outstanding at December 31, 2022 and December 31, 2021	—	—
Common stock, $0.001 par value — 500,000,000 shares authorized at December 31, 2022 and December 31, 2021; 79,470,670 and 53,031,978 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	82	56
Additional paid-in capital	1,476,018	582,844
Accumulated other comprehensive loss	(361)	(241)
Accumulated deficit	(522,126)	(298,641)
Total stockholders' equity	953,613	284,018
Total liabilities and stockholders' equity	$ 1,006,178	$ 324,337

The accompanying notes are an integral part of these financial statements.

VAXCYTE, INC.
Statements of Operations
(in thousands, except share and per share data)

	Year Ended December 31,		
	2022	**2021**	**2020**
Operating expenses:			
Research and development (including related party expenses of $0, $2,359 and $1,331 in 2022, 2021 and 2020, respectively)	$ 169,451	$ 78,411	$ 73,564
Acquired manufacturing rights (Note 6)	22,995	-	-
General and administrative	39,810	25,259	16,017
Total operating expenses	232,256	103,670	89,581
Loss from operations	(232,256)	(103,670)	(89,581)
Other income (expense), net:			
Interest expense	(2)	(7)	(7)
Interest income	8,356	344	244
Grant income	1,931	1,585	2,478
Realized gains on marketable securities	—	2	—
Loss on disposal of fixed assets	(44)	—	—
Foreign currency transaction (losses) gains	(1,470)	1,669	(2,351)
Total other income (expense), net	8,771	3,593	364
Net loss	$ (223,485)	$ (100,077)	$ (89,217)
Net loss per share, basic and diluted	$ (3.44)	$ (1.93)	$ (3.02)
Weighted-average shares outstanding, basic and diluted	64,877,988	51,922,108	29,545,810

The accompanying notes are an integral part of these financial statements.

VAXCYTE, INC.
Statements of Comprehensive Loss
(in thousands)

	Year Ended December 31,		
	2022	**2021**	**2020**
Net Loss	$ (223,485)	$ (100,077)	$ (89,217)
Other comprehensive loss:			
Unrealized losses on investments	(120)	(241)	—
Comprehensive Loss	$ (223,605)	$ (100,318)	$ (89,217)

The accompanying notes are an integral part of these financial statements.

VAXCYTE, INC.

Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

(in thousands, except share data)

	Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Series C Redeemable Convertible Preferred Stock		Series D Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance — December 31, 2019	6,225,719	$ 24,967	6,786,896	$ 55,151	7,377,480	$ 80,192	—	$ —	4,059,909	$ 7	$ 2,967	$ (109,347)	$ —	$ (106,373)
Issuance of Series D redeemable convertible preferred stock, net of issuance costs of $121	—	—	—	—	—	—	8,220,242	$ 109,879	—	—	—	—	—	—
Conversion of preferred stock	(6,225,719)	(24,967)	(6,786,896)	(55,151)	(7,377,480)	(80,192)	(8,220,242)	(109,879)	28,610,337	29	270,161		—	270,190
Conversion of common stock warrant	—	—	—	—	—	—	—	—	30,278	—	—	—	—	—
Conversion of preferred stock warrant	—	—	—	—	—	—	—	—	16,591	—	—	—	—	—
Warrant liability write-off	—	—	—	—	—	—	—	—	—	—	629	—	—	629
Issuance of common stock upon initial public offering, net of issuance costs of $3,368	—	—	—	—	—	—	—	—	17,968,750	18	263,989	—	—	264,007
Exercise of stock options	—	—	—	—	—	—	—	—	343,444	—	635	—	—	635
Issuance of common stock related to early exercised stock options	—	—	—	—	—	—	—	—	14,819	—	—	—	—	—
Issuance of common stock under Employee Stock Purchase Plan	—	—	—	—	—	—	—	—	27,465	—	374		—	374
Vesting of early exercised stock options	—	—	—	—	—	—	—	—	—	—	164	—	—	164
Issuance of preferred stock	—	—	—	—	—	—	—	—	—	—		—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	5,434	—	—	5,434
Net loss	—	—	—	—	—	—	—	—	—	—	—	(89,217)	—	(89,217)
Balance — December 31, 2020	—	$ —	—	$ —	—	$ —	—	$ —	51,071,593	$ 54	$ 544,353	$ (198,564)	$ —	$ 345,843
Exercise of stock options	—	—	—	—	—	—	—	—	931,114	—	3,012	—	—	3,012
Issuance of common stock to Lonza Ltd.	—	—	—	—	—	—	—	—	399,680	1	10,000	—	—	10,001
Issuance of common stock in connection with at-the market offering, net of issuance costs of $479	—	—	—	—	—	—	—	—	567,045	1	13,846	—	—	13,847
Issuance of common stock under Employee Stock Purchase Plan	—	—	—	—	—	—	—	—	62,546	—	888	—	—	888
Vesting of early exercised stock options	—	—	—	—	—	—	—	—	—	—	16	—	—	16
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	10,729	—	—	10,729
Unrealized losses on investment	—	—	—	—	—	—	—	—	—	—	—	—	(241)	(241)
Net loss	—	—	—	—	—	—	—	—	—	—	—	(100,077)	—	(100,077)
Balance — December 31, 2021	—	$ —	—	$ —	—	$ —	—	$ —	53,031,978	$ 56	$ 582,844	$ (298,641)	$ (241)	$ 284,018
Exercise of stock options	—	—	—	—	—	—	—	—	1,178,572	1	4,894	—	—	4,895
Issuance of common stock and pre-funded warrants in connection with public follow -on offerings, net of issuance costs of $45,814	—	—	—	—	—	—	—	—	21,062,500	21	759,160	—	—	759,181
Issuance of common stock in connection with at-the market offering, net of issuance costs of $3,107	—	—	—	—	—	—	—	—	3,921,528	4	97,295	—	—	97,299
Issuance of common stock for Sutro stock payment									167,780	—	7,995	—	—	7,995
Issuance of common stock under Employee Stock Purchase Plan	—	—	—	—	—	—	—	—	61,709	—	1,033	—	—	1,033
Release of restricted stock units									46,603	—	(861)	—	—	(861)
Vesting of early exercised stock options	—	—	—	—	—	—	—	—	—	—	8	—	—	8
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	23,650	—	—	23,650
Unrealized losses on investment	—	—	—	—	—	—	—	—	—	—	—	—	(120)	(120)
Net loss	—	—	—	—	—	—	—	—	—	—	—	(223,485)	—	(223,485)
Balance — December 31, 2022	—	$ —	—	$ —	—	$ —	—	$ —	79,470,670	$ 82	$ 1,476,018	$ (522,126)	$ (361)	$ 953,613

The accompanying notes are an integral part of these financial statements.

VAXCYTE, INC.
Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2022	2021	2020
Cash flows from operating activities:			
Net loss	$ (223,485)	$ (100,077)	$ (89,217)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	2,577	1,800	1,405
Stock-based compensation expense	23,650	10,729	5,434
Non-cash payments for acquired manufacturing rights	7,995	—	—
Change in fair value of redeemable convertible preferred stock warrant	—	—	179
Loss on disposal of assets	44	97	34
Asset impairment charges	213	—	267
Amortization of operating lease right-of-use assets	6,619	1,657	—
Net amortization of premiums on investments	(947)	1,406	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	433	(7,369)	(58)
Other assets	(465)	(3,539)	(75)
Operating lease liabilities	1,151	(12,856)	—
Accounts payable	2,896	(12,470)	26,102
Accrued compensation	(2,275)	3,170	(130)
Accrued manufacturing expenses	3,826	(8,572)	7,235
Accrued expenses	7,171	4,631	2,207
Deferred rent and other long-term liabilities	—	—	(11)
Net cash used in operating activities	(170,597)	(121,393)	(46,628)
Cash flows from investing activities:			
Purchases of property and equipment	(5,848)	(6,555)	(1,155)
Purchases of investments	(102,745)	(336,341)	—
Maturities of investments	168,691	100,500	—
Sales of investments	14,480	30,062	—
Proceeds from sales of property and equipment	7	26	50
Net cash provided by (used in) investing activities	74,585	(212,308)	(1,105)
Cash flows from financing activities:			
Payments of capital lease obligations	—	—	(61)
Proceeds from initial public offering, net of issuance costs	—	—	264,007
Proceeds from issuance of common stock and pre-funded warrants from follow-on offerings, net of issuance costs	759,181	—	—
Proceeds from issuance of common stock under ATM Sales Program, net of issuance costs	97,299	13,896	—
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	—	109,879
Proceeds from exercise of common stock options	4,895	3,012	635
Proceeds from issuance of common stock related to early exercised stock options	—	—	36
Proceeds from issuance of common stock under the Employee Stock Purchase Plan	1,033	888	374
Release of restricted stock units	(861)	—	—
Net cash provided by financing activities	861,547	17,796	374,870
Effect of exchange rate changes on cash and cash equivalents	137	(439)	87
Net increase (decrease) in cash, cash equivalents and restricted cash	765,672	(316,344)	327,224
Cash, cash equivalents and restricted cash, beginning of period	69,856	386,200	58,976
Cash, cash equivalents and restricted cash, end of period	$ 835,528	$ 69,856	$ 386,200
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 2	$ 7	$ 7
Supplemental disclosures of non-cash investing and financing activities:			
Purchases of property and equipment recorded in accounts payable and accrued expenses	$ 110	$ 766	$ 494
Issuance of common stock for acquired manufacturing rights	$ 7,995	$ —	$ —
Conversion of convertible preferred stock into common stock	$ —	$ —	$ 270,190
Stock issued for payment of accounts payable	$ —	$ 10,000	$ —
Deferred offering costs included in accounts payable and accrued expenses	$ —	$ —	$ 134

The accompanying notes are an integral part of these financial statements.

VAXCYTE, INC.
Notes to Financial Statements

1. Company Organization and Nature of Business

Vaxcyte, Inc. (“we,” “us,” “the Company,” or “Vaxcyte”), headquartered in San Carlos, California, was incorporated in the state of Delaware on November 27, 2013 as SutroVax, Inc. and we changed our name to Vaxcyte, Inc. on May 15, 2020. 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. ("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.

Our primary activities since incorporation have been to perform research and development, undertake preclinical and clinical studies and conduct manufacturing activities in support of our product development efforts; organize and staff our Company; establish our intellectual property portfolio; and raise capital to support and expand such activities.

Reverse Stock Split

On June 5, 2020, we filed a certificate of amendment to our amended and restated certificate of incorporation to affect a one-for-1.6870 reverse stock split of our issued and outstanding common stock, preferred stock, stock options and warrants effective on June 5, 2020. Accordingly, all share and per share amounts for all periods presented in the financial statements and notes thereto have been retroactively adjusted.

Initial Public Offering

In June 2020, we completed an initial public offering (“IPO”) in which we issued and sold 17,968,750 shares of common stock, including shares issued upon the exercise in full of the underwriters’ option to purchase 2,343,750 additional shares of common stock, at a public offering price of $16.00 per share. We received $264.0 million in net proceeds, after deducting underwriting discounts and commissions of $20.1 million and offering expenses of $3.4 million.

Immediately prior to the completion of our IPO, all outstanding shares of redeemable convertible preferred stock were converted into 28,610,337 shares of common stock. Subsequent to the completion of the IPO, there were no shares of redeemable convertible preferred stock outstanding.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation

These financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (“U.S. GAAP”) and applicable rules and regulations of the Securities and Exchange Commission (the “SEC”) regarding annual reporting.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities at the date of the financial statements. On an ongoing basis, we evaluate our estimates and assumptions, including those related to stock-based compensation expense, accruals for certain research and development costs, the incremental borrowing rate, the valuation of deferred tax assets and income

taxes. Management bases our estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from those estimates.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that potentially subject us to a concentration of credit risk consist primarily of cash and cash equivalents and investments. We invest in money market funds, U.S. Treasury securities, U.S. government agency securities, corporate debt, commercial paper and asset-backed securities. We maintain bank deposits in federally insured financial institutions and these deposits may exceed federally insured limits. We are exposed to credit risk in the event of a default by the financial institutions holding our cash and issuers of investments to the extent recorded on the balance sheets. Our investment policy limits investments to money market funds, certain types of debt securities issued by the U.S. Government and its agencies, corporate debt, commercial paper and asset-backed securities, and places restrictions on the credit ratings, maturities and concentration by type and issuer. We have not experienced any significant losses on our deposits of cash, cash equivalents or investments.

We are subject to supplier concentration risk from our suppliers. Although we are working to establish secondary sources of supply, we currently source several of our critical raw materials from single source suppliers. We also use one contract manufacturing organization ("CMO"), Lonza Ltd. ("Lonza"), to handle most of our manufacturing activities for our VAX-24 and VAX-31 programs. If we were to experience disruptions in raw materials supplied by our suppliers, or in manufacturing activities at Lonza, we may experience significant delays in our product development timelines and may incur substantial costs to secure alternative sources of raw materials or manufacturing.

Our future results of operations involve a number of other risks and uncertainties. Factors that could affect our future operating results and cause actual results to vary materially from expectations include, but are not limited to: our early stages of clinical vaccine development; our ability to advance vaccine candidates into, and successfully complete, clinical trials on the timelines we project; our ability to adequately demonstrate sufficient safety and immunogenicity or efficacy of our vaccine candidates; our ability to enroll subjects in our ongoing and future clinical trials; our ability to successfully manufacture and supply our vaccine candidates for clinical trials; our ability to obtain additional capital to finance our operations; our ability to obtain, maintain and protect our intellectual property rights; developments relating to our competitors and our industry, including competing vaccine candidates; general and market conditions; and other risks and uncertainties, including those more fully described in the "Risk Factors" section of this Annual Report on Form 10-K.

Segment and Geographical Information

We operate and manage our business as one reportable and operating segment. Our chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance. All of our long-lived assets are based in the United States. Long-lived assets are comprised of property and equipment.

Cash, Cash Equivalents and Restricted Cash

We consider all highly liquid investments purchased with original maturities of three months or less from the date of purchase to be cash equivalents. Cash equivalents consist primarily of amounts invested in money market funds and commercial paper and are stated at their fair values. Restricted cash consists of a standby letter of credit, which was issued in the first quarter of 2021, that serves as collateral for the lease agreement for our current corporate headquarters. Cash, cash equivalents and restricted cash as reported within the statement of cash flows consisted of the following:

	Years Ended December 31,		
	2022	2021	2020
		(in thousands)	
Cash and cash equivalents	$ 834,657	$ 68,985	$ 386,200
Restricted cash	871	871	—
Cash, cash equivalents and restricted cash	$ 835,528	$ 69,856	$ 386,200

Investments

Our investments have been classified and accounted for as available-for-sale securities. Fixed income securities consist of U.S. Treasury securities, U.S. government agency securities, corporate debt, commercial paper and asset-backed securities. These securities are recorded on the balance sheets at fair value. Unrealized gains and losses on these securities are included as a separate component of accumulated other comprehensive loss. The cost of investment securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in other income (expense), net. Realized gains and losses are also included in other income (expense), net. When the fair value of a debt security declines below its amortized cost basis, any portion of that decline attributable to credit losses, to the extent expected to be nonrecoverable before the sale of the security, is recognized in our statements of operations. When the fair value of a debt security declines below its amortized cost basis due to changes in interest rates, such amounts are recorded in other comprehensive loss, and are recognized in our statements of operations only if we sell or intend to sell the security before recovery of its cost basis.

Deferred Offering Costs

Deferred offering costs consist of fees and expenses incurred in connection with the sale of our common stock in equity transactions, including legal, accounting, printing and other issuance-related costs. Prior to the completion of equity transactions, deferred offering costs are included in Other assets on the balance sheet. In connection with and as of the closing of equity transactions, these costs are reclassified to Additional paid-in capital, representing a reduction to the gross proceeds. As of December 31, 2022 and 2021, $0 million and $0.5 million of deferred offering costs, respectively, were included in Other assets on the balance sheets.

Property and Equipment, Net

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, generally three to five years. Leasehold improvements are amortized over the shorter of the expected life or lease term. Repairs and maintenance expenditures, which are not considered improvements and do not extend the useful life of property and equipment, are expensed as incurred. When assets are retired or otherwise disposed of, the cost and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gain or loss is reflected in the statement of operations in the period realized.

Leases

Under Financial Accounting Standards Board ("FASB") Accounting Standards Update (“ASU”) No. 2016-02, *Leases (Topic 842)* and its associated amendments (“ASC 842”), we determine if an arrangement is a lease at inception. In addition, we determine whether a lease meets the classification criteria of a finance or operating lease at the lease commencement date considering whether: (i) the lease transfers ownership of the underlying asset to the lessee at the end of the lease term; (ii) the lease grants the lessee an option to purchase the underlying asset that the lessee is reasonably certain to exercise; (iii) the lease term is for a major part of the remaining economic life of the underlying asset; (iv) the present value of the sum of the lease payments and residual value guaranteed by the lessee equals or exceeds substantially all of the fair value of the underlying asset; and (v) the underlying asset is such a specialized nature that it is expected to have no alternative use to the lessor at the end of the lease term. As of December 31, 2022, our lease population consisted of real estate operating leases. As of December 31, 2022, we did not have any finance leases.

Operating leases are included in Operating lease right-of-use ("ROU") assets, Operating lease liabilities - current and Operating lease liabilities - long term in our balance sheet. ROU assets represent our right to use the underlying assets for the lease term and lease liabilities represent our obligation to make lease payments arising from the leases. Operating lease ROU assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. In determining the present value of lease payments, if the rate implicit in the lease is not readily determinable, we use our incremental borrowing rate based on the information available at the lease commencement date. We determine the incremental borrowing rate based on an analysis of corporate bond yields with a credit rating similar to us. The determination of our incremental borrowing rate requires management judgment, including development of a synthetic credit rating and cost of debt, as we currently do not carry any debt. We believe that the estimates used in determining the incremental borrowing rate are reasonable based upon current facts and circumstances. Applying different judgment to the same facts and circumstances could yield a different incremental borrowing rate. The operating lease ROU assets also include adjustments for prepayments and accrued lease payments and exclude lease incentives. ROU assets and lease liabilities may include options to extend or terminate leases if it is reasonably certain that we will exercise such options. Lease payments which are fixed and determinable are amortized as rent and lease expense on a straight-line basis over the expected lease term. Variable lease costs, which are dependent on usage, a rate or index, including common area maintenance charges, are expensed as incurred. Lease agreements that include lease and non-lease components are accounted for as a single lease component. Lease agreements with non-cancelable terms of less than 12 months are not recorded on our balance sheets.

Impairment of Long-Lived Assets

We review long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparing the carrying amount to the future undiscounted net cash flows which the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows generated by the assets. There were $0.2 million, $0 and $0.3 million of impairments of long-lived assets during the years ended December 31, 2022, 2021 and 2020, respectively.

Fair Value Measurements

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. The carrying amounts of our financial instruments, including cash and cash equivalents, prepaid and other current assets, accounts payable, accrued expenses, and other liabilities, approximate fair value due to their short-term maturities. Prior to their automatic conversion upon our IPO in June 2020, the redeemable convertible preferred stock tranche liability and redeemable convertible preferred stock warrant were carried at fair value (See Note 3, "Fair Value Measurements and Fair Value of Financial Instruments").

Research and Development

Research and development costs are expensed as incurred. Research and development costs include salaries, stock-based compensation and benefits for employees performing research and development activities, an allocation of facility and overhead expenses, expenses incurred under agreements with consultants, CMOs, contract research organizations (“CROs”) and investigative sites that conduct preclinical studies, clinical trials other supplies and costs associated with product development efforts, preclinical activities, clinical trials and regulatory operations.

Accrued Research and Development

We have entered into various agreements with CROs and CMOs. Our research and development accruals, which include accrued manufacturing expenses, are estimated based on the level of services performed, progress of the studies, including the phase or completion of events, and contracted costs. The estimated costs of research and development services provided, but not yet invoiced, are included in accrued expenses on the balance sheet. If the actual timing of the performance of services or the level of effort varies from the original estimates, we will adjust the accrual accordingly. Payments made to CROs or CMOs under these arrangements in advance of the performance of the related services are recorded as prepaid expenses and other current assets until the services are rendered. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Acquired Manufacturing Rights

In December 2022, we entered into an option agreement with Sutro Biopharma, Inc. (the "Option Agreement"). As of December 31, 2022, the option granted under the Option Agreement is a right, but not an obligation, to obtain certain exclusive rights to internally manufacture or source extract from certain CMOs and the right to independently develop and make improvements to the extract for use in connection with the exploitation of certain vaccine compositions (the “Option”). As consideration for the Option and other rights and authorizations granted to us under the Option Agreement, we paid Sutro Biopharma upfront consideration. As of December 31, 2022, we have determined there is no current alternative future use of the acquired manufacturing rights paid and accrued for the Option as of December 31, 2022. We have classified such costs incurred in entering the Option Agreement as Acquired Manufacturing Rights on the accompanying statement of operations for the year ended December 31, 2022. See Note 6, "Commitments and Contingencies, Sutro Option Agreement," for further details.

Income Taxes

We account for income taxes using the asset and liability method. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse.

In evaluating the ability to recover our deferred income tax assets, we consider all available positive and negative evidence, including our operating results, ongoing tax planning and forecasts of future taxable income on a jurisdiction-by-jurisdiction basis. In the event we determine that we would be able to realize our deferred income tax assets in the future in excess of their net recorded amount, we would make an adjustment to the valuation allowance that would reduce the provision for income taxes. Conversely, in the event that all or part of the net deferred tax assets are determined not to be realizable in the future, an adjustment to the valuation allowance would be charged to earnings in the period when such determination is made. As of December 31, 2022 and 2021, we have recorded a full valuation allowance on our deferred tax assets.

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Stock-Based Compensation Expense

For options granted to employees, non-employees and directors, stock-based compensation is measured at grant date based on the fair value of the award. We determine the grant-date fair value of the options using the Black-Scholes option-pricing model. The fair value of restricted stock and restricted stock unit ("RSU") awards is determined based on the number of units granted and the closing price of the Company's common stock as of the grant-date. The grant-date fair value of awards is amortized over the employees' requisite service period or the non-employees' vesting period as the services are rendered. Forfeitures are accounted for as they occur. Additionally, our 2020 Employee Stock Purchase Plan is deemed to be a compensatory plan and is therefore included in stock-based compensation expense.

Comprehensive Loss

Comprehensive loss includes net loss and other comprehensive loss for the period. Other comprehensive loss consists of unrealized loss on investments.

Foreign Currency Transactions

Transactions denominated in foreign currencies are initially measured in U.S. dollars using the exchange rate on the date of the transaction. Foreign currency denominated monetary assets and liabilities are subsequently re-measured at the end of each reporting period using the exchange rate at that date, with the corresponding foreign currency transaction gain or loss recorded in the statements of operations and statements of cash flows. Nonmonetary assets and liabilities are not subsequently re-measured.

Net Loss Per Share

Basic net loss per common share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common stock outstanding, including pre-funded warrants, during the period, without consideration of potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common stock and potentially dilutive securities outstanding for the period. For purposes of the diluted net loss per share calculation, redeemable convertible preferred stock, redeemable convertible preferred stock warrant, common stock subject to repurchase, and stock options are considered to be potentially dilutive securities. Shares of common stock into which the pre-funded warrants may be exercised are considered outstanding for the purposes of computing net loss per share because the shares may be issued for little consideration, are fully vested and are exercisable after the original issuance date.

Basic and diluted net loss attributable to common stockholders per share is presented in conformity with the two-class method required for participating securities as the redeemable convertible preferred stock is considered a participating security. Our participating securities do not have a contractual obligation to share in our losses. As such, the net loss was attributed entirely to common stockholders. Because we have reported a net loss for all periods presented, diluted net loss per common share is the same as basic net loss per common share for those periods.

Recently Adopted Accounting Pronouncements

In November 2021, the FASB issued ASU 2021-10, *Government Assistance (Topic 832): Disclosure by Business Entities about Government Assistance*, which requires disclosures about transactions with a government entity that are accounted for by applying a grant or contribution accounting model by analogy to other accounting guidance, such as a grant model within International Accounting Standard 20, *Accounting for Government Grants and Disclosure of Government Assistance (Subtopic 958-605), Not-For-Profit Entities - Revenue Recognition*. The required disclosures include (i) the nature of the transaction and the related accounting policy used to account for the transaction, (ii) the financial statement line items that are affected by the transactions and (iii) the significant terms and conditions of the transactions, including commitments and contingencies. This standard is effective for annual periods beginning after December 15, 2021, with early adoption and retrospective or prospective application

permitted. This standard is effective for us on January 1, 2022 and only impacts annual financial statement footnote disclosures. In Note 12, "Funding Arrangement," we included disclosures on our cost-reimbursement research award from Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator ("CARB-X"). We have adopted this standard as required by the effective date. The adoption of this standard did not have a material impact on our financial statements.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* and has subsequently issued related amendments, collectively referred to as "Topic 326." Topic 326 requires that financial assets measured at amortized cost be presented at the net amount expected to be collected. The measurement of expected credit losses is based on historical experience, current conditions and reasonable and supportable forecasts that affect collectability. Topic 326 also eliminates the concept of "other-than-temporary" impairment when evaluating available-for-sale debt securities and instead focuses on determining whether any impairment is a result of a credit loss or other factors. An entity will recognize an allowance for credit losses on available-for-sale debt securities rather than an other-than-temporary impairment that reduces the cost basis of the investment. We have adopted this standard as required by the effective date on January 1, 2022. The adoption of this standard did not have a material impact on our financial statements.

3. Fair Value Measurements and Fair Value of Financial Instruments

Assets and liabilities recorded at fair value on a recurring basis in the balance sheets, as well as assets and liabilities measured at fair value on a non-recurring basis or disclosed at fair value, are categorized based upon the level of judgment associated with inputs used to measure their fair values. The accounting guidance for fair value provides a framework for measuring fair value and requires certain disclosures about how fair value is determined. Fair value is defined as the price that would be received upon the sale of an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance also establishes a three-level valuation hierarchy that prioritizes the inputs to valuation techniques used to measure fair value based upon whether such inputs are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions made by the reporting entity. The three-level hierarchy for the inputs to valuation techniques is briefly summarized as follows:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. Our assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. Changes in the ability to observe valuation inputs may result in a reclassification of levels of certain securities within the fair value hierarchy. We recognize transfers into and out of levels within the fair value hierarchy in the period in which the actual event or change in circumstances that caused the transfer occurs.

Level 1 securities consist of highly liquid money market funds for which the carrying amounts approximate their fair values due to their short maturities. U.S. Treasury securities are valued using Level 1 inputs based on unadjusted, quoted prices in active markets that are observable at the measurement date for identical assets or liabilities. Level 2 securities, consisting of corporate debt, commercial paper, U.S. government agency securities and asset-backed securities, are measured based on other observable inputs, including broker or dealer quotations or alternative pricing sources. When quoted prices in active markets for identical assets or liabilities are not available, we rely on non-binding quotes from our investment managers, which are based on proprietary valuation models of

independent pricing services. These models generally use inputs such as observable market data, quoted market prices for similar instruments or historical pricing trends of securities relative to our peers. To validate the fair value determinations provided by our investment managers, we review the pricing movement in the context of overall market trends and trading information from our investment managers. In addition, we assess the inputs and methods used in determining the fair value in order to determine the classification of securities in the fair value hierarchy. We had no Level 3 securities either as of December 31, 2022 or 2021.

There were no transfers within the hierarchies during the years ended December 31, 2022 or 2021.

We invested in money market funds as of December 31, 2020. In January 2021, we started to invest some of our funds in corporate debt, commercial paper, U.S. Treasury securities, U.S. government agency securities and asset-backed securities. The following tables set forth our financial instruments measured at fair value on a recurring basis by level within the fair value hierarchy at December 31, 2022 and 2021:

		December 31, 2022			
	Fair Value Hierarchy Level	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets			(in thousands)		
Cash and cash equivalents:					
Cash	Level 1	$ 56,198	$ —	$ —	$ 56,198
Money market funds	Level 1	680,934	—	—	680,934
Commercial paper	Level 2	92,581	—	(34)	92,547
U.S. government agency securities	Level 2	4,978	—	—	4,978
Total cash and cash equivalents		834,691	—	(34)	834,657
Investments:					
U.S. Treasury securities	Level 1	37,651	—	(70)	37,581
Commercial paper	Level 2	28,161	—	(17)	28,144
Corporate debt	Level 2	25,402	—	(131)	25,271
Asset backed securities	Level 2	6,954	20	—	6,974
U.S. government agency securities	Level 2	25,427	19	(148)	25,298
Total investments		123,595	39	(366)	123,268
Total assets measured at fair value		$ 958,286	$ 39	$ (400)	$ 957,925

		December 31, 2021			
	Fair Value Hierarchy Level	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets			(in thousands)		
Cash	Level 1	$ 27,834	$ —	$ —	$ 27,834
Money market funds	Level 1	17,555	—	—	17,555
Commercial paper	Level 2	23,597	—	(1)	23,596
Total cash and cash equivalents		68,986	-	(1)	68,985
Investments:					
U.S. Treasury securities	Level 1	45,290	—	(73)	45,217
Commercial paper	Level 2	61,941	—	(22)	61,919
Corporate debt	Level 2	58,498	—	(74)	58,424
Asset backed securities	Level 2	13,899		(25)	13,874
U.S. government agency securities	Level 2	24,714	—	(46)	24,668
Total investments		204,342	—	(240)	204,102
Total assets measured at fair value		$ 273,328	$ -	$ (241)	$ 273,087

The following table presents the contractual maturities of our investments as of December 31, 2022 (in thousands):

	December 31, 2022
	Fair Value
Due in less than one year	$ 96,719
Due in one to five years	26,549
Total	$ 123,268

4. Balance Sheet Details

Property and Equipment, Net

Property and equipment, net as of December 31, 2022 and 2021 consisted of the following:

	December 31,	
	2022	2021
	(in thousands)	
Furniture and equipment	$ 1,608	$ 1,619
Computers and computer software	416	430
Lab equipment	13,100	9,453
Leasehold improvements	1,353	—
Total property and equipment	16,477	11,502
Less: accumulated depreciation and amortization	(6,117)	(3,548)
Property and equipment, net	$ 10,360	$ 7,954

Depreciation and amortization expense for the years ended December 31, 2022, 2021 and 2020 was $2.6 million, $1.8 million and $1.4 million respectively.

Accrued Expenses

Accrued expenses as of December 31, 2022 and 2021 consisted of the following:

	December 31,	
	2022	2021[2]
	(in thousands)	
Clinical studies	$ 1,518	$ 453
Other research and development [1]	12,446	4,676
Other accrued expenses	1,411	3,658
Total	$ 15,375	$ 8,787

(1) Includes $5.0 million and $0 of accrued manufacturing rights as of December 31, 2022 and 2021, respectively. See Note 6, "Commitments and Contingencies, Sutro Option Agreement," for further details.

(2) The breakout and categorizations of the 2021 total accrued expenses have been updated to conform to the 2022 presentation.

5. Leases

Operating Lease Obligations

In January 2021, we entered into a lease agreement for our current corporate headquarters facility located in San Carlos, California and a license agreement for temporary lab and office space in Palo Alto, California. The lease term for our current corporate headquarters facility began on January 22, 2021 and expires on December 31, 2025. We have two 60-month renewal options. The original term of the license agreement for the temporary space in Palo Alto terminated when the San Carlos office leasehold improvements were completed and we moved into our current corporate headquarters. We extended the license agreement for the Palo Alto office by 60 days to March 3, 2022 to accommodate our relocation plan. These two agreements are accounted for as a combined lease because the contracts were negotiated as a package with the same commercial objective. Upon commencement of the San Carlos lease in December 2021, we recorded a ROU asset and lease liability of $28.4 million and $12.9 million, respectively.

In July 2016, we entered into a five-year lease agreement for our previous headquarters facility located in Foster City, California. The original term of the lease was from September 1, 2016 to August 31, 2021, with two 30-month renewal options. In July 2019, we leased another facility in Foster City, California as a result of growth in personnel and lab space requirements. The original term of this lease was from July 1, 2019 to October 31, 2021, with no renewal options. In November 2020, we extended the terms of both of these leases for six months to March 1, 2022 and April 30, 2022, respectively. In February 2022, we entered into an early termination agreement for one of the facilities in Foster City and terminated our lease on February 12, 2022 instead of April 30, 2022.

Information related to our ROU assets and related lease liabilities was as follows (dollar amounts in thousands):

	December 31, 2022	December 31, 2021
Cash paid for operating lease liabilities	$ 5,374	$ 924
Operating lease right-of-use assets	$ 21,288	$ 27,958
Current operating lease liabilities	$ 5,910	$ 5,276
Non-current operating lease liabilities	12,031	11,507
Total lease liabilities	$ 17,941	$ 16,783
Weighted-average remaining lease term (in years)	2.78	3.75
Weighted-average discount rate	7.6%	7.5%

Maturities of lease liabilities as of December 31, 2022 were as follows:

Years ending December 31,	(in thousands)
2023	$ 6,684
2024	6,850
2025	7,022
Thereafter	—
Total future undiscounted lease payments	20,556
Less: Imputed interest	(2,615)
Total lease liabilities	$ 17,941

Future minimum payments required under operating leases as of December 31, 2021 were as follows:

	(in thousands)
Years ending December 31,	
2022[1]	$ (105)
2023	6,639
2024	6,805
2025	6,976
Thereafter	—
Total future undiscounted lease payments	20,315
Less: Imputed interest	(3,532)
Total lease liabilities	$ 16,783

(1) Maturities for 2022 are net of lease incentives of $0.9 million allocated to the Palo Alto office.

Rent expense recognized under the leases was $7.9 million, $3.2 million and $0.7 million for the years ended December 31, 2022, 2021 and 2020, respectively.

6. Commitments and Contingencies

Legal Contingencies

From time to time, we may become involved in legal proceedings arising from the ordinary course of business. We record a liability for such matters when it is probable that future losses will be incurred and that such losses can be reasonably estimated. Significant judgment by us is required to determine both probability and the estimated amount. We do not believe that there is any litigation or asserted or unasserted claim pending that could, individually or in the aggregate, have a material adverse effect on our results of operations or financial condition.

Guarantees and Indemnifications

In the normal course of business, we enter into agreements that contain a variety of representations and provide for general indemnification. Our exposure under these agreements is unknown because it involves claims that may be made against us in the future. To date, we have not paid any claims or been required to defend any action related to our indemnification obligations. As of December 31, 2022, we did not have any material indemnification claims that were probable or reasonably possible and consequently have not recorded related liabilities.

Indemnification

To the extent permitted under Delaware law, we have agreed to indemnify our directors and officers for certain events or occurrences while the director or officer is, or was, serving at our request in such capacity. The indemnification period covers all pertinent events and occurrences during the director's or officer's service. The maximum potential amount of future payments we could be required to make under these indemnification agreements is not specified in the agreements; however, we have director and officer insurance coverage that reduces our exposure and enables us to recover a portion of any future amounts paid. We have not incurred any material costs as a result of such indemnification and are not currently aware of any indemnification claims.

Development and Manufacturing Services Agreements

In October 2016, we entered into a non-exclusive development and manufacturing services agreement, as amended, with Lonza (the "2016 Lonza DMSA") pursuant to which Lonza is obligated to perform manufacturing process development and the manufacture of components for VAX-24, including the polysaccharide antigens, our proprietary eCRM protein carrier and conjugated drug substances.

In the September 2017, we and Lonza agreed to defer the completion payments for any stage that commenced after December 31, 2019 or had not been completed by December 31, 2019 until the earlier of the completion of all Investigational New Drug ("IND")-enabling activities or December 31, 2020. In March 2020, Lonza agreed to defer the completion payments until the earlier of the completion of all IND-enabling activities or April 30, 2021. In April 2021, Lonza further agreed to defer 50% of the completion payments until the earlier of the completion of all IND-enabling activities or December 31, 2021. Pursuant to this agreement, all deferred completion payments were paid in December 2021.

In June 2018, we entered into a letter agreement with Lonza (the "Lonza Letter Agreement") pursuant to which we agreed to certain terms for potential future payments in shares of our common stock as partial satisfaction of future obligations to Lonza. The Lonza Letter Agreement states that the initial pre-IND cash payments under the 2016 Lonza DMSA would be subject to a specified dollar cap (the "Initial Cash Cap"). After the Initial Cash Cap has been reached, we would have the option to make any further pre-IND payments owed to Lonza in cash, in shares of our common stock at then market prevailing prices, or a combination of both, at our election. In April 2021, we reached the Initial Cash Cap and notified Lonza that we would be exercising our option to issue approximately $10.0 million in shares of our common stock as payment for a portion of pre-IND payments due April 30, 2021. In June 2021, we issued 399,680 shares of our common stock to Lonza at a price of $25.02 per share to pay for $10.0 million of the pre-IND payments due April 30, 2021.

In October 2018, we entered into a second non-exclusive development and manufacturing services agreement with Lonza (the "2018 Lonza DMSA"), pursuant to which Lonza is obligated to perform services including manufacturing process development and the manufacture and supply of VAX-24 finished drug product.

In April 2022, we entered into a third non-exclusive development and manufacturing services agreement, as amended, with Lonza (the "2022 Lonza DMSA") effective as of March 22, 2022. Pursuant to the 2022 Lonza DMSA, Lonza will perform manufacturing process development and clinical manufacture and supply of our proprietary PCV.

Under each of the 2016 Lonza DMSA, 2018 Lonza DMSA and 2022 Lonza DMSA (collectively, the "Lonza Agreements"), we will pay Lonza agreed-upon fees for its performance of development and manufacturing services and pass through expenses incurred by Lonza for raw materials, as well as customary procurement and handling fees. Under each Lonza Agreement, we will own all right, title and interest in and to any and all New Customer Intellectual Property (as defined in each Lonza Agreement), and Lonza shall own all right, title and interest in New General Application Intellectual Property (as defined in each Lonza Agreement). Subject to the terms and conditions set forth in the Lonza Agreements, Lonza granted us a non-exclusive, world-wide, fully paid-up, irrevocable, transferable license, including the right to grant sublicenses, under the New General Application Intellectual Property (as defined in each Lonza Agreement), to research, develop, make, have made, use, sell and import the Product (as defined in each Lonza Agreement) manufactured under each Lonza Agreement.

Sutro Option Agreement

In December 2022, we entered into an Option Agreement with Sutro Biopharma, pursuant to which we acquired from Sutro Biopharma (i) authorization to enter into an agreement with an independent alternate CMO to directly source Sutro Biopharma's cell-free extract, allowing us to have direct oversight over financial and operational aspects of the relationship with the CMO; and (ii) a right, but not an obligation, to obtain certain exclusive rights to internally manufacture and/or source extract from certain CMOs and the right to independently develop and make improvements to extract (including the right to make improvements to the extract manufacturing process as well as cell lines) for use in connection with the exploitation of certain vaccine compositions (the "Option"). We and Sutro Biopharma have agreed to negotiate the terms and conditions of a form definitive agreement to be entered into in the event we exercise the Option, which shall include the terms and conditions set forth in an executed term sheet between us (the "Term Sheet"), and such terms that are necessary to give effect to each of the terms and conditions set forth in the Term Sheet (the "Form Definitive Agreement"). The Option period

is five years from the date of the Option Agreement, subject to potential acceleration in the event we undergo a change of control.

As consideration for the Option and other rights and authorizations granted to us under the Option Agreement, we agreed to pay Sutro Biopharma upfront consideration of $22.5 million, consisting of (i) $10.0 million in cash and $7.5 million worth of shares of our common stock (the number of shares to be calculated based on the arithmetic average of the daily volume weighted average price of our common stock as traded on Nasdaq in the three consecutive trading days immediately prior to the issuance thereof), and (ii) $5.0 million payable within five business days after we and Sutro Biopharma mutually agree in writing upon the Form Definitive Agreement. The 167,780 shares of common stock issued was recorded at fair value of $8.0 million on the date of settlement, December 22, 2022. In the event that we elect to exercise the Option, we would pay Sutro Biopharma an aggregate Option exercise price of $75.0 million in cash in two installments and, upon the occurrence of certain regulatory milestones, certain additional milestone payments totaling up to $60.0 million in cash. In the event that we undergo a change of control, certain rights and payments may be accelerated.

As of December 31, 2022, we have determined there is no current alternative future use of the acquired manufacturing rights paid and accrued for the option as of December 31, 2022. We have classified such costs incurred in entering the Option Agreement as Acquired Manufacturing Rights on the accompanying statement of operations for the year ended December 31, 2022. Part of the total cost incurred as reported on the statement of operations for the year ended December 31, 2022 is a $5.0 million accrued commitment that remains outstanding as of December 31, 2022.

Purchase Commitments

We enter into agreements in the normal course of business with CMOs and other vendors for manufacturing services and raw materials purchases. We rely on several third-party manufacturers for our manufacturing requirements. As of December 31, 2022, we had the following amounts due of non-cancelable purchase commitments related to manufacturing services and raw materials purchased due to our key manufacturing partners. These amounts represent our minimum contractual obligations, including termination fees. If we terminate certain firm orders with key manufacturing partners, we will be required to pay for the manufacturing services scheduled or raw materials purchased under our arrangements. The actual amounts we pay in the future to our vendors under such agreements may differ from the purchase order amounts.

Years ending December 31,	**(in thousands)**
2023	$ 123,099
2024	2,471
Total non-cancelable purchase commitments due to key manufacturing partners	$ 125,570

7. Redeemable Convertible Preferred Stock

There were no shares of redeemable convertible preferred stock authorized or outstanding as of December 31, 2022.

In connection with our IPO in June 2020, the outstanding shares of our Series A, Series B, Series C and Series D Redeemable Convertible Preferred Stock automatically converted into 28,610,337 shares of common stock.

8. Common Stock

Our certificate of incorporation authorizes us to issue up to 500,000,000 shares of common stock with $0.001 par value per share, of which 79,470,670 and 53,031,978 shares were issued and outstanding as of December 31, 2022 and 2021, respectively. The holders of our common stock are also entitled to receive dividends whenever funds are legally available, when and if declared by our board of directors. As of December 31, 2022 and 2021, no dividends have been declared. Each share of common stock is entitled to one vote.

In July 2021, we entered into an Open Market Sales Agreement℠ (the "ATM Sales Agreement") with Jefferies LLC ("Jefferies"), which provides that, upon the terms and subject to the conditions and limitations set forth in the ATM Sales Agreement, we may elect to issue and sell, from time to time, shares of our common stock having an aggregate offering price of up to $150.0 million through Jefferies acting as our sales agent or principal. We are obligated to pay Jefferies a commission of up to 3.0% of the gross sales proceeds of any common stock sold through Jefferies under the ATM Sales Agreement; however, we are not obligated to make any sales of common stock. As of December 31, 2022, we have sold 4,488,573 shares of our common stock under the ATM Sales Agreement at an average price of $25.56 per share for aggregate gross proceeds of $114.7 million ($111.2 million net of commissions and offering expenses).

In January 2022, we completed an underwritten public offering in which we issued 2,500,000 shares of our common stock at a price of $20.00 per share and pre-funded warrants to purchase 2,500,000 shares of our common stock at a price of $19.999 per underlying share. In February 2022, the underwriters exercised their option to purchase an additional 750,000 shares of common stock. In aggregate, we received approximately $107.6 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by us.

In October 2022, we completed an underwritten public offering in which we issued 15,000,000 shares of our common stock at a price of $32.00 per share and pre-funded warrants to purchase 3,750,000 shares of our common stock at a price of $31.999 per underlying share. The underwriters exercised their option to purchase an additional 2,812,500 shares of common stock. In aggregate, we received $651.6 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by us, and excluding the exercise of any pre-funded warrants.

Common stock reserved for future issuances under the 2020 Equity Incentive Plan (the "2020 Plan") and the 2014 Equity Incentive Plan (the "2014 Plan") was as follows, and excludes 36,710 shares issued outside of the 2014 Plan and 2020 Plan:

	December 31, 2022	December 31, 2021
Options issued and outstanding	7,715,494	5,295,007
Restricted stock units issued and outstanding	456,766	—
Shares available for future stock option grants	4,679,598	6,104,756
Total	12,851,858	11,399,763

9. Pre-Funded Warrants

In connection with our underwritten public offering in January 2022, we issued 2,500,000 shares of our common stock at a price of $20.00 per share and pre-funded warrants to purchase 2,500,000 shares of our common stock at a price of $19.999 per underlying share. Each pre-funded warrant has an exercise price of $0.001 per share.

In connection with our underwritten public offering in October 2022, we issued 15,000,000 shares of our common stock at a price of $32.00 per share and pre-funded warrants to purchase 3,750,000 shares of our common stock at a price of $31.999 per underlying share. Each pre-funded warrant has an exercise price of $0.001 per share.

The public offering price for the pre-funded warrants was equal to the public offering price of our common stock, less the $0.001 exercise price of each pre-funded warrant and was recorded as a component of stockholders' equity within additional paid-in-capital.

The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and payment of the exercise price. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. The holder of the pre-funded warrants may also satisfy its obligation to pay the exercise price through a "cashless exercise," in which the holder receives the net value of the pre-funded warrant in shares of common stock determined according to the formula set forth in the pre-funded warrant.

The pre-funded warrants will not expire until they are fully exercised. However, we may not effect the exercise of any pre-funded warrants, and a holder will not be entitled to exercise any portion of any pre-funded warrants that, upon giving effect to such exercise, would cause: (i) the aggregate number of shares of our common stock beneficially owned by such holder (together with affiliates) to exceed 4.99% or 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as applicable; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 4.99% or 9.99% of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as applicable, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder of a pre-funded warrant may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice for the holder to us. As of December 31, 2022, no shares underlying the pre-funded warrants had been exercised.

10. Equity Incentive Plans

2020 and 2014 Equity Incentive Plans

In June 2020, our board of directors adopted, and our stockholders approved, the 2020 Plan, which became effective on June 11, 2020. Under the 2020 Plan, we may grant stock options, appreciation rights, restricted stock and restricted stock units (RSUs) to employees, consultants and directors. Stock options granted under the 2020 Plan may be either incentive stock options or nonqualified stock options. Incentive stock options may be granted only to our employees, including officers and directors who are also employees. Nonqualified stock options may be granted to our employees, officers, directors, consultants and advisors. The exercise price of stock options granted under the 2020 Plan must be at least equal to the fair market value of the common stock on the date of grant, except that an incentive stock option granted to an employee who owns more than 10% of the shares of our common stock shall have an exercise price of no less than 110% of the fair value per share on the grant date and expire five years from the date of grant. The maximum term of stock options granted under the 2020 Plan is 10 years, unless subject to the provisions regarding 10% stockholders. Our stock options granted to new employees generally vest over four years at a rate of 25% upon the first anniversary of the vesting commencement date and monthly thereafter. Our other stock options granted to employees generally vest on terms consistent with stock options granted to new employees or monthly over four years from the vesting commencement date. Our RSUs granted to new employees generally vest over four years at a rate of 25% upon one year from the grant date, then 12.5% every six months thereafter. Our other RSUs granted to employees generally vest over three and a half years at a rate of 25% upon six months from the grant date, then 12.5% every six months thereafter. A total of 10,150,000 shares of common stock were approved to be initially reserved for issuance under the 2020 Plan. The number of shares that remained available for issuance under the 2014 Plan as of the effective date of the 2020 Plan, and shares subject to outstanding awards under the 2014 Plan as of the effective date of the 2020 Plan that are subsequently canceled, forfeited or repurchased by us, will be added to the shares reserved under the 2020 Plan. In addition, the number of shares of common stock available for issuance under the 2020 Plan is automatically increased on the first day of each calendar year during the 10-year term of the 2020 Plan, beginning with January 1, 2021 and ending with January 1, 2030, by an amount equal to 5% of the outstanding number of shares of our common stock on December 31 of the preceding calendar year or such lesser amount as determined by our board of directors. As of December 31, 2022, an aggregate of 4,679,598 shares of common stock were available for issuance under the 2020 Plan. Effective January 1, 2023, the number of shares of common stock available under the 2020 Plan increased by 3,973,533 shares pursuant to the evergreen provision of the 2020 Plan.

Our 2014 Plan permitted the granting of incentive stock options, non-statutory stock options, restricted stock and other stock-based awards. Subsequent to the adoption of the 2020 Plan, no additional equity awards can be made under the 2014 Plan. Shares reserved and remaining available for issuance under the 2014 Plan were added to the 2020 Plan reserve upon its effectiveness.

The terms of the 2014 Plan permit the exercise of options granted prior to vesting, subject to required approvals. The unvested shares are subject to our lapsing repurchase right upon termination of employment at the original purchase price. Shares purchased by employees pursuant to the early exercise of stock options are not deemed, for accounting purposes, to be issued until those shares vest according to their respective vesting schedules. Cash received for early exercised stock options is recorded as other liabilities on the balance sheet and is reclassified to common stock and additional paid-in capital as such shares vest.

As of December 31, 2022, 2,576,161 shares and 5,596,099 shares of common stock were subject to outstanding options and RSUs under the 2014 Plan and 2020 Plan, respectively.

At December 31, 2022 and 2021, 3,705 shares and 7,410 shares, respectively, remained subject to our right of repurchase as a result of the early exercised stock options. The remaining liabilities related to early exercised shares as of December 31, 2022 and 2021 were both less than $0.1 million and were recorded in other liabilities.

Stock Option Activity

Stock option activity under our 2020 Plan and 2014 Plan, which excludes options to purchase 36,710 shares granted outside of the 2020 Plan and 2014 Plan, was as follows:

		Options Outstanding			
Stock Option and Restricted Stock Units Activity	Options and RSUs Available for Grant	Number of Options	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Balances — December 31, 2020	4,651,149	5,121,549	$ 4.99		
Additional shares authorized	2,553,579	—			
Options granted	(1,616,021)	1,616,021	$ 21.83		
Options exercised	—	(926,514)	$ 3.25		
Options forfeited	516,049	(516,049)	$ 16.70		
Balances — December 31, 2021	6,104,756	5,295,007	$ 9.30		
Additional shares authorized	2,651,598	—			
Options granted	(3,850,981)	3,850,981	$ 27.67		
Options exercised	385 (1)	(1,153,285)	$ 4.25		
Options forfeited	277,209	(277,209)	$ 23.54		
Restricted Stock Units granted	(581,047)				
Restricted Stock Units withheld	32,626				
Restricted Stock Units forfeited	45,052				
Balances — December 31, 2022	4,679,598	7,715,494	$ 18.70	8.20	$ 225,667
Vested and expected to vest — December 31, 2022		7,715,494	$ 18.70	8.20	$ 225,667
Exercisable at December 31, 2022		2,921,091	$ 9.41	6.81	$ 112,585

(1) Net exercise - shares returned to the Plan.

During the years ended December 31, 2022, 2021 and 2020, 1,153,285, 926,514 and 358,264 shares of stock options, respectively, were exercised for cash at a weighted-average price per share of $4.25, $3.25 and $1.88, respectively. The weighted-average grant date fair value of options granted for the years ended December 31, 2022, 2021 and 2020 was $18.88, $14.65 and $9.62, respectively. The intrinsic value of the stock options exercised was $34.0 million, $18.9 million and $7.8 million for the years ended December 31, 2022 , 2021 and 2020, respectively.

Restricted Stock Units Activity

In March 2022, our board of directors authorized the issuance of RSUs under our 2020 Plan and adopted a form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement (the "RSU Agreement"), which is intended to serve as a standard form agreement for RSU grants issued to employees. RSU activity for the year ended December 31, 2022 was as follows:

	Shares	Weighted-Average Grant-Date Fair Value
Unvested at December 31, 2021	—	$ —
Granted	581,047	26.25
Vested and released	(79,229)	24.79
Cancelled	(45,052)	24.32
Unvested at December 31, 2022	456,766	$ 26.70

The weighted-average grant date fair value of RSUs granted during the year ended December 31, 2022 was $26.25. The aggregate fair value of unvested RSU is calculated using the closing price of our common stock on the grant date. As of December 31, 2022, the unrecognized stock-based compensation cost of unvested RSUs was $10.8 million, which is expected to be recognized over a weighted-average period of 3.0 years.

2020 Employee Stock Purchase Plan

In June 2020, our board of directors adopted, and our stockholders approved, the 2020 Employee Stock Purchase Plan (the “2020 ESPP”), which became effective on June 11, 2020. The 2020 ESPP permits participants to purchase common stock through payroll deductions of up to 15% of their eligible compensation. Employees enrolled in the 2020 ESPP, purchase shares of common stock at a price per share equal to 85% of the lower of the fair market value at the start or end of the six-month purchase periods within the two-year offering period. A total of 650,000 shares of common stock were approved to be initially reserved for issuance under the 2020 ESPP. In addition, the number of shares of common stock available for issuance under the 2020 ESPP is automatically increased on the first day of each calendar year during the 10-year term of the 2020 Plan, beginning with January 1, 2021 and ending with January 1, 2030, by an amount of 1% of the outstanding number of shares of our common stock on December 31 of the preceding calendar year or such lesser amount as determined by our board of directors. Activity under our 2020 ESPP was as follows:

	Shares
Balance - December 31, 2019	—
Shares authorized	650,000
Shares purchased	(27,465)
Balance - December 31, 2020	622,535
Additional shares authorized	510,715
Shares purchased	(62,546)
Balance - December 31, 2021	1,070,704
Additional shares authorized	530,319
Shares purchased	(61,709)
Balance - December 31, 2022	1,539,314

Effective January 1, 2023, the number of shares of common stock available under the 2020 ESPP increased by 794,706 shares pursuant to the evergreen provision of the 2020 ESPP.

Stock-based Compensation

We estimated the fair value of employee stock options using the Black-Scholes option-pricing model for the years ended December 31, 2022, 2021 and 2020 using the following weighted-average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Fair Value Assumptions			
Expected volatility	78.1% - 85.1%	81.0% - 84.1%	81.2% - 94.1%
Expected dividend yield	0%	0%	0%
Expected term (in years)	5.3 - 5.5	5.3 - 5.5	5.6 - 6.1
Risk-free interest rate	1.6% - 4.4%	0.5% - 1.3%	0.3% - 1.4%

We estimated the fair value of shares under the 2020 ESPP using the Black-Scholes option-pricing model for the years ended December 31, 2022, 2021 and 2020 using the following weighted-average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Fair Value Assumptions			
Expected volatility	78.8% - 99.7%	79.6% - 126.3%	105.8% - 158.2%
Expected dividend yield	0%	0%	0%
Expected term (in years)	0.5 - 2.0	0.5 - 2.0	0.4 - 2.0
Risk-free interest rate	0.1% - 4.7%	0.0% - 0.5%	0.1% - 0.2%

We recorded total stock-based compensation expense for the years ended December 31, 2022, 2021 and 2020 related to the 2014 Plan, the 2020 Plan and the 2020 ESPP in the statements of operations and allocated the amounts as follows:

	Year Ended December 31,		
	2022	2021	2020
		(In thousands)	
Research and development	$ 9,899	$ 3,954	$ 1,861
General and administrative	13,751	6,775	3,573
Total	$ 23,650	$ 10,729	$ 5,434

Upon our IPO, 362,935 performance-based awards vested and, as a result, we recognized $0.3 million of stock-based compensation expense during the three months ended June 30, 2020, which amount is included in the above table for the year ended December 31, 2020.

As of December 31, 2022, there was $87.7 million of unrecognized stock-based compensation expense related to the employee and non-employee awards, which is expected to be recognized over a weighted-average period of 2.9 years.

11. Retirement Plan

The Company sponsors a qualified 401(k) Plan. The retirement plan is a defined contribution plan covering eligible employees. Participants may contribute a portion of their annual compensation limited to a maximum annual amount set by the Internal Revenue Service. For the year ended December 31, 2022, the Company contributed $0.8 million to the retirement plan.

12. Funding Arrangement

In July 2019, we received a cost-reimbursement research award from Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator ("CARB-X"), a public-private partnership funded under a Cooperative Agreement from Assistant Secretary for Preparedness and Response/Biomedical Advanced Research and Development Authority ("BARDA") and by awards from Wellcome Trust, Germany's Federal Ministry of Education and Research, the United Kingdom Global Antimicrobial Resistance Innovation Fund and the Bill & Melinda Gates Foundation. In connection with this funding, we entered into a cost-reimbursement sub-award agreement with the Trustees of Boston University, the administrator of the program. The initial award provided the potential for funding up to four years to develop a universal vaccine to prevent infections caused by Group A Strep bacteria, which include pharyngitis, impetigo and necrotizing fasciitis. The initial award committed initial funding of up to $1.6 million for our VAX-A1 program and, subject to a CARB-X decision to extend the options, up to $15.1 million in total funding available upon achievement of development milestones over the next four years. Specified research expenditures are reimbursable expenses associated with agreed-upon activities needed to advance the research project supported by the grant. These expenditures can include labor, laboratory supplies, travel, consulting and third-party vendor research and development support costs. CARB-X has awarded us total funding to date of $6.6 million, with potential funding of up to $29.7 million upon the achievement of future VAX-A1 development milestones. In January 2022, CARB-X revised the parameters for the contribution of CARB-X funding and implemented maximum funding levels for all grant recipients. As a result, our total funding available upon achievement of development milestones through Phase 1 human clinical trials was revised from $29.7 million to $14.6 million.

In April 2021, we received a cost-reimbursement research award from the National Institutes of Health ("NIH"). In connection with this funding, we entered into a cost-reimbursement sub-award agreement with the University of Maryland, Baltimore, the administrator of the program. The award provides for potential funding up to five years totaling approximately $0.5 million to develop a vaccine to prevent infections caused by Shigella.

Income from grants is recognized in the period during which the related specified expenses are incurred, provided that the conditions under which the grants were provided have been met. We recognized $1.9 million, $1.6 million and $2.5 million of grant income and recorded the amounts in Other income (expense), net in the statement of operations during the years ended December 31, 2022, 2021, and 2020 respectively. A grant receivable of $1.0 million and $1.2 million representing unreimbursed, eligible costs incurred under the CARB-X agreement was recorded and included in Prepaid expenses and other current assets in the balance sheets as of December 31, 2022 and 2021, respectively.

13. Net Loss Per Share

The following table sets forth the computation of basic and diluted net loss per share and excludes shares which are legally outstanding, but subject to repurchase by us:

	Year Ended December 31,		
	2022	2021	2020
Net loss (in thousands)	$ (223,485)	$ (100,077)	$ (89,217)
Weighted-average shares outstanding used in computing net loss per share, basic and diluted[(1)]	64,877,988	51,922,108	29,545,810
Net loss per share, basic and diluted	$ (3.44)	$ (1.93)	$ (3.02)

(1) Includes shares of common stock into which pre-funded warrants may be exercised. See Note 9, "Pre-Funded Warrants".

The following potentially dilutive securities were excluded from the computation of diluted net loss per share for the period presented because including them would have been antidilutive:

	Year Ended December 31,		
	2022	2021	2020
Stock options	7,752,204	5,357,389	5,188,531
Restricted stock units	456,766	—	-
Employee stock purchase plans	113,240	66,404	87,887
Total	8,322,210	5,423,793	5,276,418

14. Income Taxes

Our pre-tax book loss was derived from our business operations within the United States.

A reconciliation of our effective tax rate to the statutory U.S. federal rate is as follows:

	Year Ended December 31,		
	2022	2021	2020[1]
Statutory rate	21.0%	21.0%	21.0%
Stock-based compensation	1.5%	2.2%	0.8%
Credits	0.8%	1.1%	0.6%
Change in valuation allowance	(21.3)%	(23.0)%	(22.1)%
Section 162(m) limitation	(1.8)%	(1.1)%	(0.1)%
Other	(0.2)%	(0.2)%	(0.2)%
Total	0.0%	0.0%	0.0%

(1) The 2020 effective tax rate reconciliation has been updated to conform to the 2021 and 2022 presentation.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of the assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The following table presents significant components of our deferred tax assets as of December 31, 2022 and 2021:

	As of December 31,	
	2022	2021
	(in thousands)	
Deferred tax assets:		
Net operating losses	111,555	85,574
Fixed assets	1,062	1,700
Accrued & others[1]	1,103	2,174
R&D Credits	5,436	2,865
Capitalized R&D expenditures	32,873	2,984
Accrued manufacturing expenses	2,063	1,006
Lease liability	5,358	6,674
Intangible assets	6,867	—
Stock compensation[1]	4,474	1,956
Total deferred tax assets	170,791	104,934
Deferred tax liabilities:		
ROU asset	(6,357)	(8,349)
Total deferred tax liabilities	(6,357)	(8,349)
Net deferred tax asset	164,433	96,585
Valuation allowance	(164,433)	(96,585)
Net deferred taxes	$ —	$ —

(1) The 2021 Accrued & others and Stock compensation lines have been updated to conform to the 2022 presentation.

At December 31, 2022, we have net operating loss carryforwards of approximately $340.2 million and $453.1 million available to reduce future taxable income, if any, for federal and state income tax purposes, respectively. The federal and state net operating loss carryforwards, except the federal loss carryforward arising in tax years beginning after December 31, 2017, begin to expire in 2034 unless previously utilized. Federal net operating losses arising in tax years beginning after December 31, 2017 have an indefinite carryover period and do not expire.

At December 31, 2022, we have research credit carryforwards of $4.4 million and $2.8 million available to offset future income tax liabilities, if any, for federal and California income tax purposes, respectively. The federal research and development tax credit carryforwards expire beginning in 2039 unless previously utilized. The California tax credits can be carried forward indefinitely.

We have evaluated the positive and negative evidence bearing upon the realizability of our deferred tax assets. Based on our history of operating losses, we have concluded that it is more likely than not that the benefit of our deferred tax assets will not be realized. Accordingly, we have provided a full valuation allowance for deferred tax assets as of December 31, 2022 and 2021.

Utilization of the net operating loss carryforward and research credit carryforward may be subject to an annual limitation due to the ownership percentage change limitations under Section 382 and Section 383, respectively, provided by the Internal Revenue Code of 1986, as amended (the "Code"), and similar state provisions. The annual limitation may result in the expiration of the net operating loss before utilization. We have experienced ownership changes in the past. There were no ownership changes identified in 2022, as such we have determined that no federal research credits will expire unutilized or are excluded from our research credit carryforwards. The Company does not expect any ownership changes during the year ended December 31, 2022 to result in a limitation that would materially reduce the total amount of net operating loss carryforwards and credits that can be utilized. Subsequent ownership changes may affect the limitation in future years.

We have uncertain tax benefits ("UTBs") totaling $1.8 million and $0.9 million as of December 31, 2022 and 2021, respectively, which were netted against deferred tax assets subject to valuation allowance. The UTBs had no effect on the effective tax rate. We recognize interest and penalties related to UTBs, when they occur, as a component of income tax expense. To the extent accrued interest and penalties do not ultimately become payable, amounts accrued will be reduced and reflected as a reduction of the provision for income taxes in the period such determination is made. There were no interest or penalties recognized for the years ended December 31, 2022 and 2021. We do not expect our UTBs to change significantly over the next 12 months.

A reconciliation of the beginning and ending unrecognized tax benefit amount is as follows:

	December 31,		
	2022	2021	2020
	(in thousands)		
Balance at the beginning of the year	$ 924	$ 393	$ 271
Additions based on tax positions related to current year	876	461	287
Reductions based on tax positions related to prior years	(46)	70	(165)
Balance at end of year	$ 1,754	$ 924	$ 393

We file U.S. federal and state tax returns. In general, the Company is no longer subject to tax examination by the Internal Revenue Service or state taxing authorities for years before 2017. Although the federal and state statutes are closed for purposes of assessing additional income tax in those prior years, the taxing authorities may still make adjustments to the net operating loss, or NOL, and credit carryforwards used in open years. Therefore, the tax statutes should be considered open as it relates to the NOL and credit carryforwards used in open years. We do not have any tax audits or other issues pending.

On March 27, 2020, the President of the United States signed into law the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act"). The CARES Act, among other things, includes certain income tax provisions for individuals and corporations; however, these benefits do not impact our current tax provision.

On December 21, 2020, the President of the United States signed into law the "Consolidated Appropriations Act, 2021" which includes further COVID-19 economic relief and extension of certain expiring tax provisions. The relief package includes a tax provision clarifying that businesses with forgiven Paycheck Protection Program, or PPP, loans can deduct regular business expenses that are paid for with the loan proceeds. Additional pandemic relief tax measures include an expansion of the employee retention credit, enhanced charitable

contribution deductions and a temporary full deduction for business expenses for food and beverages provided by a restaurant. These benefits do not have a material impact on the current tax provision.

The Infrastructure Investment and Jobs Act was signed on November 15, 2021, and it contained several tax provisions including changes to the Employee Retention Tax Credit and changes to excise taxes. These provisions do not have a material impactful to the Company's current tax provision.

In accordance with the 2017 Tax Act, research and experimental (R&E) expenses under Internal Revenue Code Section 174 are required to be capitalized beginning in 2022. R&E expenses are required to be amortized over a period of five years for domestic expenses and 15 years for foreign expenses. The Company has capitalized research and experimental expenditures in its current tax provision as a result.

The Inflation Reduction Act of 2022 specifically introduces the topic of corporate alternative minimum tax ("CAMT") on adjusted financial statement income on applicable corporations for taxable years beginning after December 31, 2022. There is no impact to the Company's current tax provision.

The American Rescue Plan Act was signed on March 11, 2021. One of the provisions of the Act included expanding the definition of covered employees subject to IRC 162(m) to include an additional top five highest compensated officers beyond the CEO, CFO, and three highest paid employees currently covered under IRC 162(m). This expanded provision is applicable for tax years beginning after Dec 31, 2026. The Company does not believe that this update to IRC 162(m) would have a material impact on its income tax provision currently and will continue to monitor this.

15. Related Party Transactions

We have an ongoing relationship with Sutro Biopharma. In 2013, Sutro Biopharma provided support to facilitate the establishment of our Company. As of December 31, 2021 and 2020, Sutro Biopharma owned approximately 1.6 million shares of our common stock. As of December 31, 2019, Sutro Biopharma also owned warrants to purchase 31,857 shares of our common stock (the "Common Stock Warrant") at an exercise price of $0.79289 per share and 59,276 shares of our Series C redeemable convertible stock (the "Preferred Stock Warrant") at an exercise price of $11.5215 per share. The Common Stock Warrant and the Preferred Stock Warrant were automatically net exercised pursuant to their terms for 30,278 shares and 16,591 shares, respectively, of our common stock in connection with the IPO. In the agreements and amendments identified herein, we licensed certain intellectual property and acquired certain supply rights from Sutro Biopharma, including the right to use the XpressCF platform to discover and develop vaccine candidates for the treatment or prophylaxis of infectious diseases. On October 12, 2015, we and Sutro Biopharma ("the Parties") entered into the Sutro Biopharma License Agreement, which amended and restated an agreement dated August 1, 2014. The Sutro Biopharma License Agreement was subsequently amended on May 9, 2018 ("License Amendment A1") and May 29, 2018 ("License Amendment A2"). In consideration for the License Amendment A2, we issued to Sutro Biopharma the Preferred Stock Warrant to purchase 59,276 shares of Series C redeemable convertible preferred stock at a purchase price of $11.5215 per share. We also entered into a separate supply agreement with Sutro Biopharma on May 29, 2018 (the "Sutro Biopharma Supply Agreement"). As of June 2, 2021, Sutro Biopharma was no longer considered a related party.

Under the Sutro Biopharma License Agreement, Sutro Biopharma granted us an exclusive, worldwide license to research, develop, manufacture and commercialize vaccine products addressing infectious disease, which are discovered or produced based on the use of Sutro Biopharma's proprietary cell-free protein expression technology, known as XpressCF, which utilizes extracts derived from strains of *E. coli*. In connection with the Sutro Biopharma License Agreement, under the Sutro Biopharma Supply Agreement, Sutro Biopharma has agreed to manufacture and supply extracts and reagents for us on a cost-plus basis. In consideration for the rights licensed, we are obligated to pay a 4% royalty on worldwide aggregate annual net sales of our vaccine products for human health and a 2% royalty on annual net sales of vaccine products for animal health. In License Amendment A1, the Parties amended the license agreement to remove a pre-IND regulatory meeting as a diligence milestone and to agree that certain other diligence milestones had been satisfied. In License Amendment A2, the Parties amended the license agreement to add certain terms confirming our obligation to purchase Sutro Biopharma's proprietary extract from *E. coli* ("Extract") from Sutro Biopharma. In addition, the Parties amended the license agreement to specify our rights

to a transfer of certain know-how relating to the manufacture of Extract in the event of a declaration of bankruptcy by Sutro Biopharma. Finally, the Parties agreed to terms providing for injunctive relief in the event of a breach or threatened breach by the other party.

In the Sutro Biopharma Supply Agreement, the Parties agreed to terms for the supply of manufactured Extract and custom reagents by Sutro Biopharma for us to use in manufacturing vaccine compositions in non-clinical research or in Phase 1 or Phase 2 clinical trials. The term of the Sutro Biopharma Supply Agreement is from execution until the later of July 31, 2021 and the date the parties enter into and commence activities under the supply agreement unless extended through a subsequent supply agreement for the supply of Extract and custom reagents for vaccine compositions for Phase 3 and commercial uses as contemplated in the Supply Agreement. In February 2021, we entered into an amendment to the Sutro Biopharma Supply Agreement and extended the term to July 31, 2022.

As Sutro Biopharma was no longer considered a related party as of June 2, 2021, we excluded expenses after that date from related party transaction expenses. We recognized expense related to the Supply Agreement of $0.0 million, $2.4 million and $1.2 million for the years ended December 31, 2022, 2021 and 2020, respectively. In addition, we recorded $0, $0 and $0.2 million in the change in fair value of the Preferred Stock Warrant for the years ended December 31, 2022, 2021 and 2020, respectively. The expense related to the changes in the fair value of the warrant is included in research and development expenses in the statements of operations.

16. Subsequent Events

Subsequent to December 31, 2022, through February 24, 2023, we sold a total of 507,136 shares of our common stock under the ATM Sales Agreement at an average price of $45.79 per share, generating aggregate gross proceeds of $23.0 million ($22.5 million net of commissions and offering expenses).

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, control may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Our management, with the participation of our Chief Executive Office, or CEO, and our Chief Financial Officer, or CFO, our principal executive officer and principal financial officer, respectively, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as of December 31, 2022. Based on this evaluation, our CEO and CFO have concluded that our disclosure controls and procedures as of December 31, 2022 were effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There have been no changes in our internal control over financial reporting during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in its 2013 Internal Control - Integrated Framework. Based on this assessment, our management has concluded that our internal control over financial reporting was effective as of December 31, 2022. Pursuant to Section 404(c) of the Sarbanes-Oxley Act, our independent registered public accounting firm has issued an attestation report on the effectiveness of our internal control over financial reporting for the year ended December 31, 2022, which is included below.

Report of Independent Registered Public Accounting Firm

To the stockholders and the Board of Directors of Vaxcyte, Inc.

Opinion on Internal Control over Financial Reporting

We have audited the internal control over financial reporting of Vaxcyte, Inc. (the "Company") as of December 31, 2022, based on criteria established in Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control — Integrated Framework (2013) issued by COSO.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the balance sheets, the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows as of and for the year ended December 31, 2022, of the Company and our report dated February 27, 2023, expressed an unqualified opinion on those financial statements.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Deloitte & Touche LLP

San Francisco, California
February 27, 2023

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K since we intend to file our definitive proxy statement for our 2023 Annual Meeting of Stockholders (the "2023 Proxy Statement") pursuant to Regulation 14A of the Exchange Act, not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and certain information to be included in the 2023 Proxy Statement is incorporated herein by reference.

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item of Form 10-K will be included under the captions "Proposal No. 1— Election of Directors," "Executive Officers," "Delinquent Section 16(a) Reports," "Corporate Governance and Board Matters," and "Code of Business Conduct and Ethics" in our 2023 Proxy Statement, and is incorporated herein by reference.

We have adopted a written Code of Business Conduct and Ethics ("Ethics Code") that applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The Ethics Code is available on our website at www.vaxcyte.com. If we make any substantive amendments to the Ethics Code or grant any waiver from a provision of the Ethics Code to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website or in a Current Report on Form 8-K.

Item 11. Executive Compensation.

The information required by this item of Form 10-K will be included under the captions "Executive Officers," "Executive Compensation," "Director Compensation," "Corporate Governance and Board Matters," and "Certain Relationships and Related Person Transactions" in our 2023 Proxy Statement, and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item of Form 10-K will be included under the captions "Security Ownership of Certain Beneficial Owners and Management," "Director Compensation," and "Executive Compensation" in our 2023 Proxy Statement, and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item of Form 10-K will be included under the captions "Certain Relationships and Related Person Transactions," and "Corporate Governance and Board Matters" in our 2023 Proxy Statement, and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item of Form 10-K will be included under the caption "Proposal No. 2— Ratification of Independent Registered Public Accounting Firm" in our 2023 Proxy Statement, and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this Annual Report on Form 10-K:

(1) All Financial Statements

The financial statements and Report of Independent Registered Public Accounting Firm filed as part of this Annual Report on Form 10-K are listed in the "Index to Financial Statements" under Part II, Item 8 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

All financial statement schedules have been omitted because of the absence of conditions under which they are required or because the required information, where material, is shown in the financial statements, financial notes or supplementary financial information.

(3) Exhibits

The list of exhibits filed with this Annual Report on Form 10-K is set forth in the Exhibit Index preceding the signature page and is incorporated herein by reference or filed with this Annual Report on Form 10-K, in each case as indicated herein (numbered in accordance with Item 601 of Regulation S-K).

Item 16. Form 10-K Summary

None.

Exhibit Index

Exhibit	Description	Incorporated by Reference			
		Schedule/Form	File Number	Exhibits	Filing Date
3.1	Amended and Restated Certificate of Incorporation of Vaxcyte, Inc., as amended	8-K	001-39323	3.1	June 16, 2020
3.2	Amended and Restated Bylaws of Vaxcyte, Inc.	8-K	001-39323	3.2	June 16, 2020
4.1	Form of common stock certificate of the Registrant	S-1/A	333-238630	4.1	June 8, 2020
4.2	Description of Capital Stock.	10-K	001-39323	4.2	March 29, 2021
4.3	Form of Pre-Funded Warrant	8-K	001-39323	4.1	January 13, 2022
4.4	Form of Pre-Funded Warrant	8-K	001-39323	4.1	October 27, 2022
10.1#	Vaxcyte, Inc. Amended and Restated 2014 Equity Incentive Plan and forms of agreements thereunder.	S-1	333-238630	10.2	May 22, 2020
10.2#	Vaxcyte, Inc. 2020 Equity Incentive Plan and forms of agreements thereunder.	S-1/A	333-238630	10.3	June 8, 2020
10.3#	Form of Restricted Stock Unit Grant Notice	10-Q	001-39323	10.2	May 9, 2022
10.4#	Vaxcyte, Inc. 2020 Employee Stock Purchase Plan.	S-1/A	333-238630	10.4	June 8, 2020
10.5	Form of Indemnification Agreement entered into by and between the Registrant and each director and executive officer.	S-1	333-238630	10.5	May 22, 2020
10.6#	Executive Employment Agreement entered into by and between the Registrant and Grant Pickering, dated January 21, 2016.	S-1	333-238630	10.6	May 22, 2020
10.7#	Executive Employment Agreement entered into by and between the Registrant and Jeff Fairman, dated January 21, 2016.	S-1	333-238630	10.7	May 22, 2020

Exhibit	Description	Incorporated by Reference			
		Schedule/Form	File Number	Exhibits	Filing Date
10.8#	Offer Letter entered into by and between the Registrant and Paul Sauer, dated April 12, 2016.	S-1	333-238630	10.8	May 22, 2020
10.9#	Executive Employment Agreement entered into by and between the Registrant and Jim Wassil, dated November 15, 2019.	S-1	333-238630	10.11	May 22, 2020
10.10#	Offer Letter entered into by and between the Registrant and Andrew Guggenhime, dated April 16, 2020.	S-1	333-238630	10.13	May 22, 2020
10.11#	Offer Letter entered into by and between the Registrant and Harpreet Dhaliwal, dated September 29, 2021.				X
10.12#	Offer Letter entered into by and between the Registrant and Mikhail Eydelman, dated March 4, 2022.	10-Q	001-39323	10.1	May 9, 2022
10.13#	Form of Executive Change in Control and Severance Agreement entered into by and between the Registrant and each eligible employee.	S-1	333-238630	10.14	May 22, 2020
10.14+†	Development and Manufacturing Services Agreement by and between the Registrant and Lonza Ltd, dated October 29, 2018.	S-1	333-238630	10.15	May 22, 2020
10.15+†	Development and Manufacturing Services Agreement by and between the Registrant and Lonza Ltd, dated October 21, 2016, as amended.				X
10.16+†	Letter Agreement by and between the Registrant and Lonza Ltd, dated June 19, 2018.	S-1	333-238630	10.17	May 22, 2020
10.17+†	Master Services Agreement for Drug Product Development and Manufacturing between Registrant and Lonza Ltd., dated March 22, 2022, as amended.				X

Exhibit	Description	Incorporated by Reference			
		Schedule/Form	File Number	Exhibits	Filing Date
10.18+†	Amended and Restated SutroVax Agreement by and between the Registrant and Sutro Biopharma, Inc., dated October 12, 2015, as amended.	S-1	333-238630	10.18	May 22, 2020
10.19+†	Supply Agreement by and between the Registrant and Sutro Biopharma, Inc., dated May 29, 2018, as amended.				X
10.20+†	Option Grant Agreement by and between Registrant and Sutro Biopharma, Inc., dated December 19, 2022.				X
10.21+†	License Agreement by and between the Registrant and The Regents of the University of California, represented by its San Diego campus, dated February 4, 2019.	S-1	333-238630	10.20	May 22, 2020
10.22+†	Lease Agreement by and between the Company and ARE-San Francisco No. 63, LLC, dated as of January 21, 2021	8-K	001-39323	10.1	January 25, 2021
23.1	Consent of Independent Registered Public Accounting Firm				X
24.1	Power of Attorney. Reference is made to the signature page hereto.				X
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended.				X

Exhibit	Description	Incorporated by Reference			
		Schedule/Form	File Number	Exhibits	Filing Date
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended.				X
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 13a-14(b) or 15d-14(b) of the Securities Exchange Act, as amended, and 18 U.S.C. Section 1350.				X
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.				X
101.SCH	Inline XBRL Taxonomy Extension Schema Document				X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document				X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				X
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101				X

X Filed herewith.

+ Pursuant to Item 601(b)(10)(iv) of Regulation S-K, certain portions of this exhibit have been omitted (indicated by "[***]") because we have determined that the information is not material and is the type that we treat as private or confidential.

† Schedules and exhibits to this exhibit have been omitted pursuant to Item 601(a)(5) of Regulation S-K. A copy of any omitted schedule or exhibit will be furnished to the SEC upon request; provided, however, that we may request confidential treatment pursuant to Rule 24b-2 of the Exchange Act for any schedule or exhibit so furnished.

* The certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Vaxcyte, Inc.

Date: February 27, 2023

By: /s/ Grant E. Pickering
Grant E. Pickering
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Grant E. Pickering and Andrew Guggenhime, and each of them, as his or her true and lawful attorneys-in-fact, each with full power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the SEC, hereby ratifying and confirming all that each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Grant E. Pickering **Grant E. Pickering**	Chief Executive Officer and Director *(Principal Executive Officer)*	February 27, 2023
/s/ Andrew Guggenhime **Andrew Guggenhime**	President and Chief Financial Officer *(Principal Financial Officer)*	February 27, 2023
/s/ Elvia Cowan **Elvia Cowan**	Senior Vice President, Finance *(Principal Accounting Officer)*	February 27, 2023
/s/ Carlos Paya, M.D., Ph.D. **Carlos Paya, M.D., Ph.D.**	Director	February 27, 2023
/s/ Annie Drapeau **Annie Drapeau**	Director	February 27, 2023
/s/ Halley Gilbert **Halley Gilbert**	Director	February 27, 2023
/s/ Peter Hirth, Ph.D. **Peter Hirth, Ph.D.**	Director	February 27, 2023
/s/ Michael Kamarck, Ph.D. **Michael Kamarck, Ph.D.**	Director	February 27, 2023
/s/ Teri Loxam **Teri Loxam**	Director	February 27, 2023
/s/ Heath Lukatch, Ph.D. **Heath Lukatch, Ph.D.**	Director	February 27, 2023

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