PROSPECTUS SUPPLEMENT

(To Prospectus dated March 11, 2020)



Common Stock

We have entered into an Open Market Sale AgreementSM, or sales agreement, with Jefferies LLC, or Jefferies, relating to shares of our common stock, par value \$0.0001 per share, offered by this prospectus supplement. In accordance with the terms of the sales agreement, pursuant to this prospectus supplement we may offer and sell shares of our common stock having an aggregate offering price of up to \$11.5 million, from time to time through Jefferies, acting as sales agent. We will be required to file another prospectus supplement in the event we want to offer more than \$11.5 million of shares of our common stock in accordance with the sales agreement.

Sales of the shares of common stock, if any, under this prospectus supplement will be made by any method permitted that is deemed an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Jefferies is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Jefferies will be entitled to compensation at a commission rate of 3.0% of the gross sales price of the shares sold under the sales agreement. See "Plan of Distribution" beginning on page S-12 for additional information regarding the compensation to be paid to Jefferies. In connection with the sale of shares of common stock on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Jefferies with respect to certain liabilities, including civil liabilities under the Securities Act.

As of the date of this prospectus supplement, the aggregate market value of our outstanding common stock held by non-affiliates and calculated in accordance with General Instruction I.B.6 of Form S-3 is approximately \$49.6 million, which is based on 5,920,473 shares of our outstanding common stock held by non-affiliates and a price per share of \$8.37, which was the closing sale price of our Common Stock on the Nasdaq Capital Market on January 28, 2020. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we offer to sell, pursuant to the registration statement of which this prospectus supplement forms a part, securities in a public primary offering with a value exceeding one-third of the aggregate market value of our common stock held by non-affiliates in any 12-month period, so long as the aggregate market value of our outstanding common stock held by non-affiliates remains below \$75 million. During the 12 calendar months prior to and including the date of this prospectus supplement, we have offered \$5.0 million of shares of our common stock pursuant to General Instruction I.B.6 of Form S-3. As a result of the one-third limitation and prior offers, we are now able to offer and sell up to \$11,518,119 of shares of our common stock.

Our common stock trades on the Nasdaq Capital Market under the symbol "VCNX". On March 25, 2020, the last reported sale price of our common stock on the Nasdaq Capital Market was \$4.40 per share.

We are an "emerging growth company" as defined by the Jumpstart Our Business Startups Act of 2012 and, as such, we are eligible for reduced public company reporting requirements. Please see "Summary—Implications of Being an Emerging Growth Company."

Investing in our common stock involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" beginning on page S-7 of this prospectus supplement, page 6 of the accompanying base prospectus, and under similar headings in the documents incorporated by reference into this prospectus supplement and the accompanying base prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or determined if this prospectus supplement and the accompanying base prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Jefferies

The date of this prospectus supplement is March 27, 2020

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of our common stock and also adds to and updates information contained in the accompanying base prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying base prospectus. The second part, the accompanying base prospectus, dated March 11, 2020, including the documents incorporated by reference into it, provides more general information, some of which may not apply to the shares of common stock offered by this prospectus supplement. Generally, when we refer to this "prospectus," we are referring to both parts of this document combined.

To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying base prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference in this prospectus supplement or the accompanying base prospectus — the statement in the document having the later date modifies or supersedes the earlier statement unless otherwise specified.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference into this prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreement, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should rely only on the information contained in or incorporated by reference into this prospectus and any free writing prospectus prepared by or on our behalf that we have authorized for use in connection with this offering. We have not, and Jefferies has not, authorized any dealer, salesperson or other person to provide any information or to make any representation other than those contained or incorporated by reference into this prospectus or into any free writing prospectus prepared by or on our behalf or to which we have referred you. If anyone provides you with additional, different or inconsistent information, you should not rely on it. We and Jefferies take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not, and Jefferies is not, making an offer to sell our common stock in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing or incorporated by reference into this prospectus and in any free writing prospectus prepared by or on our behalf that we have authorized for use in connection with this offering is accurate only as of the date of each such respective document. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus, including the documents incorporated by reference, and any free writing prospectus prepared by or on our behalf that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents we have referred you to in the sections of this prospectus supplement and the accompanying base prospectus entitled "Incorporation By Reference" and "Where You Can Find Additional Information"

Other than in the United States, no action has been taken by us or Jefferies that would permit a public offering of the common stock offered by this prospectus in any jurisdiction where action for that purpose is required. The common stock offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of the shares be distributed or published in any jurisdiction, except under circumstances that will result in compliance

with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to this offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy the common stock offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

References in this prospectus supplement to "Vaccinex," the "Company," "we," "our," or "us" mean Vaccinex, Inc. and its subsidiaries except where the context otherwise requires.

FORWARD-LOOKING STATEMENTS

This prospectus supplement contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which statements involve substantial risks and uncertainties. All statements contained in this prospectus supplement other than statements of historical fact, including statements regarding our future results of operations and financial position, our business strategy and plans, and our objectives for future operations, are forward-looking statements. The words "may," "will," "should," "expects," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "intends," "continue" and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements. Forward-looking statements included in this prospectus supplement include, but are not limited to, statements regarding:

- our ability to continue as a going concern;
- the impact on our operations of public health crises in the United States or internationally, including the current COVID-19 coronavirus outbreak;
- our estimates regarding our expenses, future revenues, anticipated capital requirements and our needs for additional financing;
- the implementation of our business model and strategic plans for our business and technology;
- the timing and success of the commencement, progress and receipt of data from any of our preclinical and clinical trials;
- our expectations regarding the potential safety, efficacy or clinical utility of our product candidates;
- the expected results of any clinical trial and the impact on the likelihood or timing of any regulatory approval;
- the difficulties in obtaining and maintaining regulatory approval of our product candidates;
- the rate and degree of market acceptance of any of our product candidates;
- the success of competing therapies and products that are or become available;
- regulatory developments in the United States and foreign countries;
- current and future legislation regarding the healthcare system;
- the scope of protection we establish and maintain for intellectual property rights covering our technology;
- developments relating to our competitors and our industry;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the performance of third parties, including collaborators, contract research organizations and third-party manufacturers;
- the development of our commercialization capabilities, including the need to develop or obtain additional capabilities;
- the enforceability of the exclusive forum provisions in our amended and restated certificate of incorporation; and
- our use of the proceeds from the offerings of our common stock.

These statements are only current predictions and are subject to known and unknown risks, uncertainties and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements. We discuss many of these risks in greater detail in the risk factors in Item 1A of our 2019 Annual Report on Form 10-K and under the heading "Risk Factors" beginning on page S-7 of this prospectus supplement and page 6 of the accompanying base prospectus. You should not rely upon forward-looking statements as predictions of future events.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, after the date of this prospectus supplement, we are under no duty to update or revise any of the forward-looking statements, whether as a result of new information, future events or otherwise.

PROSPECTUS SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus. This summary is not complete and does not contain all of the information that you should consider in making your investment decision. For a more complete understanding of our company and this offering, you should read carefully this entire prospectus, including the information incorporated by reference into this prospectus, and any free writing prospectus prepared by or on our behalf that we have authorized for use in connection with this offering, including the "Risk Factors" section beginning on page S-7 of this prospectus supplement, page 6 of the accompanying base prospectus, our consolidated financial statements and the related notes thereto and the other documents incorporated by reference into this prospectus.

Our Company

We are a clinical-stage biotechnology company engaged in the discovery and development of targeted biotherapeutics to treat serious diseases and conditions with unmet medical needs, including cancer, neurodegenerative diseases, and autoimmune disorders. We believe we are the leader in the field of semaphorin 4D, or SEMA4D, biology and that we are the only company targeting SEMA4D as a potential treatment for cancer, neurodegenerative diseases, or autoimmune disorders. SEMA4D is an extracellular signaling molecule that regulates the migration of immune and inflammatory cells to sites of injury, cancer or infection. We are leveraging our SEMA4D antibody platform and our extensive knowledge of SEMA4D biology to develop our lead product candidate, pepinemab (also known as VX15/2503), an antibody that we believe utilizes novel mechanisms of action. We are focused on the development of pepinemab for the treatment of non-small cell lung cancer, or NSCLC, Huntington's disease, or HD, and Alzheimer's disease, or AD. Additionally, third party investigators are studying pepinemab in clinical trials in osteosarcoma and melanoma as well as in "window of opportunity" studies in other indications. We have developed multiple proprietary platform technologies and are developing product candidates to address serious diseases or conditions that have a substantial impact on day-to-day functioning and for which treatment is not addressed adequately by available therapies. We employ our proprietary platform technologies, including through our work with our academic collaborators, to identify potential product candidates for sustained expansion of our internal product pipeline and to facilitate strategic development and commercial partnerships.

Our lead platform technologies include our SEMA4D antibody platform and our ActivMAb antibody discovery platform.

- Our SEMA4D antibody platform is the application of our extensive knowledge of SEMA4D biology to develop our lead product
 candidate pepinemab for the treatment of various indications, including cancer and neuroinflammatory and neurodegenerative
 diseases. Pepinemab's mechanisms of action block the SEMA4D signal and activate innate physiological mechanisms to respond to
 tumors or tissue injury. We have demonstrated in preclinical studies in animal models that the biological activities associated with an
 antibody blockade of SEMA4D can promote immune cell infiltration into tumors and the repair or prevention of neurological damage
 in neuroinflammatory and neurodegenerative diseases.
- Our ActivMAb® antibody discovery platform is a proprietary human antibody discovery platform based on a novel method for expressing large and diverse libraries of high affinity, full-length human monoclonal antibodies on the surface of vaccinia, a mammalian virus. We believe our ActivMAb technology offers (i) rapid generation of high affinity, full-length, human monoclonal antibodies synthesized and naturally modified in mammalian cells, (ii) expression and selection of antibodies that easily and predictably transition to manufacturing in mammalian lines, and (iii) an innovative and efficient method for selecting antibodies against multi-pass membrane proteins, an important class of

pharmacological targets. Our product candidate VX5 was generated by our ActivMAb platform and is currently in preclinical development for the treatment of MS and potentially for other autoimmune disorders. We intend to continue to utilize our ActivMAb platform to identify additional product candidates for our own pipeline development and for strategic collaborations.

In addition, we and our academic collaborators are using our Natural Killer T, or NKT, vaccine platform to discover product candidates that target and extend the activity of NKT cells. NKT cells work directly to kill certain types of parasites and cells, including tumor cells and virus-infected cells. We are applying our agonists to direct NKT cells to the site of tumors, potentially enhancing tumor-specific immunity through recruitment and activation of cytotoxic T cells, or CTL, and antibody-armed natural killer, or NK, cells that will work to eradicate the tumor.

Vaccinex Product Pipeline

Research/Preclinical	Phase 1	Phase 2	Phase 3
Pepinemab Antibody Platform			
Neurology			
Pepinemab in Huntington's Disease (Orphan Drug and Fast Tra	ack Designations)		SIGNAL
Pepinemab in Alzheimer's Disease	SIGNAL-AD		
Oncology			
Pepinemab in Non-Small Cell Lung Cancer (Collaboration with	Merck KGaA, Darmstadt, Germ	any)	CLASSICAL - Lung
Pepinemab in Melanoma (in combination with check point inhib	itors) IST spon	sored by UCLA (with BMS)	
Pepinemab in Osteosarcoma	IST spon	sored by Children's Oncolog	y Group/NCI
Pepinemab in Multiple "Window of Opportunity" Studies	Multiple I	ST sponsored by Emory Unive	ersity, Winship Cancer Institute
ActivMAb Antibody Platform			
VX5 (Anti-CXCL13) for Autoimmune Diseases			

Pepinemab is currently in clinical development by us for the treatment of NSCLC, and HD, in investigator-sponsored trials, or ISTs, for the treatment of osteosarcoma and melanoma, and in multiple "window of opportunity" studies in other indications. Our additional product candidates, VX5 and VX25, are in earlier stages of development and were generated using our ActivMAb and NKT vaccine platforms, respectively. VX5 is a human antibody to CXCL13, a molecule that regulates the formation of immune tissues, and is currently in preclinical development for the treatment of MS and potentially for other autoimmune disorders. VX25, a bi-specific NKT cell stimulator, is being evaluated in various preclinical cancer models and seeks to address challenges for the therapeutic application of NKT cell stimulation for cancer immunotherapy. We believe our multiple platform technologies position us well for continued pipeline expansion and partnership opportunities going forward.

Pepinemab

Pepinemab is a humanized monoclonal antibody that binds and blocks the signaling activity of SEMA4D. We are advancing pepinemab with what we believe to be novel mechanisms of action for the treatment of cancer and certain neurodegenerative diseases, including HD. As of December 31, 2019, 521 patients have been treated or enrolled in seven Phase 1 clinical trials and two Phase 2 clinical trials of pepinemab in separate indications.

Cancer

Pepinemab is currently being studied as a treatment for advanced solid tumors, including in clinical trials in NSCLC, osteosarcoma, and melanoma. We have demonstrated in preclinical tumor models that SEMA4D regulates infiltration of immune precursor cells into tumor tissue. Our preclinical data suggest that blocking SEMA4D promotes infiltration of immune cells that can eradicate the tumor. We have also demonstrated in preclinical models the potential for synergy between pepinemab and a checkpoint inhibitor when used in combination. We completed a Phase 1 clinical trial of pepinemab as a single-agent cancer therapy and released top-line data in October 2014. Pepinemab was well tolerated in this clinical trial.

In October 2017 in collaboration with Merck KGaA, we initiated the CLASSICAL—Lung clinical trial, a Phase 1b/2 clinical trial of pepinemab in combination with avelumab, an inhibitor of the PD-1/PD-L1 checkpoint pathway, in patients with NSCLC who have not previously been treated with immunotherapy. In July 2018, an additional cohort of patients who failed prior immunotherapy was added to the trial. The CLASSICAL-Lung trial consists of a dose escalation phase and a subsequent dose expansion phase. We announced in August 2019 that we had completed enrollment in the dose expansion phase. We anticipate near topline data for this trial in the first half of 2020.

In February 2018, The Children's Oncology Group, or COG, with financial support from the National Cancer Institute, initiated a Phase 1/2 clinical trial of pepinemab as a single agent in pediatric patients with recurrent, relapsed, or refractory solid tumors, including osteosarcoma. In March 2020, COG notified us of its intention to discontinue this study. In June 2018, a Phase 1 IST of pepinemab in combination with Yervoy® or with Opdivo® began at the UCLA Jonsson Comprehensive Cancer Center in patients with advanced melanoma who have progressed on prior anti-PD-1/PD-L1 based therapies. In addition, Emory University has initiated three separate Phase 1 IST "window of opportunity" studies evaluating pepinemab as a single agent and in combination with ipilimumab or nivolumab in multiple other indications. We anticipate that we will present interim analysis of these window of opportunity studies at the American Society of Clinical Oncology, or ASCO, Annual Meeting in May/June 2020.

Huntington's Disease

We are studying pepinemab as a treatment for HD, which is a neurodegenerative genetic disorder that typically manifests in mid-adult life. Our study of pepinemab in HD is based on our prior research of neurodegenerative disease mechanisms, in which we demonstrated in preclinical models that SEMA4D triggers activation of both microglia and astrocytes, the innate inflammatory cells of the central nervous system, or CNS. The chronic activation of microglia and astrocytes has been implicated as an important disease mechanism in HD, Alzheimer's disease, or AD, progressive MS, and other neurodegenerative disorders. We initiated the SIGNAL study, a Phase 2 clinical trial, in July 2015 in early manifest and late prodromal (pre-manifest) HD patients. This clinical trial builds on preclinical studies in an animal model of HD and safety data from a Phase 1 dose-escalation clinical trial of pepinemab in MS patients that we completed in November 2014. The SIGNAL study has an adaptive design, and interim analysis of Cohort A data for 36 randomized patients was completed in April 2017. Data from this cohort showed that treatment with pepinemab induced a sharp increase in glucose metabolism in the brain during HD disease progression as detected by conventional FDG-PET imaging. On the

basis of this data, the design of the Cohort B study was modified, and enrollment in Cohort B was completed in December 2018. We anticipate publication of data from Cohort A of the SIGNAL trial in the second half of 2020. Cohort B includes a total of 265 subjects in two cohorts: 179 patients who have early manifest disease, and 86 who are late prodromal. All subjects are randomized to receive monthly infusions of either pepinemab or placebo for 18 months in double-blind fashion without crossover. The estimated primary completion date, which is the date on which the last participant in a clinical study is examined or receives an intervention to collect the final data for the primary outcome measure, for the SIGNAL Phase 2 trial is the second half of 2020, with topline data expected in October 2020. The U.S. Food and Drug Administration, or FDA, has granted both Orphan Drug designation and Fast Track designation to pepinemab for HD.

Alzheimer's Disease

We intend to initiate a clinical study of pepinemab as a potential treatment for AD in 2020. This study of pepinemab in AD, which we refer to as "SIGNAL-AD," will be based on our prior research of neurodegenerative disease mechanisms in which we demonstrated in preclinical models that SEMA4D triggers activation of both microglia and astrocytes. In December 2019, we announced a funding grant of \$750,000 from the Alzheimer's Association and an award in the form of investment in our common stock of up to \$3 million from the Alzheimer's Drug Discovery Foundation, each in support of SIGNAL-AD. We expect to receive the funding in 2020. As noted above, the chronic activation of microglia and astrocytes has been implicated as an important disease mechanism in AD as well as in other neurodegenerative disorders. The design for this study is based on evidence from Cohort A of the SIGNAL clinical trial in HD showing that treatment with pepinemab induced a sharp increase in glucose metabolism in the brain during HD disease progression as detected by conventional FDG-PET imaging. Previous studies in AD have shown that decline in glucose metabolism correlates with cognitive decline. Recently, it has been reported that FDG-PET is superior to the more established Aß amyloid-PET as an indicator of cognitive decline in early AD, which gives us greater confidence in relying on the evidence from Cohort A of our SIGNAL clinical trial in HD to inform the SIGNAL-AD trial. SIGNAL-AD will be a 60 patient, randomized, placebo-controlled, multi-center phase 1b clinical study. We had intended to enroll the first patient in this trial in mid-2020, with top-line data anticipated early 2022. However, the initial enrollment date is now delayed subject to evaluating further developments and risks related to the COVID-19 coronavirus.

Corporate Information

We were incorporated under the laws of the State of Delaware in April 2001. Our principal executive offices are located at 1895 Mount Hope Avenue, Rochester, New York 14620, and our telephone number is (585) 271-2700. Our website address is *www.vaccinex.com*. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this prospectus. You should not rely on any such information in making your decision to purchase our common stock.

Implications of Being an Emerging Growth Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earliest of: (i) December 31, 2023; (ii) the last day of the first fiscal year in which our annual gross revenues are \$1.07 billion or more; (iii) the date on which we have, during the previous three-year period, issued more than \$1.0 billion in non-convertible debt securities; or (iv) the last day of the first fiscal year in which the market value of our common stock held by non-affiliates exceeded \$700 million as of the end of the second quarter of that fiscal year.

For as long as we remain an "emerging growth company," we may take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not "emerging growth companies" including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation and financial statements in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote to approve executive compensation and shareholder approval of any golden parachute payments not previously approved. We may take advantage of one or more of these reporting exemptions until we are no longer an "emerging growth company."

The JOBS Act provides that an "emerging growth company" can take advantage of an extended transition period for complying with new or revised accounting standards, and we have elected to do so.

THE OFFERING

Common stock offered by us:

Shares having an aggregate offering price of up to \$11,500,000.

Common stock to be outstanding following the offering:

Up to 17,500,783 shares (as more fully described in the notes following this table), assuming sales of 2,613,636 shares of our common stock in this offering at an offering price of \$4.40 per share, which was the last reported sale price of our shares on the Nasdaq Capital Market on March 25, 2020. The actual number of shares issued will vary depending on the sales price under this offering.

Plan of Distribution:

"At the market offering" that may be made from time to time on the Nasdaq Capital Market or other existing trading markets for our common stock through our sales agent, Jefferies. See "Plan of Distribution" on page S-12 of this prospectus supplement.

Use of Proceeds:

We intend to use the net proceeds from this offering for the development of pepinemab for the treatment of NSCLC and other cancer indications including, in particular, head and neck squamous cell carcinoma, or HNSCC, HD, and AD and for general corporate purposes, which may include working capital, capital expenditures, research and development expenditures and clinical trial expenditures, among other things. See "Use of Proceeds."

Risk Factors:

Investing in our common stock involves a high degree of risk. Please read the information contained in and incorporated by reference under the heading "Risk Factors" beginning on page S-7 of this prospectus supplement, the "Risk Factors" section beginning on page 6 of the accompanying base prospectus and the documents incorporated by referenced into this prospectus.

Nasdaq Capital Market symbol:

"VCNX"

The number of shares of our common stock to be outstanding after this offering is based on 14,887,147 shares of our common stock outstanding as of December 31, 2019 and excludes:

- 1,468,563 shares of our common stock issued in a private placement on January 23, 2020;
- 579,731 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2019 at a weighted-average exercise price of \$8.04 per share;
- 1,173,500 shares of our common stock issuable upon the exchange of Vaccinex Products, LP units;
- 1,318,787 shares of our common stock issuable upon the exchange of VX3 (DE) LLP units; and
- 230,952 shares of our common stock available for future issuance under our 2018
 Omnibus Incentive Plan, or the 2018 Plan, as of December 31, 2019.

RISK FACTORS

We operate in rapidly changing business environments that present numerous risks, many of which are driven by factors we cannot control or predict. You should consider carefully the risks and uncertainties described below, together with the documents incorporated by reference into this prospectus, including the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2019, which is incorporated by reference into this prospectus, as updated by annual, quarterly and other reports and documents we file with the SEC after the date of this prospectus supplement and that are incorporated by reference into this prospectus. We cannot assure you that any of the events discussed below will not occur. These events as well as additional risks and uncertainties we are unaware of, or currently believe are not material, could have a material and adverse impact on our business, results of operations, financial condition and cash flows.

Risks Related to This Offering

A substantial number of shares of our common stock may be sold in the market following this offering, which may depress the market price for our common stock.

Sales of a substantial number of shares of our common stock in the public market following this offering could cause the market price of our common stock to decline. Although there can be no assurance that any of the \$11.5 million worth of shares being offered under this prospectus supplement will be sold or the price at which any such shares might be sold, assuming that an aggregate of 2,613,636 shares of our common stock are sold during the term of the sales agreement with Jefferies, in each case, for example, at a price of \$4.40 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on March 25, 2020, upon completion of this offering, based on 14,887,999 shares outstanding as of December 31, 2019, we will have outstanding an aggregate of 17,500,783 shares of common stock, assuming no exercise of outstanding stock options or exchange of Vaccinex Products, LP units or VX3 (DE) LLP units. All of the shares sold in this offering upon issuance will be, freely tradable without restriction or further registration under the Securities Act, unless these shares are owned or purchased by "affiliates" as that term is defined in Rule 144 under the Securities Act.

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

In order to raise additional capital, we may in the future offer additional shares of common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares of common stock or other securities convertible into or exchangeable for our shares in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing common stock or other securities convertible into or exchangeable for our common stock in the future could have rights superior to existing shareholders. The price per share at which we sell additional shares of common stock or other securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

As a result of this offering, we are further limited in the securities we may issue under our shelf registration statement, which may have an adverse effect on our liquidity.

We have filed a shelf registration statement on Form S-3 with the SEC of which this prospectus supplement and accompanying prospectus are a part. In order to issue securities under this registration statement, we must rely on Instruction I.B.6 of Form S-3, which imposes a limitation on the maximum amount of securities that we may offer and sell pursuant to the registration statement during any twelve-month period. At the time we offer securities pursuant to the registration statement, the amount of securities to be offered and sold plus the amount of any securities we have offered and sold during the prior twelve months in reliance on Instruction I.B.6 may not exceed one-third of the aggregate market value of our outstanding common stock held by non-affiliates

as of a day during the 60 days immediately preceding such sale, as computed in accordance with Instruction I.B.6. After giving effect to this offering, we will be substantially limited in our ability to effect any other offering pursuant to our effective registration statement on Form S-3 in the near term, unless and until the market value of our outstanding common stock held by non-affiliates increases significantly. If we cannot sell securities under our shelf registration statement, we may be required to utilize more costly and time-consuming means of accessing the capital markets, which could materially adversely affect our liquidity and cash position.

We have broad discretion in how we use the net proceeds of this offering, and we may not use these proceeds effectively or in ways with which you agree.

Our management will have broad discretion as to the use of the net proceeds from this offering. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Accordingly, you will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds will be used appropriately. These net proceeds could be applied in ways that do not improve our operating results or increase the value of your investment. See "Use of Proceeds" on page S-10 of this prospectus supplement for a description of our proposed use of proceeds from this offering.

Investors in this offering will experience immediate dilution in the book value per share of the common stock purchased in the offering.

The common stock sold in this offering, if any, will be sold from time to time at various prices. However, the expected offering price of our common stock will be substantially higher than the net tangible book deficit per share of our outstanding common stock. After giving effect to the sale of shares of our common stock in the aggregate amount of \$11.5 million at an assumed offering price of \$4.40 per share, the last reported sale price of our common stock on March 25, 2020 on the Nasdaq Capital Market, and after deducting estimated commissions and estimated offering expenses, our as-adjusted net tangible book value as of December 31, 2019 would have been approximately \$8.7 million, or approximately \$0.50 per share. This represents an immediate increase in net tangible book value of approximately \$0.65 per share to our existing shareholders and an immediate dilution in as-adjusted net tangible book deficit of approximately \$3.90 per share to new investors participating in this offering. See "Dilution" on page S-11 of this prospectus supplement.

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

Subject to certain limitations in the sales agreement with Jefferies and compliance with applicable law, we have the discretion to deliver placement notices to Jefferies at any time throughout the term of the sales agreement. The number of shares that are sold by Jefferies after delivering a placement notice will fluctuate based on the market price of the common stock during the sales period and limits we set with Jefferies.

We do not expect to pay dividends in the foreseeable future. As a result, you must rely on stock appreciation for any return on your investment.

We have never paid do not anticipate paying cash dividends on shares of our common stock in the foreseeable future. Any payment of cash dividends will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Accordingly, you will have to rely on capital appreciation, if any, to earn a return on your investment in our common stock. Furthermore, we may in the future become subject to additional contractual restrictions on, or prohibitions against, the payment of dividends.

The COVID-19 coronavirus could adversely impact our business, including our clinical development plans.

In December 2019, a novel strain of coronavirus, COVID-19, was reported to have surfaced in Wuhan, China. Since then, the COVID-19 coronavirus has spread to multiple countries, including the United States, and has caused significant disruptions around the world. For example, we had previously anticipated beginning enrollment in mid-2020 in our study of pepinemab in AD, but the initial enrollment date is now delayed, the extent of such delay is subject to evaluating further developments and risks related to COVID-19. We may experience further disruptions as a result of the COVID-19 pandemic that could severely impact our business, including:

- interruption of key manufacturing, research and clinical development activities due to limitations on work and travel imposed or recommended by federal or state governments, employers and others;
- delays or difficulties in clinical trial site operations, including difficulties in recruiting clinical site investigators and clinical site staff and difficulties in enrolling patients or treating patients in active trials;
- interruption of key business activities due to illness and/or quarantine of key individuals and delays associated with recruiting, hiring and training new temporary or permanent replacements for such key individuals, both internally and at our third party service providers;
- delays in research and clinical trial sites receiving the supplies and materials needed to conduct preclinical studies and clinical trials, due to work stoppages, travel and shipping interruptions or restrictions or other reasons;
- difficulties in raising additional capital needed to pursue the development of our programs due to the slowing of our economy and near term and/or long term negative effects of the pandemic on the financial, banking and capital markets;
- changes in local regulations as part of a response to the COVID-19 coronavirus outbreak that may require us to change the ways in which research, including clinical development, is conducted, which may result in unexpected costs; and
- delays in necessary interactions with regulators, ethics committees and other important agencies and contractors due to limitations in employee resources, travel restrictions or forced furlough of government employees.

The global outbreak of the COVID-19 coronavirus continues to rapidly evolve. The extent to which the COVID-19 coronavirus may impact our business will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the virus.

USE OF PROCEEDS

We may issue and sell our shares of common stock having aggregate sales proceeds of up to \$[•] million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that, in the future, we will sell any shares under or fully utilize the sales agreement with Jefferies as a source of financing.

We currently intend to use the net proceeds from this offering for the development of pepinemab for the treatment of NSCLC and other cancer indications including, in particular, HNSCC, and for neurodegenerative diseases including HD and AD, and for general corporate purposes, which may include working capital, capital expenditures, research and development expenditures and clinical trial expenditures, among other things.

The precise amount and timing of the application of these net proceeds will depend upon a number of factors, such as the timing and progress of our research and development efforts and the timing and progress of any partnering efforts. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds from this offering. Depending on the outcome of our efforts and other unforeseen events, our plans and priorities may change and we may apply the net proceeds of this offering in different manners than we currently anticipate. Accordingly, our management will have broad discretion in the timing and application of these net proceeds.

DILUTION

If you invest in our securities in this offering, you will experience immediate dilution to the extent of the difference between the price per share of our common stock in this offering and the net tangible book deficit per share of our common stock immediately after this offering. As of December 31, 2019, our historical net tangible book deficit was approximately \$2.3 million, or \$0.15 per share of our common stock. Our historical net tangible book deficit per share represents our total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding as of December 31, 2019.

After giving effect to the assumed sale of our shares of common stock in the aggregate amount of \$11.5 million at an assumed offering price of \$4.40 per share, the last reported sale price of our common stock on March 26, 2020 on the Nasdaq Capital Market, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our adjusted net tangible book value as of December 31, 2019 would have been approximately \$8.7 million, or approximately \$0.50 per share of our common stock. This amount represents an immediate increase in net tangible book value of \$0.65 per share to our existing stockholders and immediate dilution of \$3.90 per share of our common stock to purchasers in this offering. The following table illustrates this calculation on a per share basis:

Assumed public offering price per share of common stock		\$4.40
Net tangible book value (deficit) per share as of December 31, 2019	\$(0.15)	
Increase in net tangible book value per share of common stock attributable to investors purchasing our common stock in this		
offering	0.65	
Adjusted net tangible book value per share of common stock immediately after this offering		0.50
Dilution per share of common stock to investors purchasing shares of our common stock in this offering		\$3.90

The number of shares of our common stock to be outstanding after this offering is based on 14,887,147 shares of our common stock outstanding as of December 31, 2019 and excludes:

- 1,468,563 shares of our common stock issued in a private placement on January 23, 2020;
- 579,731 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2019 at a weighted-average exercise price of \$8.04 per share;
- 1,173,500 shares of our common stock issuable upon the exchange of Vaccinex Products, LP units;
- 1,318,787 shares of our common stock issuable upon the exchange of VX3 (DE) LLP units; and
- 230,952 shares of our common stock available for future issuance under our 2018 Omnibus Incentive Plan, or the 2018 Plan, as of December 31, 2019.

To the extent that any of our outstanding options are exercised, Vaccinex Products, LP or VX3 (DE) LLP units are exchanged, new options are issued under the 2018 Plan or pursuant to inducement awards, or we issue additional shares of common stock in the future, there will be further dilution to new investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Jefferies, under which we may offer and sell shares of common stock from time to time through Jefferies acting as agent. Sales of our shares of common stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act.

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

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

We will pay Jefferies a commission equal to a rate of 3.0% of the aggregate gross proceeds we receive from each sale of our shares of common stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. In addition, we have agreed to reimburse Jefferies for the fees and disbursements of its counsel, payable upon execution of the sales agreement, in an amount not to exceed \$50,000, in addition to certain ongoing disbursements of its legal counsel. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Jefferies under the terms of the sales agreement, will be approximately \$162,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Jefferies will provide written confirmation to us before the open on The Nasdaq Capital Market on the day following each day on which shares of common stock are sold under the sales agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to us.

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

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

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of the sales agreement will be filed as an exhibit to a current report on Form 8-K filed under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and will be incorporated by reference in this prospectus supplement.

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

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

LEGAL MATTERS

The validity of the shares of common stock offered hereby is being passed upon for us by Hogan Lovells US LLP, Baltimore, Maryland. Jefferies LLC is being represented in connection with this offering by Cooley LLP, New York, New York.

EXPERTS

The consolidated financial statements of Vaccinex, Inc. and its subsidiaries incorporated in this prospectus by reference from the Company's Annual Report on Form 10-K for the year ended December 31, 2019 have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which report expresses an unqualified opinion on the consolidated financial statements and includes an explanatory paragraph describing conditions that raise substantial doubt about Vaccinex, Inc.'s ability to continue as a going concern as described in Note 1 to the consolidated financial statements, which is herein incorporated by reference. Such consolidated financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The SEC file number for each of the documents incorporated by reference in this prospectus supplement is 001-38624. The following documents incorporated by reference into this prospectus supplement contain important information that you should read about us:

- our Annual Report on Form 10-K for the year ended December 31, 2019, filed on March 9, 2020;
- our Current Reports on Form 8-K filed with the SEC on <u>January 23, 2020</u> and <u>February 26, 2020</u>; and
- the description of our capital stock included under the caption "Description of Capital Stock" contained in our Registration Statement on Form 8-A filed with the SEC on <u>August 8, 2018</u>, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference into this prospectus supplement all documents (other than portions of documents that are either described in paragraph (e) of Item 201 of Regulation S-K or paragraphs (d)(1)-(3) and (e)(5) of Item 407 of Regulation S-K promulgated by the SEC and current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial registration statement of which this prospectus supplement forms a part but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Vaccinex, Inc., Attn: Corporate Secretary, 1895 Mount Hope Avenue, Rochester, New York 14620. In addition, copies of any or all of the documents incorporated herein by reference may be accessed at our website at www.vaccinex.com. The information on such website is not incorporated by reference and is not a part of this prospectus.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy and information statements and other information with the SEC. This prospectus supplement is part of a registration statement that we have filed with the SEC relating to the common stock to be offered under this prospectus supplement. This prospectus supplement does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the common stock to be offered under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement.

The SEC maintains an internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, where you may read and copy the registration statement, as well as our reports, proxy and information statements and other information. The address of the SEC's web site is www.sec.gov.

Copies of certain information filed by us with the SEC are also available on our website at *www.vaccinex.com*. Information contained in or accessible through our website does not constitute a part of this prospectus and is not incorporated by reference in this prospectus.

PROSPECTUS



\$125,000,000

Common Stock

We may offer and sell up to an aggregate of \$125,000,000 of common stock from time to time in one or more offerings in amounts, at prices and on terms described in one or more supplements to this prospectus.

This prospectus provides a general description of the common stock we may offer. Each time we offer common stock, we will provide specific terms of the common stock offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. A prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the common stock being offered.

This prospectus may not be used to sell our common stock unless accompanied by a prospectus supplement.

We may offer and sell our common stock to or through one or more agents, underwriters, dealers or other third parties or directly to one or more purchasers on a continuous or delayed basis. If agents, underwriters or dealers are used to sell our common stock, we will name them and describe their compensation in a prospectus supplement. The price to the public of our common stock and the net proceeds we expect to receive from the sale of such common stock will also be set forth in a prospectus supplement.

Our common stock is listed on the Nasdaq Capital Market under the symbol "VCNX." On February 12, 2020, the closing price of our common stock was \$6.48 per share.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 6 of this prospectus and under similar headings in the documents incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 11, 2020.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we have filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this registration statement, we may sell from time to time in one or more offerings the common stock described in this prospectus for an aggregate offering price of up to \$125,000,000. This prospectus provides you with a general description of our common stock being offered.

Each time we offer shares of common stock under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of the offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. This prospectus may not be used to sell our common stock unless accompanied by a prospectus supplement. Each such prospectus supplement and any free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents incorporated by reference into this prospectus.

You should carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference and the information below under the captions "Where You Can Find More Information" and "Incorporation by Reference" before you invest in our common stock. The information contained in this prospectus is not complete and may be changed. You should rely only on the information contained or incorporated by reference in this prospectus or in any prospectus supplement, or documents to which we otherwise refer you. We have not authorized any other person to provide you with different information. If anyone provides you with additional, different or inconsistent information, you should not rely on it. This prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement, if any, constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information in this prospectus, any documents we incorporate by reference herein, or the accompanying prospectus supplement, if any, is accurate as of any date other than the date on the front of each such document. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus and the documents that are incorporated by reference herein contain certain market data and industry statistics and forecasts that are based on studies and clinical trials sponsored by Vaccinex or third parties, independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not verified any of this data. Further, many of these statements involve risks and uncertainties and are subject to change based on various factors, including those discussed under the caption "Risk Factors" in this prospectus and under similar captions in the documents that are incorporated by reference herein. Accordingly, investors should not place undue reliance on this information.

References in this prospectus to the terms "Vaccinex," "the Company," "we," "our" and "us" or other similar terms mean Vaccinex, Inc. and our subsidiaries, unless we state otherwise or the context indicates otherwise.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this prospectus or the documents incorporated herein by reference regarding our strategy, future operations, future product research or development, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "goals," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus include, among other things, statements about:

- our estimates regarding our expenses, future revenues, anticipated capital requirements and our needs for additional financing;
- the implementation of our business model and strategic plans for our business and technology;
- the timing and success of the commencement, progress and receipt of data from any of our preclinical and clinical trials;
- our expectations regarding the potential safety, efficacy or clinical utility of our product candidates;
- the expected results of any clinical trial and the impact on the likelihood or timing of any regulatory approval;
- the difficulties in obtaining and maintaining regulatory approval of our product candidates;
- the rate and degree of market acceptance of any of our product candidates;
- the success of competing therapies and products that are or become available;
- regulatory developments in the United States and foreign countries;
- current and future legislation regarding the healthcare system;
- the scope of protection we establish and maintain for intellectual property rights covering our technology;
- developments relating to our competitors and our industry;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the performance of third parties, including collaborators, contract research organizations and third-party manufacturers;
- the development of our commercialization capabilities, including the need to develop or obtain additional capabilities; and
- the enforceability of the exclusive forum provisions in our amended and restated certificate of incorporation.

These statements are only current predictions and are subject to known and unknown risks, uncertainties and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements. We discuss many of these risks in greater detail in the risk factors in Item 1A of our 2018 Annual Report on Form 10-K. You should not rely upon forward-looking statements as predictions of future events.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, after the date of this prospectus, we are under no duty to update or revise any of the forward-looking statements, whether as a result of new information, future events or otherwise.

THE COMPANY

Company Overview

We are a clinical-stage biotechnology company engaged in the discovery and development of targeted biotherapeutics to treat serious diseases and conditions with unmet medical needs, including cancer, neurodegenerative diseases, and autoimmune disorders. We believe we are the leader in the field of SEMA4D biology and that we are the only company targeting SEMA4D as a potential treatment for cancer, neurodegenerative diseases, or autoimmune disorders. SEMA4D is an extracellular signaling molecule that regulates the migration of immune and inflammatory cells to sites of injury, cancer or infection. We are leveraging our SEMA4D antibody platform and our extensive knowledge of SEMA4D biology to develop our lead product candidate, pepinemab (VX15), which we believe utilizes novel mechanisms of action. We are focused on the development of pepinemab for the treatment of non-small cell lung cancer, osteosarcoma, melanoma and Huntington's disease. We have developed multiple proprietary platform technologies and are developing product candidates to address serious diseases or conditions that have a substantial impact on day-to-day functioning and for which treatment is not addressed adequately by therapies available on the market. We employ our proprietary platform technologies, including through our work with our academic collaborators, to identify potential product candidates for sustained expansion of our internal product pipeline and to facilitate strategic development and commercial partnerships.

Our lead platform technologies include our SEMA4D antibody platform and our ActivMAb antibody discovery platform.

- Our SEMA4D antibody platform is the application of our extensive knowledge of SEMA4D biology to develop our lead product candidate pepinemab for the treatment of various indications, including cancer and neuroinflammatory and neurodegenerative diseases. We believe pepinemab's mechanisms of action block the SEMA4D signal and activate innate physiological mechanisms to respond to tumors or tissue injury. We have demonstrated in animal models in preclinical studies that the biological activities associated with an antibody blockade of SEMA4D can promote immune cell infiltration into tumors and the repair or prevention of neurological damage in neuroinflammatory and neurodegenerative diseases.
- Our ActivMAb® antibody discovery platform is a proprietary human antibody discovery platform based on a novel method for expressing large and diverse libraries of high affinity, full-length human monoclonal antibodies on the surface of vaccinia, a mammalian virus. We believe our ActivMAb technology offers (i) rapid generation of high affinity, full-length, human monoclonal antibodies synthesized and naturally modified in mammalian cells, (ii) expression and selection of antibodies that easily and predictably transition to manufacturing in mammalian lines, and (iii) an innovative and efficient method for selecting antibodies against multi-pass membrane proteins, an important class of pharmacological targets. Our product candidate VX5 was generated by our ActivMAb platform and is currently in preclinical development for the treatment of multiple sclerosis, or MS, and potentially for other autoimmune disorders. We intend to continue to utilize our ActivMAb platform to identify additional product candidates for our own pipeline development and for strategic collaborations.

In addition, we and our academic collaborators are using our Natural Killer T, or NKT, vaccine platform to discover product candidates that target and extend the activity of NKT cells. NKT cells work directly to kill certain types of parasites and cells, including tumor cells and virus-infected cells. We are applying our agonists to direct NKT cells to the site of tumors, potentially enhancing tumor-specific immunity through recruitment and activation of cytotoxic T cells and antibody-armed natural killer cells that will work to eradicate the tumor.

Vaccinex Product Pipeline



Our lead product candidate pepinemab is currently in clinical development for the treatment of NSCLC, osteosarcoma, melanoma and Huntington's disease, through our efforts or through investigator-sponsored trials, or ISTs. Our additional product candidates VX5 and VX25 are in earlier stages of development and were generated using our ActivMAb and NKT vaccine platforms, respectively. VX5 is a human antibody to CXCL13, a molecule that regulates the formation of immune tissues, and is currently in preclinical development for the treatment of MS and potentially for other autoimmune disorders. VX25, a bi-specific NKT cell stimulator, is being evaluated in various preclinical cancer models and seeks to address challenges for the therapeutic application of NKT cell stimulation for cancer immunotherapy. We believe our multiple platform technologies position us well for continued pipeline expansion and partnership opportunities going forward.

Pepinemab

Pepinemab is a humanized monoclonal antibody that binds and blocks the signaling activity of SEMA4D. We are advancing pepinemab with what we believe to be novel mechanisms of action for the treatment of cancer and certain neurodegenerative diseases, including Huntington's disease.

Cancer - NSCLC, Osteosarcoma and Melanoma

Pepinemab is currently being studied as a treatment for advanced solid tumors, including NSCLC, osteosarcoma, and melanoma. We have demonstrated in preclinical tumor models that SEMA4D regulates infiltration of immune precursor cells into tumor tissue. Our preclinical data suggest that blocking SEMA4D promotes infiltration of immune cells that can eradicate the tumor. We have also demonstrated in preclinical models the potential for synergy between pepinemab and a checkpoint inhibitor when used in combination. We completed a Phase 1 clinical trial of pepinemab as a single-agent cancer therapy and released top-line data in October 2014. Pepinemab was well tolerated in this clinical trial. In October 2017 in collaboration with Merck KGaA, we initiated the CLASSICAL—Lung clinical trial, a Phase 1b/2 clinical trial of pepinemab in combination with avelumab, an inhibitor of the PD-1/PD-L1 checkpoint pathway, in patients with NSCLC who have not previously been treated with immunotherapy. In July 2018, an additional cohort was added to the CLASSICAL—Lung study to include patients who failed prior immunotherapy. The CLASSICAL—Lung clinical trial has completed enrollment. We anticipate topline data for this trial in the first half of 2020. In February 2018, The Children's Oncology Group with financial support of the National Cancer Institute, initiated a Phase 1/2 clinical trial of pepinemab as a single agent in pediatric patients with recurrent, relapsed, or refractory solid tumors,

including osteosarcoma. In June 2018, a Phase 1 IST of pepinemab in combination with *Yervoy*® or with *Opdivo*® began at the UCLA Jonsson Comprehensive Cancer Center in patients with advanced melanoma who have progressed on prior anti-PD-1/PD-L1 based therapies.

Huntington's Disease

We are studying pepinemab as a treatment for Huntington's disease, which is a neurodegenerative genetic disorder that typically manifests in mid-adult life. Our study of pepinemab in Huntington's disease is based on our prior research of neurodegenerative disease mechanisms, where we demonstrated in preclinical models that SEMA4D triggers activation of both microglia and astrocytes, the innate inflammatory cells of the central nervous system. The chronic activation of microglia and astrocytes has been implicated as an important disease mechanism in Huntington's disease, progressive MS, and other neurodegenerative disorders. We initiated the SIGNAL study, a Phase 2 clinical trial, in July 2015 in early manifest and late prodromal Huntington's disease patients. This clinical trial builds upon preclinical studies in an animal model of Huntington's disease and safety data from a Phase 1 dose-escalation clinical trial of pepinemab in MS patients that we completed in November 2014. We anticipate topline data from the SIGNAL trial in the second half of 2020. The U.S. Food and Drug Administration, or the FDA, has granted both Orphan Drug designation and Fast Track designation to pepinemab for Huntington's disease.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in April 2001. Our principal executive offices are located at 1895 Mount Hope Avenue, Rochester, New York 14620, and our telephone number is (585) 271-2700. Our website address is www.vaccinex.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this prospectus. You should not rely on any such information in making your decision to purchase our common stock.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

RISK FACTORS

Investing in our common stock involves a high degree of risk. The prospectus supplement applicable to each offering of our common stock will contain a discussion of the risks applicable to an investment in our common stock. You should carefully consider and evaluate all of the information contained in this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you decide to purchase our common stock. In particular, you should carefully consider and evaluate the risks and uncertainties described in "Part I – Item 1A. Risk Factors" of our most recent Annual Report on Form 10-K, as updated by the additional risks and uncertainties set forth or incorporated by reference herein. Additional risks and uncertainties that we are unaware of or that we believe are not material at this time could also materially adversely affect our business, financial condition or results of operations. Any of these risks and uncertainties could materially and adversely affect the trading price or value of our common stock. As a result, you could lose all or part of your investment.

This prospectus also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks faced by us described below and elsewhere in this prospectus. See "Special Note Regarding Forward-Looking Statements" for information relating to these forward-looking statements.

Our amended and restated certificate of incorporation contains exclusive forum provisions, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.

Our amended and restated certificate of incorporation provides that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will, to the fullest extent permitted by law, be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws or any action asserting a claim that is governed by the internal affairs doctrine.

In addition, our amended and restated certificate of incorporation provides that, unless we consent in writing to an alternative forum, the federal courts of the United States will, to the fullest extent permitted by law, be the sole and exclusive forum for any claim arising under the Securities Act of 1933, as amended, or the Securities Act. However, as previously disclosed in our Current Report on Form 8-K filed on March 4, 2019, in light of the Court of Chancery's opinion in Sciabacucchi v. Salzberg, C.A. No. 2017-0931-JTL, invalidating provisions in the certificates of incorporation of Delaware companies that purport to limit to federal court the forum in which a stockholder could bring a claim under the Securities Act unless and until the Court of Chancery's decision is reversed by the Delaware Supreme Court on appeal or otherwise abrogated, we do not intend to enforce this provision of our amended and restated certificate of incorporation. If the Delaware Supreme Court affirms the Court of Chancery's decision or otherwise makes a determination that provisions such as these are invalid, then we will seek approval by our stockholders to amend our amended and restated certificate of incorporation at our next regularly scheduled annual meeting of stockholders to remove the provision. As a result of the Court of Chancery's decision or a decision by the Supreme Court of Delaware affirming the Court of Chancery's decision, we may incur additional costs associated with this provision, which could have an adverse effect on our business, financial condition or results of operations.

For the avoidance of doubt, the exclusive forum provisions described above do not apply to any claims arising under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder.

These choice of forum provisions may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers, employees or agents, which may discourage such lawsuits against us and our directors, officers, employees and agents even though an action, if successful, might benefit our stockholders. The applicable courts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. With respect to the provision making the Court of Chancery the sole and exclusive forum for certain types of actions, stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near Delaware. Finally, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could have a material adverse effect on our business, financial condition or results of operations.

USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement relating to a specific offering, we intend to use the net proceeds from the sale of common stock by us under this prospectus for general corporate purposes, which may include working capital, capital expenditures, research and development expenditures, clinical trial expenditures, commercial expenditures, debt service costs and repayment, acquisitions of new technologies, products or businesses, and investments. Additional information on the use of net proceeds from the sale of common stock by us under this prospectus may be set forth in the prospectus supplement relating to the specific offering.

PLAN OF DISTRIBUTION

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

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

We may also sell the securities covered by this registration statement in an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price on or through the facilities of the Nasdaq Capital Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale. Such at the market offerings, if any, may be conducted by underwriters acting as principal or agent.

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

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

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any overallotment or other option. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

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

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

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

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any underwriters or agents who are qualified market makers on the Nasdaq Capital Market may engage in passive market making transactions in the securities on the Nasdaq Capital Market in accordance with Rule 103 of Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

The validity of the shares of common stock offered hereby is being passed upon for us by Hogan Lovells US LLP, Baltimore, Maryland.

EXPERTS

The consolidated financial statements of Vaccinex, Inc. and its subsidiaries incorporated in this prospectus by reference from the Company's Annual Report on Form 10-K for the year ended December 31, 2018 have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such consolidated financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The SEC file number for each of the documents incorporated by reference in this prospectus is 001-38624. The documents incorporated by reference into this prospectus contain important information that you should read about us.

The following documents are incorporated by reference into this document:

- our Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on March 13, 2019;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2018 from our Definitive Proxy Statement on Schedule 14A filed with the SEC on <u>April 9, 2019</u>;
- our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2019, June 30, 2019 and September 30, 2019, filed with the SEC on May 15, 2019, August 14, 2019 and November 12, 2019, respectively;
- our Current Reports on Form 8-K (other than portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits accompanying such reports that relate to such items) filed with the SEC on <u>January 24, 2019</u>, <u>March 4, 2019</u>, <u>March 11, 2019</u>, <u>May 15, 2019</u>, <u>July 19, 2019</u>, <u>July 31, 2019</u> and <u>January 23, 2020</u>; and
- the description of our capital stock included under the caption "Description of Capital Stock" contained in our Registration Statement on Form 8-A filed with the SEC on <u>August 8, 2018</u>, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference into this prospectus all documents (other than portions of documents that are either described in paragraph (e) of Item 201 of Regulation S-K or paragraphs (d)(1)-(3) and (e)(5) of Item 407 of Regulation S-K promulgated by the SEC and current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial registration statement of which this prospectus forms a part but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Vaccinex, Inc., Attn: Corporate Secretary, 1895 Mount Hope Avenue, Rochester, New York 14620. In addition, copies of any or all of the documents incorporated herein by reference may be accessed at our website at www.vaccinex.com. The information on such website is not incorporated by reference and is not a part of this prospectus.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy and information statements and other information with the SEC. This prospectus is part of a registration statement that we have filed with the SEC relating to the common stock to be offered under this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the common stock to be offered under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement.

The SEC maintains an internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, where you may read and copy the registration statement, as well as our reports, proxy and information statements and other information. The address of the SEC's web site is http://www.sec.gov.

Copies of certain information filed by us with the SEC are also available on our website at http://www.vaccinex.com. Information contained in or accessible through our website does not constitute a part of this prospectus and is not incorporated by reference in this prospectus.



Common Stock

PRO	SPECTU	JS SUP	PLEM1	ENT

Jefferies

March 27, 2020