UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 26, 2023

Vaccinex, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-38624**	**16-1603202**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

1895 Mount Hope Avenue, Rochester, New York	**14620**
(Address of principal executive offices)	**(Zip Code)**

(585) 271-2700
(Registrant's telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.0001 per share	VCNX	Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

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

Item 7.01 Regulation FD Disclosure.

On September 26, 2023, Vaccinex, Inc. (the "Company") issued a press release announcing that it will present findings supporting development of Pepinemab for the treatment of neurodegenerative diseases and cancer at (1) the Keystone Symposia, B Cells and Tertiary Lymphoid Structures: Emerging Targets in Cancer Therapeutics, on October 1-5, 2023, and (2) the 16th edition of the Clinical Trials on Alzheimer's Disease Conference to be held in Boston on October 24-27, 2023.

The information furnished pursuant to this Item 7.01, including Exhibit 99.1 shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities under such section and shall not be deemed to be incorporated by reference into any filing of the Company under the Securities Act of 1944, as amended, or the Exchange Act.

Item 9.01 Financial Statements and Exhibits.

Exhibit No.	Description
99.1	Press Release, dated September 26, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

VACCINEX, INC.

Date: September 26, 2023

By: /s/ Scott E. Royer
Scott E. Royer
Chief Financial Officer

Exhibit 99.1

Vaccinex Reports Groundbreaking Findings at Medical Conferences Supporting Development of Pepinemab for the Treatment of Neurodegenerative Diseases and Cancer

"Pepinemab, a SEMA4D blocking antibody, is a novel potential treatment for neurodegenerative disease" will be a podium presentation at the 16th edition of the Clinical Trials on Alzheimer's Disease Conference to be held in Boston on October 24-27, 2023.

"Inhibition of Semaphorin 4D in Combination with Immune Checkpoint Therapy Induces Organized Lymphoid Structures within the Tumor Microenvironment that Correlate with Clinical Outcome" will be a podium presentation at the Keystone Symposia, B Cells and Tertiary Lymphoid Structures: Emerging Targets in Cancer Therapeutics, October 1-5, 2023.

ROCHESTER, N.Y., September 26, 2023 — Vaccinex, Inc. (Nasdaq: VCNX), a clinical-stage biotechnology company will report on novel findings for its lead product, pepinemab, with implications for treatment of Alzheimer's and other slowly progressive neurodegenerative diseases and for cancer immunotherapy at two upcoming Medical Conferences.

- Results from our phase 2 SIGNAL trial suggest pepinemab is the **first therapeutic agent that appears to have the potential to prevent decline in brain metabolic activity and to slow or halt cognitive decline** in Huntington's disease (HD) [1], a slowly progressive, orphan neurodegenerative disease with many pathological similarities to the much more prevalent Alzheimer's disease (AD). Encouraged by these findings, a separate, randomized, phase 1/2a study in AD is ongoing in which the last patient is anticipated to complete the planned 12-months of treatment in early June 2024.
- Pepinemab in combination with a checkpoint inhibitor is, to our knowledge, the **first treatment that has shown the potential to induce formation of lymphoid structures in tumors** that promote efficient immune responses and are known to be associated with improved outcomes in head and neck cancer. Clinical results indicate an approximate doubling of objective responses (ORR) and progression free survival (PFS) relative to historical results with checkpoint monotherapy in patients with hard-to-treat tumors that express low levels of PD-L1 (CPS<20) (described in detail below).

Alzheimer's Disease

Vaccinex completed enrollment in the randomized, double-blind SIGNAL-AD phase 1/2a study (NCT04381468) for early AD in May 2023. The last patient is anticipated to complete the planned 12 months of treatment by early June 2024 at which time the database will be locked and results analyzed. Key endpoints include brain metabolic activity (FDG-PET, a biomarker of disease progression) along with measures of cognition specific to AD (CDR-SB, ADAS-Cog13) that have been recognized as clinically meaningful by the U.S. Food and Drug Administration (FDA). Investors will be aware of recent excitement surrounding full FDA approval of Eisai and Biogen's drug Leqembi (lecanemab), the first anti-Aß amyloid antibody for treatment of AD. A second such drug from Eli Lilly, donanemab, has reported equivalent data and may be FDA approved before year end. Clinical consensus is that Leqembi and donanemab provide a modest but real benefit to patients at a very early stage of disease. Common side

effects associated with these drugs, however, include an inflammatory and hemorrhagic response in brain denoted as ARIA. Although ARIA often resolves itself, it has proven to be life-threatening in a small percentage of patients. As a result, all patients treated with these drugs must be followed carefully with significant effort and expense to avoid complications. **It is important to appreciate that pepinemab has a very different mechanism of action than Leqembi or donanemab and, in clinical studies conducted to date, has not been found to be associated with inflammatory responses in the brain.**

We believe that use of pepinemab to treat slowly progressive neurodegenerative diseases like AD has been substantially de-risked by results from our completed phase 2 study in HD. We have had the opportunity to meet with several major pharmaceutical companies. We believe from their responses that they have prioritized improving treatments for AD ("Our team was really intrigued by the data you presented and would like to continue our dialogue. However, we see your upcoming AD data as being essential to confirm the signal obtained in HD, and we would therefore gladly re-engage then."; "…we are enthused by the mechanism of Sema4D. We would be interested in re-engaging once your on-going Phase 2 [AD] is available."; "Let's meet again when you are able to discuss the AD data with pepinemab.")

We believe that the prevalence of AD (6 million people diagnosed with AD in the US alone) and current concerns about the limitations of anti-Aß amyloid antibodies would make pepinemab attractive as a potential alternative to anti-Aß antibodies or possibly for use in combination with an anti-Aß for greater efficacy. The potential impact of the AD program on Vaccinex valuation and financial resources, therefore, make this Vaccinex's most important near term catalyst. **Our highest priority in the coming months will be to complete the SIGNAL-AD trial, which we believe may make substantial resources available for our initiatives in cancer and other neurodegenerative diseases such as HD.**

Cancer

The Phase 2 KEYNOTE-B84 study (NCT04815720) evaluated Vaccinex's pepinemab antibody in combination with Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab) for immunotherapy of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC). Results of a preplanned interim analysis of the first 36 patients treated in this study indicated that the Objective Response (ORR) for the PD-L1 low population, CPS <20 (N=19), was 21.1% (2 CR and 2 PR) and median progression free survival (PFS) was 5.79 months, which are approximately twice that of historical ORR and PFS for checkpoint monotherapy in this population [2]. In contrast, in the CPS ≥20 (N=17) subgroup, the ORR and PFS for combination therapy was similar to historical checkpoint monotherapy. The improvement in response to treatment is important for the 55% of HNSCC patients whose tumors are characterized as CPS <20. These data are also consistent with a prior study in which we observed that the combination of pepinemab with PD-L1 inhibitor BAVENCIO® (avelumab) appeared to approximately double ORR in patients with PD-L1-low non-small cell lung cancer (NCT03268057) [3].

In view of these clinical findings, we investigated the changes in the tumor immune environment that might correlate with response to pepinemab treatment by analyzing pre-treatment and on-treatment tumor biopsies collected during the KEYNOTE-B84 study. The results indicate that treatment with **pepinemab in combination with KEYTRUDA appears to induce formation of highly organized lymphoid aggregates in the tumor** of patients who demonstrate disease control (complete response plus partial response plus stable disease). Such aggregates are characterized by a high density of B cells, antigen-presenting dendritic cells and activated T cells (**Figure 1A**); further, treatment-induced increase in the number of aggregates correlates with Disease Control (**Figure 1B**) and with Progression Free Survival (**Figure 1C**).

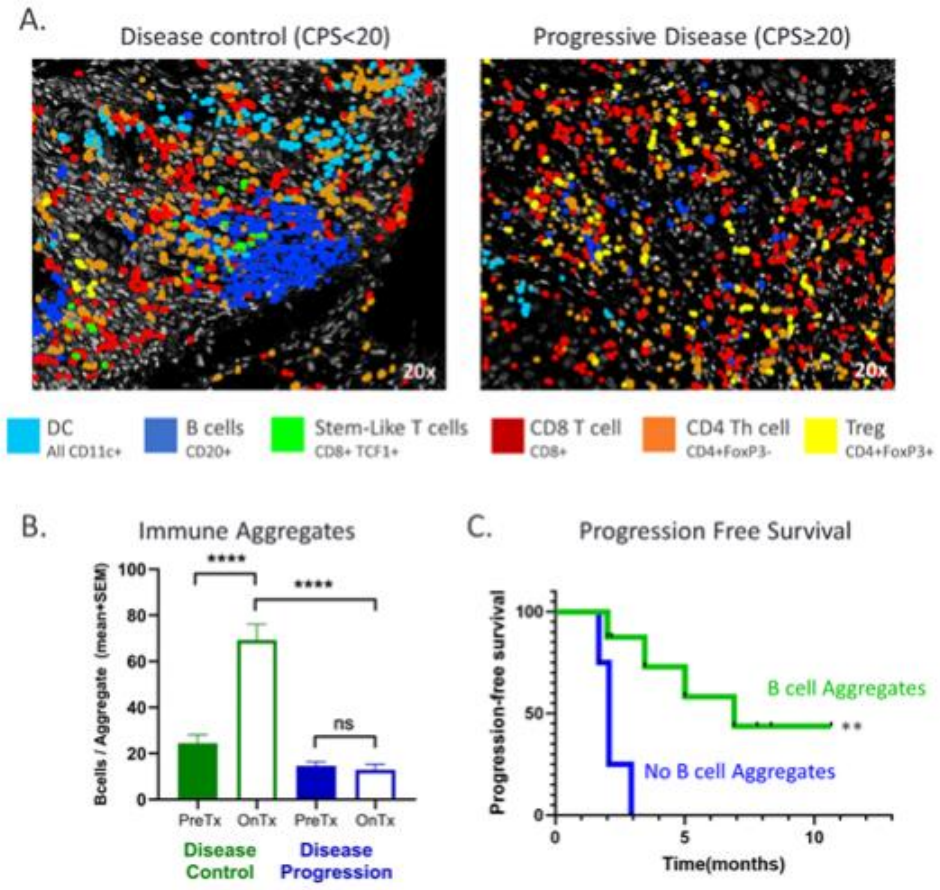

Figure 1. **Treatment with pepinemab in combination with KEYTRUDA appears to induce formation of highly organized lymphoid structures in tumors that correlate with disease control.**

A. Representative images of 5-week on-treatment biopsies. Left: from a patient with stable disease, tumor biopsy contains highly organized immune aggregates consisting of high density antigen presenting cells (B cells, DC dendritic cells) as well as T lymphocytes. Right: from a patient with progressive disease, immune cells in the tumor biopsy are disorganized and include relatively high levels of inhibitory T regulatory (Treg) cells, but relatively few antigen presenting cells (B cells, DC).

B. Patients who experience clinical benefit (Disease Control) during treatment with pepinemab and KEYTRUDA have a higher frequency of mature immune aggregates with a high density of B cells in their on-treatment biopsy compared to their pre-treatment biopsies, $p<0.0001$. This difference is not observed in on- and pre-treatment biopsies from patients whose cancer progresses rapidly. One-way ANOVA, **** $p<0.0001$; ns = not significant, $p\geq0.05$.

C. Immune Aggregates correlate with PFS. On-treatment patient biopsies with B cell aggregates positively correlate with longer progression-free survival. Log Rank survival analysis, $p= 0.0056$.

We and our collaborators at the Winship Cancer Center of Emory University have reported similar observations indicating that combination immunotherapy with pepinemab induces mature lymphoid structures in tumors of patients with metastatic melanoma treated in the neoadjuvant setting (NCT03690986) [4].

Based on these findings, we and our pharmaceutical collaborator, Merck Sharp & Dohme LLC, a subsidiary of Merck and Co., Inc., Rahway, NJ, USA, are in the preliminary testing and design stages of a potential extension of this study that may focus on treatment with pepinemab and KEYTRUDA in combination with chemotherapy. In previous studies of checkpoint monotherapy, addition of chemotherapy has been observed to approximately double the frequency of ORR. We believe that a similar effect is likely for addition of chemotherapy to treatment with pepinemab in combination with KEYTRUDA. We hope to subsequently determine whether, in the setting of more mature lymphoid structures in tumors, such treatment also prolongs overall survival.

Vaccinex has global commercial and development rights to pepinemab and is the sponsor of the KEYNOTE-B84 study which is being performed in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck and Co., Inc., Rahway, NJ, USA. Additional information about the study is available at: clinicaltrials.gov .

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

References:

1. Feigin AS, Evans EE, Fisher TL, et al. Pepinemab antibody blockade of SEMA4D in patients with early Huntington's Disease: a randomized, placebo-controlled, Phase 2 trial. *Nature Medicine*, 2022 Aug 8;1-11. doi: 10.1038/s41591-022-01919-8.

2. Burtness B, Harrington KJ, Greil R, et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. *The Lancet* 2019; 394: 1915-1928. doi:10.1016/ S0140-6736(19)32591-7

3. Shafique MR, Fisher TL, Evans EE, Leonard JE, et al. A Phase Ib/II Study of Pepinemab in Combination with Avelumab in Advanced Non-Small Cell Lung Cancer. *Clin Cancer Res.* 2021 Jul 1;27(13):3630-3640. doi: 10.1158/1078-0432.CCR-20-4792.

4. Olson B, Mallow C, Reilly C, et al. Neoadjuvant SEMA4D blockade with nivolumab alters suppressive myeloid cells while elevating B cell and CD26hi T cell infiltration in the tumors of patients with resectable stage III melanoma. *Journal for ImmunoTherapy of Cancer* 2022;10: doi: 10.1136/jitc-2022-SITC2022.0613

About Pepinemab

Pepinemab is a humanized IgG4 monoclonal antibody designed to block SEMA4D, which can trigger collapse of the actin cytoskeleton and loss of homeostatic functions of astrocytes and glial cells in the brain and dendritic cells in immune tissue. Pepinemab has been administered to more than 400 patients and appears to be well-tolerated and to have a favorable safety profile.

About Vaccinex Inc.

Vaccinex, Inc. is pioneering a differentiated approach to treating slowly progressive neurodegenerative diseases and cancer through the inhibition of semaphorin 4D (SEMA4D). The Company's lead drug candidate, pepinemab, is designed to block SEMA4D, a potent biological effector that is believed to trigger damaging inflammation in chronic diseases of the brain and inhibit immune infiltration and activation in tumors. In neurodegenerative diseases, pepinemab is being studied as a monotherapy in the Phase 1/2a SIGNAL-AD study in Alzheimer's Disease, with ongoing exploration of potential Phase 3 development in Huntington's disease. In oncology, pepinemab is being evaluated in combination with KEYTRUDA® in the Phase 1b/2 KEYNOTE-B84 study in recurrent or metastatic head and neck cancer (HNSCC) and in combination with BAVENCIO® in a Phase 1b/2 study in patients with metastatic pancreatic adenocarcinoma (PDAC). The oncology clinical program also includes several investigator-sponsored studies in solid tumors including breast cancer and melanoma.

Forward Looking Statements

To the extent that statements contained in this presentation are not descriptions of historical facts regarding Vaccinex, Inc. ("Vaccinex," "we," "us," or "our"), they are forward-looking statements reflecting management's current beliefs and expectations. Such statements include, but are not limited to, statements about our plans, expectations and objectives with respect to the results and timing of the SIGNAL-AD clinical trial; the direct or indirect effect the SIGNAL-AD clinical trial will have on our financial resources available for our innovative initiatives; expectations and objectives with respect to the results and timing of the KEYNOTE-B84 clinical trial, the use and potential benefits of pepinemab in neurodegenerative diseases like AD and HD, and cancer; our plans, expectations and objectives with respect to the results and timing of a trial of treatment with pepinemab and KEYTRUDA in combination with chemotherapy in R/M HNSCC, lung cancer, metastatic PDAC and other indications, the potential for benefits as compared to single agent KEYTRUDA® or BAVENCIO®, expectations with respect to the collaboration of Merck, the expected timeline for disclosure of trial results at scientific conferences or through publications, and other statements identified by words such as "anticipate," "believes," "hope," "being," "may," "will," "appears," "expect," "continue," "ongoing," "potential", "possibly," "prevents," "suggest", and similar expressions or their negatives (as well as other words and expressions referencing future events, conditions, or circumstances). Forward-looking statements involve substantial risks and uncertainties that could cause the outcome of our research and pre-clinical development programs, clinical development programs, future results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, uncertainties inherent in the execution, cost and completion of preclinical studies and clinical trials, that interim and preliminary data may not be predictive of final results and does not ensure success in later clinical trials,

uncertainties related to regulatory approval, risks related to our dependence on our lead product candidate pepinemab, the impact of the COVID-19 pandemic, the possible delisting of our common stock from Nasdaq if we are unable to regain compliance with the Nasdaq listing standards, and other matters that could affect our development plans or the commercial potential of our product candidates. Except as required by law, we assume no obligation to update these forward-looking statements. For a further discussion of these and other factors that could cause future results to differ materially from any forward-looking statement, see the section titled “Risk Factors” in our periodic reports filed with the Securities and Exchange Commission (“SEC”) and the other risks and uncertainties described in the Company’s annual year-end Form 10-K and subsequent filings with the SEC.

Investor Contact

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