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): July 31, 2024

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 8.01 Other Events.

On July 31, 2024, Vaccinex, Inc. (the "Company") issued a press release announcing positive results of its early stage SIGNAL-AD clinical trial of pepinemab antibody in Alzheimer's Disease ("AD") and that topline results of the trial were presented at the Alzheimer's Association International Conference in Philadelphia. A copy of the press release is attached as Exhibit 99.1 and incorporated by reference herein.

Item 9.01 Financial Statements and Exhibits.

Exhibit No.	Description
99.1	Press Release, dated July 31, 2024
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: July 31, 2024

By: /s/ Jill Sanchez
Jill Sanchez
Chief Financial Officer

Exhibit 99.1

Vaccinex Reports Positive Data for SIGNAL-AD Phase 1b/2 trial of Pepinemab in Alzheimer's Disease

Results affirm expectation of a novel mechanism of action targeting astrocyte activation to delay progression of Alzheimer's disease from early stage Mild Cognitive Impairment

Findings echo previous phase 2 results in Huntington's disease based on similarities to neuroimmune pathology in Alzheimer's

ROCHESTER, N.Y., July 31, 2024 - Vaccinex, Inc. (Nasdaq: VCNX), a clinical-stage biotechnology company pioneering treatment of Alzheimer's disease (AD) with anti-Semaphorin 4D (SEMA4D) antibody, today announced positive results of its early stage SIGNAL-AD clinical trial of pepinemab antibody in AD. Topline results were presented by Eric Siemers, MD, Principal Investigator of the SIGNAL-AD trial, at the Alzheimer's Association International Conference in Philadelphia.

The clinical trial met its designated primary endpoint of safety by indicating that pepinemab is well-tolerated by patients with AD. **No Serious Treatment Emergent Adverse Events (TEAE) Related to Treatment were reported** by investigators at any of the 16 clinical sites that participated in this study. The only TEAE leading to discontinuation in the entire trial was in the placebo group. Vaccinex had previously reported that pepinemab (VX15/2503) was well-tolerated by patients with Huntington's disease (HD) and multiple sclerosis (MS).

An important secondary endpoint of the study was to determine whether pepinemab prevents decline in brain metabolic activity consistent with blocking astrocyte reactivity as evidenced by an increase in FDG-PET imaging signal in a major brain region known to be affected by disease progression. This was determined over the course of 12-months treatment with pepinemab relative to placebo. **We report that pepinemab treatment resulted in a statistically significant increase (p=0.0297) in FDG-PET signal** in the medial temporal cortex of patients with Mild Cognitive Impairment (MCI) due to AD. The medial temporal region of brain includes hippocampus and entorhinal cortex known to be affected during early disease progression in many patients with MCI. A similar significant result of pepinemab treatment on brain metabolic activity was previously shown in our phase 2 study of HD which we believe highlights mechanistic similarities in the pathology of these two neurodegenerative diseases.

Although the present study was not sufficiently powered to detect cognitive effects or changes in some additional secondary endpoints with statistical significance, we previously reported that, in a larger study that enrolled approximately 90 HD patients/arm with early symptoms of cognitive deficits, seemingly similar to MCI in AD, pepinemab treatment improved performance on key cognitive and psychological measures.

Business Considerations

“We believe that results of the SIGNAL-AD study demonstrate that pepinemab has a similar effect in Alzheimer’s to those we previously described for a key outcome in Huntington’s disease, preventing the characteristic disease-related decline of brain metabolic activity in a brain region known to be affected early in disease progression,” said the Company’s CEO, Maurice Zauderer, PhD. This positive data release suggests that pepinemab has the potential to benefit patients with MCI due to AD. AD and HD share important pathological features and clinical symptoms, and we believe our approach of confirming similar treatment effects of pepinemab in these two different neurodegenerative diseases is strongly supportive of pepinemab as a potentially well-tolerated and effective treatment for both Alzheimer’s and Huntington’s disease.”

“Our study indicates that pepinemab may be most effective in patients with very early stage symptoms, e.g. Mild Cognitive Impairment (MCI) due to AD, but not subsequent dementia,” Dr. Zauderer added. “This suggests that a promising treatment strategy would be to identify people with MCI as early as possible and to treat with pepinemab to keep them from progressing for as long as possible. We believe that, to date, no disease modifying therapy has been shown to be effective in later stages of AD dementia. Perhaps for AD, as for cancer, if you wait, new pathologies come into play and drugs that may have been helpful earlier become less effective.”

The Alzheimer’s Association estimates that 12% to 18% of people aged 60 or older are living with MCI due to AD and that about one-third of these patients will develop dementia within five years. A drug that can slow progression of MCI could significantly extend a rewarding and productive life for people at risk.

Pepinemab has been well-tolerated in clinical trials that enrolled a total of more than 600 patients primarily in neurological indications, AD, HD, and MS. Current concerns about the limitations of treatment with approved anti-Aß amyloid antibodies such as Leqembi™ (Eisai and Biogen) and Kisunla™ (Eli Lilly) might make pepinemab, if approved, attractive as either an alternative for patients at high risk for adverse events related to treatment with Leqembi or Kisunla, or as a complementary treatment that might enhance the benefit to patients of treatment with such anti-Aß antibodies.

The SIGNAL-AD study was funded in part by a grant from the Alzheimer’s Association as well as by investments from the Alzheimer’s Drug Discovery Foundation (ADDF).

Vaccinex is actively exploring the potential for continuing late stage development in AD together with a major pharmaceutical partner.

About the SIGNAL-AD trial (NCT04381468)

The NCT04381468, or SIGNAL-AD, trial is a Phase 1b/2, double-blind, randomized, placebo-controlled, multicenter study of pepinemab in 50 patients who have MCI due to AD or early Alzheimer's dementia, with amyloid positive status and CDR-GS of 0.5-1 and MMSE 17-26. The study's primary endpoint related to safety and tolerability; secondary endpoint includes assessment of brain metabolic activity determined by FDG-PET. Patients received pepinemab (40 mg/kg) randomized 1:1 to placebo, every four weeks for 12 intravenous infusions. Prior clinical results of pepinemab treatment for Huntington's disease indicate that pepinemab may be capable of preventing decline in brain metabolic activity consistent with blocking astrocyte reactivity and associated with apparent improvements in cognition (NCT02481674). Results of the Phase 2 NCT02481674 trial were published in Nature Medicine, December 2022.

About Pepinemab

Pepinemab is a humanized IgG4 monoclonal antibody designed to block SEMA4D, which can otherwise bind to plexin-B1 receptors to trigger collapse of the actin cytoskeleton in cells and lead to loss of homeostatic functions of astrocytes and other glial cells in the brain and of dendritic cells in immune tissue. Pepinemab appears to have been well-tolerated with a favorable safety profile in multiple clinical trials in different neurological and cancer indications.

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, blocks SEMA4D, a potent biological effector that it believes triggers damaging inflammation in chronic diseases of the brain and prevents infiltration and activation of immune cells in tumors. Pepinemab was studied as a monotherapy in the Phase 1b/2 SIGNAL-AD study in Alzheimer's Disease, and the Company has previously published promising Phase 2 data in Huntington's disease. Vaccinex believes pepinemab could also be an important contributor to combination therapy in AD. 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.

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 Corp, a subsidiary of Merck and Co, Inc. Kenilworth, NJ, USA.

KEYTRUDA is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., Kenilworth, NJ, USA. BAVENCIO®/avelumab is provided by Merck KGaA, Darmstadt, Germany, previously as part of an alliance between the healthcare business of Merck KGaA, Darmstadt, Germany and Pfizer.

Forward Looking Statements

To the extent that statements contained in this press release 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 the use and potential benefits of pepinemab treatment in patients with AD and HD; the potential for use of pepinemab as an alternative or complement to other treatments; the potential and prospects for continuing late stage development of pepinemab; our plans, expectations and objectives with respect to the results of the KEYNOTE-B84 clinical trial; the use and potential benefits of pepinemab in oncology indications; the potential for benefits as compared to single agent KEYTRUDA® or BAVENCIO®; expectations with respect to the collaboration of Merck; and other statements identified by words such as "believe," "being," "will," "appear," "expect," "ongoing," "potential," "promising," "indicate," "suggest," "apparent", 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, risks related to reliance on third parties, 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 possible delisting of our common stock from Nasdaq if the Company is unable to regain and sustain 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, the Company assumes 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 and the other risks and uncertainties described in the Company’s annual year-end Form 10-K and subsequent filings with the SEC.

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