Vaccinex Reports Completion of Last Patient Visit in Randomized, SIGNAL-AD Phase 1b/2 Study of Pepinemab Treatment for Alzheimer's Disease

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Company expects to lock database in June and
remains on track to report key outcomes later in July.

Pepinemab targets astrocyte reactivity and neuroinflammation,
believed to be key drivers of neurodegeneration.

ROCHESTER, N.Y., June 06, 2024 (GLOBE NEWSWIRE) -- Vaccinex, Inc. (Nasdaq: VCNX), a clinical-stage biotechnology company pioneering a differentiated approach to treating neurodegenerative disease and cancer through the inhibition of Semaphorin 4D (SEMA4D), today announced that the last patient completed their last visit in its randomized, placebo-controlled double-blind study of pepinemab treatment for Alzheimer's disease.

What can we expect to learn from this study?

- Vaccinex scientists discovered and published that SEMA4D, a molecule that binds to high affinity plexin-B1 receptors predominantly expressed on astrocytes in the brain, is highly upregulated on stressed or damaged neurons during progression of Alzheimer's Disease (AD) .
- Astrocytes, which are key brain cells that support the health and function of neurons, undergo substantial changes in morphology and gene expression when SEMA4D binds to their plexin-B1 receptors. As a result, they switch from normal supportive functions to neurotoxic inflammatory activity that is believed to accelerate and aggravate progression of AD.
- The Company's hypothesis, which is being tested in the SIGNAL-AD study, is that treating with pepinemab antibody can block signaling by SEMA4D and prevent some or all the damaging consequences of astrocyte activation.
- The Company has previously reported that antibody blockade of SEMA4D appears to protect and restore healthy astrocyte functions and to slow or prevent disease progression in patients with Huntington's disease by several different measures.
- Key outcomes of the SIGNAL-AD study will include safety and tolerability and the impact of pepinemab treatment on brain metabolic activity as detected by FDG-PET and astrocyte reactivity reflected in plasma levels of glial fibrillary acidic protein (GFAP), a molecule known to be released into blood by reactive astrocytes. Together, these are key biomarkers of disease progression.
- Deposition of Aβ amyloid in the brain is considered to be the earliest recognized event in the pathologic cascade leading to AD. Aggregates of Aβ are believed to trigger a series of subsequent events, including astrocyte reactivity and formation of toxic tau tangles in neurons, which are believed to be key drivers of neurodegeneration. Accordingly, secondary endpoints will also include plasma levels of phosphorylated tau peptide (p-tau 217), a biomarker released into blood during formation of tau tangles in neurons. In addition, several validated cognitive scales will be employed as exploratory endpoints to evaluate potential treatment effects on cognitive decline, the main clinical symptom of AD.
- The Company believes that the prevalence of AD (6 million people diagnosed with AD in the US alone) and current concerns about the limitations of treatment with anti-Aβ amyloid antibodies such as Leqembi (Eisai and Biogen) and donanemab (Eli Lilly) could make pepinemab, if approved, attractive as a potential alternative treatment or possibly for use in combination with anti-Aβ to enhance the benefit to patients. Pepinemab has, to date, been well-tolerated in clinical trials that enrolled a total of more than 600 patients.

The SIGNAL-AD study was funded in part by two investments from the Alzheimer's Drug Discovery Foundation (ADDF) for a total of $4.75 million, and by an $0.75 million grant from the Alzheimer's Association.

About Pepinemab
Pepinemab is a humanized IgG4 monoclonal antibody designed to block SEMA4D, which can 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 immune infiltration into tumors. Pepinemab is being studied as a monotherapy in the Phase 1b/2 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.

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. Additional information about the study is available at: clinicaltrials.gov.

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 expectations and objectives with respect to the results and timing of the SIGNAL-AD clinical trial; expectations with respect to compliance with Nasdaq listing standards; our plans, expectations and objectives with respect to the results and timing of the SIGNAL-AD and KEYNOTE-B84 clinical trials; the use and potential benefits of pepinemab in R/M HNSCC, lung cancer, metastatic pancreatic adenocarcinoma (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 potential to initiate a Phase 3 trial in Huntington's disease; and other statements identified by words such as "anticipate," "believe," "plans," "schedule," "being," "will," "appears," "expect," "ongoing," "potential," "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 possible delisting of our common stock from Nasdaq if the Company is 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, 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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