Vaccinex Completes Enrollment in Phase 1b/2 SIGNAL-AD (Alzheimer's Disease) Study of Pepinemab

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Topline data anticipated in mid-2024

SIGNAL-AD builds on promising data from the Phase 2 SIGNAL Study in Huntington's Disease

ROCHESTER, N.Y., April 25, 2023 (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 SEMA4D, today announced that it has completed enrollment goal in the SIGNAL-AD clinical trial for people with mild dementia due to Alzheimer's Disease (NCT04381468). Topline data from the study are expected in mid-2024, after the last enrolled patients will have received 12 months of treatment.

The randomized, double-blinded, placebo-controlled Phase 1b/2 SIGNAL-AD study was designed to evaluate the safety, tolerability and effects on cognition and brain metabolism of the SEMA4D inhibitor, pepinemab. The one-year study enrolled 40 patients with mild Alzheimer's dementia. The SIGNAL-AD study was designed to build on the exciting data obtained in the Phase 2 SIGNAL study of pepinemab in Huntington's disease (HD), another neurodegenerative disease with many similarities in pathology to AD. Data from the SIGNAL-HD study were published in Nature Medicine (2022).

"Completing enrollment in the SIGNAL-AD study is a major accomplishment for Vaccinex and the first of several important milestones anticipated in the second quarter of 2023," said Maurice Zauderer, Ph.D., President and Chief Executive Officer of Vaccinex. "While the treatment phase of the SIGNAL-AD study is ongoing, we are expecting FDA response to proposed plans for the design of a Phase 3 study in HD. Study data have been submitted to the FDA and a response is anticipated on or before May 16, 2023."

"Multiple prior clinical studies in AD have shown that, as in HD, a decline in brain metabolic activity correlates with disease progression. Pepinemab is the only clinical intervention to date that has been shown to reduce or prevent decline in brain metabolic activity while also appearing to slow or prevent cognitive decline. Based on the clinical data and favorable profile from the SIGNAL study in HD, we are hopeful that treatment with pepinemab can open the door to a safe and effective, disease modifying treatment option for patients with Alzheimer's Disease. Disease-related stress, such as is induced by accumulation of toxic aggregates of beta-amyloid in AD and mutant huntingtin protein in HD, activate inflammatory cells in brain that inhibit normal healthy functions of neurons and aggravate neurodegeneration. We believe that blocking neuroinflammatory signals with pepinemab represents a novel approach to treating NDD with the potential to complement independent amyloid-lowering strategies," continued Dr. Zauderer. "We are very appreciative of patients and their families for their dedication to advancing research by participating in this and similar important studies. We look forward to share the results of this study with the NDD/AD communities in mid-2024 and will continue to work with our advisors and regulators to chart a course for potential next steps for pepinemab in treatment of neurodegenerative disease."

About the SIGNAL-AD Study
The SIGNAL-AD study was designed to evaluate the treatment of pepinemab in patients with mild AD. The randomized, double-blinded, placebo-controlled study enrolled 40 patients at 16 sites in the U.S. Patients were randomized 1:1 to receive pepinemab, administered as an intravenous infusion (IV) every 4 weeks for 44 weeks (12 infusions at 40 mg/kg). The study is 52 weeks in duration, including a safety and efficacy evaluation four weeks after the last dose of study drug. Outcome measures include safety, an evaluation of brain metabolism and a battery of standard cognitive assessments specific to AD. Additional outcomes include measures of pepinemab immunogenicity and biomarkers associated with NDD including neurofilament light chain (NfL), Aß amyloid, tau, and immune and inflammatory markers. Vaccinex received funding support for this trial from the Alzheimer's Drug Discovery Foundation and the Alzheimer's Association under its Part the Cloud Program.

About Pepinemab
Pepinemab is a humanized IgG4 monoclonal antibody that inhibits SEMA4D, which regulates the actin cytoskeleton of cells that plays an important role in inflammatory reactions in the brain as well as in tumor immune evasion. Data show that by preventing deleterious inflammatory gliosis during disease progression, pepinemab preserves normal function of astrocytes and microglia, two types of glial cells that play a crucial role in the function and health of neurons in the brain. Additional preclinical and clinical data show that pepinemab promotes infiltration and activation of dendritic cells and CD8+ T cells and reverses immunosuppression within the tumor microenvironment. Pepinemab is being evaluated in several studies in neurodegenerative disease and oncology. Pepinemab has been administered to more than 400 patients and appears to have a favorable safety and tolerability profile.

About Vaccinex Inc.
Vaccinex, Inc. is pioneering a differentiated approach to treating slowly progressive neurodegenerative diseases (NDD) 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. In NDD, 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 (R/M 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. The Company has also developed a proprietary drug discovery platform, ActivMAb®, that it is leveraging through strategic collaborations, particularly by applying its unique capability to select high value antibodies against important multi-pass membrane receptors.

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 KEYNOTE-B84 clinical trial, planned interim analysis, 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®, the expected timeline for publication and disclosure of trial results, and other statements identified by words such as “may,” “will,” “appears,” “expect,” “planned,” “anticipate,” “estimate,” “intend,” “hypothesis,” “potential,” “suggest”, “advance,” 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.

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