Vaccinex to report topline data for SIGNAL-AD Phase 1b/2 trial of Pepinemab in Alzheimer's Disease at the Alzheimer's Association International Conference, Philadelphia, July 31, 2024

07/17/24

Pepinemab is believed to block astrocyte reactivity, a key pathology driving Alzheimer's progression

ROCHESTER, N.Y., July 17, 2024 (GLOBE NEWSWIRE) -- Vaccinex, Inc. (Nasdaq: VCNX), a clinical-stage biotechnology company pioneering a differentiated approach to treating Alzheimer's disease (AD) and cancer through the inhibition of Semaphorin 4D (SEMA4D), today announced that it will **present topline data for its randomized, double-blind, phase 1b/2 SIGNAL-AD study of pepinemab treatment for Alzheimer's disease at the Alzheimer's Association International Conference in Philadelphia, July 28- Aug 1, 2024**. Eric Siemers, MD, Principal Investigator, will present results of the study in a Featured Research Session.

Presentation title: Results of SIGNAL-AD, a randomized, phase 1b/2 trial to evaluate safety and efficacy of targeting reactive astrocytes with pepinemab, SEMA4D blocking antibody, in people with MCI or mild Alzheimer's dementia

Presenter: Eric Siemers, MD

Featured Research Session: Glial biomarkers and Alzheimer's disease therapeutics

Date: Wednesday July 31st, 2024. 9:00 AM EST.

Venue: Ballroom A, Pennsylvania Convention Center, 1101 Arch St., Philadelphia, PA 19107, USA

What can we expect to learn from results of 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 aggravate and accelerate progression of AD.
- The Company's hypothesis, which is being tested in the SIGNAL-AD study, is that treating with pepinemab antibody that binds SEMA4D can block signaling through its receptor on astrocytes and slow or prevent the damaging consequences of astrocyte activation.
- The Company has previously reported that antibody blockade of SEMA4D appears to protect healthy astrocyte functions and to slow disease progression in patients with early manifest Huntington's disease by several different biomarker and clinical measures. An important goal of the present study is to determine whether pepinemab treatment is effective at one or more defined stages of AD progression.
- Key outcomes of the SIGNAL-AD study will include safety and tolerability and the impact of pepinemab treatment on brain metabolic activity determined by FDG-PET and astrocyte reactivity as detected by plasma levels of glial fibrillary acidic protein (GFAP), a molecule known to be released into blood by reactive astrocytes and believed to be a key biomarker of disease progression.
- Deposition of Aβ amyloid in the brain is currently 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, believed to be key drivers of neurodegeneration. It is, therefore, of considerable interest to determine whether blocking SEMA4D-induced astrocyte reactivity might also slow disease progression as evidenced by increasing plasma levels of phosphorylated tau peptide (p-tau 217), a biomarker released into blood during formation of tau tangles in neurons.
- 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 approved anti-Aβ amyloid antibodies such as Leqembi™ (lecanemab) or Kisunla™ (donanemab) could 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 to further enhance the benefit of anti-Aβ antibodies to patients. In this regard, it is important that pepinemab has a very different mechanism of action than anti-Aβ antibodies. 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 a grant from the Alzheimer's Association as well as by investments from the Alzheimer's Drug Discovery Foundation (ADDF).

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 is being 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. Pepinemab could 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. 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," "promising," "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 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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