Science in the service of medicine

Vaccinex Announces Initiation of Single-Arm Open Label, Phase Ib/2 Study to Evaluate Pepinemab in Combination with Avelumab as Second Line Combination Immunotherapy for Patients with Metastatic Pancreatic Ductal Adenocarcinoma (PDAC)

The study is intended to assess whether pepinemab can reverse the suppressive tumor microenvironment found in PDAC, thereby facilitating the anti-tumor activity of immune checkpoint blockade

This Vaccinex-sponsored study will be conducted at the University of Rochester

Primary funding support is provided by Gateway Discovery Award, administered by ASCO's "Conquer Cancer Foundation"

ROCHESTER, N.Y., March 21, 2023 -- Vaccinex, Inc. (Nasdaq: VCNX), a clinical-stage biotechnology company pioneering a differentiated approach to treating cancer and neurodegenerative disease through the inhibition of SEMA4D, today announced the initiation of a **single-arm open label, Phase Ib/2 study to evaluate pepinemab in combination with avelumab as second line combination immunotherapy for patients with metastatic pancreatic adenocarcinoma (PDAC)**, NCT05102721.

The principal goal of this proof-of-concept study is to investigate the safety and efficacy of the combination of pepinemab and the PD-L1 immune checkpoint inhibitor (ICI), avelumab, in patients with PDAC, with particular attention to changes in the tumor microenvironment.

"We are very pleased to be working with Dr. David Linehan and his team at the University of Rochester Cancer Center and Wilmot Cancer Institute to conduct this important proof-of-concept study evaluating pepinemab and avelumab in PDAC. The team **received a grant from the Gateway Discovery Award to support the trial** concept," said Maurice Zauderer, CEO of Vaccinex. "Metastatic pancreatic adenocarcinoma is the third leading cause of cancer-related deaths. The profoundly immunosuppressive tumor microenvironment (TME) in PDAC remains a significant barrier to effective cytotoxic and immune based therapies. Low response rates to current chemotherapy regimens are evidenced by a 5-year survival rate of only 5-10%, underscoring the significant need for new treatment options. We believe that pepinemab has demonstrated a favorable safety profile when used in combination with the immune checkpoint inhibitor (ICI) avelumab[1], and the combination may represent a novel treatment option for patients with this devastating disease."

Dr. Zauderer continued, "The hypothesis for evaluating pepinemab in combination with ICIs in PDAC is supported by a robust body of preclinical studies and human clinical data. These data suggest that treatment with the semaphorin 4D (SEMA4D) blocking antibody, pepinemab, may reverse immunosuppression to promote the infiltration and activation of dendritic cells and CD8+ cells into the TME, rendering "cold" tumors "hot" and leading to enhanced efficacy of ICIs such as avelumab."

Dr. Luis Ruffolo, MD, University of Rochester Medical Center, will be presenting details of these PDAC studies at SSO 2023, International Conference on Surgical Cancer Care in Boston, MA on March 23.

Potential Mechanism of Action for pepinemab in combination with ICIs in PDAC

Tumors that are characterized by a high level of immunosuppressive myeloid cells may be potential candidates for treatment with pepinemab. The tumor microenvironment (TME) of PDAC is characterized

by dense fibrotic tissue and abundance of highly suppressive myeloid cells that creates an immunologically "cold" setting with a minimal adaptive T-cell response that limit the efficacy of immune therapies.

In PDAC, both SEMA4D and PD-1 are expressed on CD8+T cells in the TME. Myeloid cells within the TME express a high level of SEMA4D receptors and signaling through this pathway induces their suppressive activity. This suggests that blocking SEMA4D may represent a novel immunotherapeutic strategy for PDAC. In preclinical oncogene driven PDAC tumor models, treatment with Sema4D blocking antibody in combination with immune checkpoint blockade and standard of care chemotherapy increased penetration of effector T cells and improved response to treatment.

These observations in PDAC are consistent with a large body of preclinical and clinical data showing that pepinemab promotes infiltration and activation of dendritic cells and CD8+ T-cells and reverses immunosuppression within the tumor microenvironment.

About the Phase 1b/2 Study in Patients with PDAC

The single-arm, open label Phase 1b/2 study was designed to evaluate the use of pepinemab, a humanized IgG4 monoclonal antibody that inhibits SEMA4D, in combination with the anti-PD-L1 immune checkpoint inhibitor (ICI), avelumab, as second line treatment for patients with metastatic pancreatic adenocarcinoma who have received first line treatment with either 5-floururacil (5-FU) or gemcitabine.

The trial was designed at the ASCO-AACR Clinical Trial workshop to integrate evaluation of safety and efficacy. The study will be conducted in two segments utilizing a Simon two-stage design. The Phase 1b stage is intended to establish the tolerability (defined as the maximally tolerated dose) of the combination. Phase 2 begins after 16 subjects are enrolled at the recommended Phase2 dose and successful completion of futility evaluation in Phase 1b. The Phase 2 expansion stage is intended to assess the efficacy of the combination therapy. Efficacy, defined as objective response rate, will be assessed by RECIST1.1 criteria and iRECIST. When combined with the 16 patients from the Phase 1b segment, the overall study cohort will have an evaluable sample of 40 patients. Robust correlative analysis of TME and genomic profiling of tumor biopsies will be conducted to ascertain mechanisms of treatment response and failure.

Vaccinex has global commercial and development rights to pepinemab. The Company is the sponsor of the study which is being primarily funded by a grant from the Gateway Discovery Award (administered by the Conquer Cancer Foundation/ASCO). Pepinemab is being provided by Vaccinex and avelumabis being provided by Merck KGaA, Darmstadt, Germany and Pfizer, Inc. Additional information about the study is available at: clinicaltrials.gov.

Avelumab is co-developed and co-commercialized by Merck KGaA, Darmstadt, Germany and Pfizer Inc

1. Shafique MR, Fisher TL, Evans EE, Leonard JE, et al. Clin Cancer Res. 2021 Jul 1;27(13):3630-3640. doi: 10.1158/1078-0432.CCR-20-4792.

About Vaccinex, Inc.

Vaccinex, Inc. is pioneering a differentiated approach to treating cancer and slowly progressive neurodegenerative diseases (NDD) through the inhibition of semaphorin 4D (SEMA4D). The Company's lead drug candidate, pepinemab, blocks SEMA4D, a potent biological effector that it believes prevents immune infiltration into tumors and triggers inflammation in chronic diseases of the brain. In oncology,

pepinemab is being evaluated in combination with KEYTRUDA® in the Phase 1b/2 KEYNOTE B-84 study in recurrent or metastatic head and neck cancer (R/M HNSCC) and in combination with avelumab 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 and melanoma. In NDD, pepinemab is being studied as a monotherapy in a Phase 1/2a study in the SIGNAL-AD Alzheimer's Disease study, with ongoing exploration of potential Phase 3 development in Huntington's disease. 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 and other indications, the potential for benefits as compared to single agent KEYTRUDA® or avelumab, 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, 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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