Vaccinex New ActivMab® application published in Nature Communications for Directed Evolution of GPCRs in Mammalian Cells

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GPCRs play a key role in many important physiological processes which makes them an important class of drug targets; however, their biophysical properties have made many GPCRs "difficult to drug"

New technology makes it possible to present GPCR and ion channels in a novel and simplified membrane context that has the potential to make them more tractable for functional studies and drug discovery

ROCHESTER, N.Y., April 12, 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 a new publication in the March 30, 2023 issue of Nature Communications describing a novel way that the ActivMab® platform can be used for functional studies and drug discovery of the "hard to drug" class of membrane-associated G protein-coupled receptors (GPCRs) and ion channels.

The *Nature Communications* article, titled "*A Vaccinia-based system for directed evolution of GPCRs in mammalian cells*" provides an overview of how Vaccinex and its collaborators at the University of Zurich created an elegant system to make highly diverse libraries of functional GPCR variants and to enrich for variants with improved expression levels and stability while maintaining functional aspects of GPCR signaling. GPCRs are a very important class of drug targets because of their critical role in physiological processes. However, low expression levels and dependence on the mammalian membrane environment for conformational stability and function make them difficult targets for drug selection. The authors demonstrate that the ActivMAb technology overcomes these limitations by engineering directed protein evolution libraries in a mammalian signaling environment allowing GPCR expression that is amenable to structural studies. This novel application could be utilized to decipher the functional properties of GPCR for drug discovery or to incorporate GPCR membrane receptors into novel drug screening assays.

"Vaccinex is very pleased that this pioneering work by our scientists in collaboration with the group of Dr. Andreas Plückthun of the University of Zurich has been published in *Nature Communications*," said Ernest Smith, Ph.D., Sr. Vice President Research and Chief Scientific Officer. "GPCRs are a very important class of drug targets because of their critical role in physiological processes. The complex biophysical properties of these important targets embedded in the cell membrane can make them "difficult to drug". We believe that our novel directed evolution system will allow us to generate improved variants of any GPCR in a mammalian signaling system, better enabling us and our partners to study the functional properties of these complex receptors and develop new and valuable drugs against these important targets. We believe this new technology application will further enhance our ActivMab® offering, and we look forward to sharing it with our partners."

About ActivMAb®
Vaccinex has developed a proprietary mammalian cell-based antibody discovery platform with unique capabilities for multi-pass membrane targets such as G-protein-coupled receptors (GPCRs). The ActivMAb® technology has five main applications: complex membrane antigen presentation, antibody or antigen discovery, directed evolution and protein optimization. The first clinical candidate selected through use of this technology (SRF114, a fully human monoclonal antibody targeting CCR8 for the potential treatment of solid tumors), recently entered development in a Phase 1/2 study sponsored by our licensee, Surface Oncology. Vaccinex has entered into multiple antibody discovery collaborations with leading biopharmaceutical companies.

About Vaccinex, Inc.
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 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. 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 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 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 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 is 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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