Vaccinex and its Collaborators Present Two Abstracts Related to Pepinemab Combination Immunotherapy Trials at 37th Annual Meeting of Society for Immunotherapy of Cancer

November 10, 2022

New Biomarkers of Response and Resistance that Suggest Pepinemab Could Offer New Combination Treatment Options

ROCHESTER, N.Y., Nov. 10, 2022 (GLOBE NEWSWIRE) -- Vaccinex, Inc. (Nasdaq: VCNX), a clinical-stage biotechnology company pioneering a differentiated approach to treating cancer and neurodegenerative diseases through the inhibition of semaphorin 4D (SEMA4D), and its collaborators at Emory University and the Moffitt Cancer Center today announced that two abstracts, including an oral presentation and a poster related to investigator-sponsored trials for pepinemab combinations, are being presented at The Society for Immunotherapy of Cancer's (SITC) 37th Annual Meeting.

These studies describe novel biomarkers of response and resistance to immunotherapy that inform new potential treatment options in combination with Vaccinex's pepinemab antibody.

Oral Presentation of pepinemab combinations with immune checkpoint blockade for neoadjuvant treatment of Stage III melanoma:
Dr. Brian Olson of Winship Cancer Institute at Emory University presented results of a collaborative study with Vaccinex investigating biomarkers and benefit of neoadjuvant combination immunotherapy including Vaccinex's pepinemab antibody in patients with resectable Stage III melanoma who went on to receive adjuvant therapy with nivolumab after surgery (NCT03769155). 100% of patients who received the triple combination of pepinemab, nivolumab and ipilimumab were recurrence free at 24 months. This contrasted with recurrence free survival of less than 40% in patients who received the dual combination of pepinemab and nivolumab or pepinemab and ipilimumab.

Importantly, it was observed that the LAG-3 immune checkpoint is increased on T cells in tumors from the subset of patients who did not respond to the combination of pepinemab plus nivolumab. This provides a strong rationale for a triple combination treatment with pepinemab and inhibitors of both the PD-1 and LAG-3 checkpoint pathways. Further characterization of the tumors resected from these patients demonstrated that combination treatments that include pepinemab give rise to highly organized lymphoid structures consisting of B lymphocytes in close proximity to activated CD8+ and CD4+ T cells. These organized lymphoid structures are believed to provide an environment that supports efficient differentiation of immunoprotective as opposed to immunosuppressive cells.

Poster Presentation of pepinemab combination with adoptive cell therapy for patients with HER2+ metastatic breast cancer:
The important role of CD4+ T cells in directing a productive immune response was also the rationale for an independent adoptive cell therapy trial in breast cancer presented by collaborators, Dr. Hyo S. Han and Dr. Brian Czerniecki of the Moffitt Cancer Center (NCT05378464). In preclinical studies, it was shown that SEMA4D antibody blockade in combination with a dendritic cell vaccine improved trafficking of dendritic cells to tumors and stimulated expansion of tumor-specific B and T cells, resulting in improved regression of both primary and distant tumors. A Phase 1/2 trial involving combination of pepinemab and trastuzumab with a dendritic cell vaccine followed by adoptive transfer of expanded autologous CD4+ T cells is now enrolling patients with HER2+ metastatic breast cancer.

Maurice Zauderer, Ph.D., President and Chief Executive Officer of Vaccinex, remarked, "The investigator-sponsored collaborative studies reported at SITC 2022 provide safety information and describe novel biomarkers of response and resistance to immunotherapy that inform new potential treatment options in combination with Vaccinex's pepinemab antibody. **We plan to explore such strategies with partners interested in rational combinations to enhance the activity of their drugs through an independent mechanism of action, without notable additional toxicity**."

Dr. Zauderer concluded, "Vaccinex is conducting a Phase 1b/2 study in patients with pepinemab in combination with KEYTRUDA for recurrent and metastatic head and neck squamous cell cancer (R/M HNSCC), the KEYNOTE-B84 study. We have previously reported promising initial results from this study, including complete responses in patients with difficult to treat tumors that express low levels of PD-L1. These exciting data build on our understanding of the potent activity of pepinemab in orchestrating and amplifying immune responses in combinations with companion immunotherapies. We continue to observe strikingly improved responses in this patient population and expect to report results of interim analysis from this study in 1Q 2023."

Oral Presentation Details:

"Neoadjuvant SEMA4D blockade with nivolumab alters suppressive myeloid cells while elevating B cell and CD26hi T cell infiltration in the tumors of patients with resectable stage III melanoma".

Abstract number: 613
Presentation Date/Time: Friday November 11 at 5:20 PM, EST
Session: 210: Cancer Surgery in the Age of Immunotherapy
Presenter: Dr. Brian Olson of Winship Cancer Institute at Emory University

This Phase 1 open label integrated biomarker study was designed to evaluate immune responses in tumor and blood before and after neoadjuvant treatment with immunotherapy combinations (n=8) compared to standard of care surgery without treatment (n=6). Objectives included biomarker correlates, as well as safety and tolerability in the neoadjuvant setting, and clinical response in terms of pathologic response and recurrence-free survival (RFS). In September 2022, Dr. Michael Lowe from the Emory team presented the clinical safety and efficacy data at the 2022 ESMO Congress in Paris, France, reporting that pepinemab enhanced RFS of nivolumab and ipilimumab combinations, yet was well-tolerated and did not enhance toxicities associated with the companion immune checkpoint blockade (ICB) drugs (1). At SITC, Dr. Olson reports the biomarker correlates of this study.

The first of several important findings is that LAG3 expression appears to be an escape mechanism to treatment with the combination of pepinemab plus nivolumab. LAG3 was significantly upregulated on CD8+ and CD4+ T cells in patients who experienced recurrence of cancer within 24 months of treatment, while LAG3 remained low in patients who were recurrence-free. Together with previously reported preclinical data demonstrating dramatic synergy of blocking antibodies to SEMA4D and LAG3, as well as the favorable safety profiles for both pepinemab and LAG-3 antibodies in clinical studies, this provides rationale to evaluate combinations of pepinemab with LAG3 and PD-1/PD-L1 targeted therapies.

Secondly, results demonstrate a striking increase in the formation of tertiary lymphoid structures (TLS) in tumors of patients responding to treatment with combination therapies that include pepinemab, but not single agent nivolumab. These highly organized TLS consist of activated and proliferating B cells surrounded by activated (CD69+) CD8+ and CD4+ T cells. Notably, a significant increase in $CD26^{high}$ CD4+ T cells was induced in all pepinemab combinations, especially in the highly effective triple combination. These cells were previously described by team member, Dr. Chrystal Paulos, to have enhanced multi-functionality, a rich profile of cytokine and chemokine secretion, and, importantly, long-term persistence and memory with improved cytotoxic function and activity in preclinical models of adoptive cell therapy (2, 3). This suggests that addition of pepinemab to adoptive cell and/or CAR-T therapies may more effectively augment or rescue anti-tumor immune responses in patients.

Poster Presentation Details:

"**Phase I Study of Adoptive T Cell Therapy Following HER2-Pulsed Dendritic Cell Vaccine and Pepinemab/Trastuzumab in Patients with Metastatic HER2-Positive Breast Cancer (NCT05378464)**".

Abstract number: 645
Presentation Date/Time: Thursday November 10 at 9:00 AM, EST
Session: Clinical Trials In Progress
Presenter: Dr. Hyo Han of Moffitt Cancer Center

Co-authors from Moffitt Cancer Center and Vaccinex present a newly initiated and actively enrolling trial to evaluate safety and efficacy of a combination therapy involving treatment with pepinemab/trastuzumab/DC-1 dendritic cell vaccine, followed by collection, expansion, and adoptive transfer of CD4+ Th1 cells in patients with trastuzumab-refractory metastatic breast cancer. Primary endpoints include safety and tolerability, with additional assessments of clinical efficacy as well as immune biomarkers in the tumors and blood.

About Pepinemab
Pepinemab is a humanized IgG4 monoclonal antibody that inhibits SEMA4D, which regulates chronic inflammation in the tumor microenvironment. Preclinical and clinical data show that pepinemab promotes infiltration/activation of dendritic cells/ CD8+ T-cells and reverses immunosuppression within the tumor (4,5).

Results of a Phase 1b/2 study to evaluate the combination of pepinemab with checkpoint inhibitor, BAVENCIO® (avelumab, Merck KGaA) were presented at ASCO 2020 and were highlighted in the July 2021 publication of Clinical Cancer Research. Vaccinex reported that results of this Phase 1b/2 CLASSICAL-Lung trial showed a 25-33% Overall Response Rate (ORR) for patients with difficult to treat PD-L1 low/negative tumors treated with the combination. The study report also indicated that pepinemab did not increase immune-related toxicities of BAVENCIO but increased penetration of cytotoxic T cells (6). The publication is available electronically at: Clinical Cancer Research.

Vaccinex has global commercial and development rights to pepinemab, and is 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: https://www.vaccinex.com/clinical-trials-oncology/
KEYTRUDA is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., Kenilworth, NJ, USA.

About Vaccinex, Inc.
Vaccinex, Inc. is pioneering a differentiated approach to treating cancer and slowly progressive neurodegenerative diseases 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. Pepinemab is being evaluated in a Phase 1b/2 study in recurrent or metastatic head and neck cancer (R/M HNSCC) and in a Phase 1/2a study in Alzheimer's Disease, 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 thru strategic collaborations, particularly by exploiting 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, the use and potential benefits of pepinemab in R/M HNSCC, lung cancer and other indications, the potential for benefits as compared to single agent KEYTRUDA, 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.

References

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