Alpine Immune Sciences Advances Oncology Programs with New ALPN-202 Preclinical Data and Key Additions to Scientific Advisory Board

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ALPN-202 Preclinical Data Presented at the Society for Immunotherapy of Cancer's (SITC) 33rd Annual Meeting Supports First-In-Class Triple Mechanism of Action for the Treatment of Cancer

Company Strengthens Scientific Advisory Board with Slate of Oncology Leaders

SEATTLE--(BUSINESS WIRE)--Nov. 9, 2018-- Alpine Immune Sciences, Inc. (NASDAQ:ALPN), a leading immunotherapy company focused on developing innovative treatments for cancer, autoimmune/inflammatory, and other diseases, today announced advancements in the company's oncology program. Following promising preclinical data presented today at the Society for Immunotherapy of Cancer (SITC) 33rd Annual Meeting in Washington, D.C., the company remains on track to initiate human clinical trials of ALPN-202, a PD-L1/CTLA-4 dual antagonist with PD-L1 dependent CD28 costimulation, in the fourth quarter of 2019. Additionally, Alpine has strengthened its Scientific Advisory Board with the addition of key oncology leaders – Rafi Ahmed, Ph.D., James Welsh, M.D., and John Thompson, M.D.

ALPN-202 Preclinical Study Results Presented at SITC's 33 rdAnnual Meeting

Alpine presented the results of a preclinical study of ALPN-202 in a poster session today, strongly supporting the proposed mechanism of action of ALPN-202 via activation of the immune system in a differentiated way from current checkpoint therapies. ALPN-202 is a novel molecule designed to block the inhibitory immune checkpoints PD-L1 and CTLA-4 while providing PD-L1 dependent T cell activation via the CD28 costimulatory pathway. It has previously been demonstrated to have efficacy in an MC38-based colorectal cancer model, superior to the FDA-approved PD-L1 inhibitor durvalumab. Today's poster correlates these findings with superior intratumoral immune cell infiltration and effector gene signatures, as well as favorable changes in T cell receptor profiles, consistent with ALPN-202's proposed multi-modal mechanism of action.

"ALPN-202 is differentiated from currently approved checkpoint inhibitors by providing T cell costimulation in addition to dual checkpoint antagonism. We believe that the provision of costimulation, such as via CD28, will be critical to improving response rates during checkpoint inhibition," said Stanford Peng, M.D., Ph.D., Executive Vice President of Research and Development and Chief Medical Officer of Alpine. "In this way, ALPN-202 could result in superior monotherapy efficacy over single or even dual checkpoint antagonists. We anticipate initiating human clinical trials of ALPN-202 for the treatment of advanced malignancies in the fourth quarter of 2019."

The preclinical study evaluated the anti-tumor responses of ALPN-202 compared with durvalumab in mice implanted with human PD-L1 transduced MC38 tumors. Results showed ALPN-202:

- Produced dose-dependent anti-tumor responses, including potent single-dose activity
- Induced a greater tumor inflammation gene signature than durvalumab
- Induced increased T cell infiltration and T cell-related effector gene signatures compared to durvalumab
- Promoted both increased T cell receptor clonality and richness, consistent with ALPN-202's multiple mechanisms of action

NKp30/ICOSL vIgD-Fc program demonstrates tumor-localized costimulation

In a second preclinical study, Alpine used its variant immunoglobin domain (vIgD) platform to engineer novel NKp30/ICOSL vIgD fusion proteins. The resulting therapeutic is designed to agonize two T cell costimulatory receptors ICOS and CD28 only in the presence of B7-H6, a tumor antigen overexpressed in certain cancer types such as some forms of esophageal, kidney, rectal, and stomach cancers.

Results showed the NKp30-ICOSL vIgD-Fc fusion proteins:

- Conferred potent T cell costimulation *in vitro*, with enhanced T cell proliferation and cytokine production only in response to B7-H6-expressing target cells. In contrast, ICOSL and NKp30 vIgDs alone in the absence of B7-H6 were not inflammatory.
- Demonstrated efficacy in a B7-H6-positive CT26 mouse colon cancer model, especially when administered in combination with a PD-1 inhibitor. The proteins were not effective on a B7-H6-negative parental CT26 tumors, demonstrating target specificity.

Dr. Peng added, "These results are encouraging because they indicate that NKp30/ICOSL vIgD-Fc fusion proteins in particular may provide a novel therapeutic strategy to provide tumor-specific immunomodulation in a B7-H6-dependent fashion and support the utility of Alpine's platform in developing novel targeted agents in oncology."

Scientific Advisory Board Appointments

Drs. Rafi Ahmed, James Welsh, and John Thompson have been appointed to the Alpine Immune Sciences Scientific Advisory Board. They join a team of distinguished translational and clinical scientists including Andrew Scharenberg, M.D, Scientific Advisory Board Chair, Manish Butte, M.D, Ph.D, and Paul Tumeh, M.D.

“We welcome Rafi, James, and John to the Alpine Scientific Advisory Board,” said Andy Scharenberg, M.D. “The support of these scientific leaders and their belief in Alpine’s vision to bring novel molecules to patients will be important as we work to advance our oncology programs into the clinic next year.”

Dr. Rafi Ahmed, Ph.D. is a highly respected researcher who has contributed significant influential work over the past decade in shaping the current understanding of memory T cell differentiation and anti-viral T and B cell immunity. He is the Charles Howard Candler Professor of Microbiology and Immunology at Emory University, where he is also Director of the Emory Vaccine Center, and a Georgie Research Alliance Eminent Scholar in Vaccine Research. He is also a member of the National Academy of Sciences.

“I am looking forward to working with the Alpine team as they have a unique approach of targeting T cells,” said Dr. Ahmed. “My lab previously published research showing how CD28/B7 pathway costimulation is required for anti PD-1 antibody efficacy, so I’m particularly excited work with Alpine on their ALPN-202 program.”

Dr. James Welsh, M.D. is a Tenured Physician Scientist at The University of Texas MD Anderson Cancer Center, where he serves as the Head of the Immune Radiation programwith the goal of using radiation to turn the tumor into an “in-situ” vaccine in order to prime T cells, turning radiation into a systemic therapy. Dr. Welsh and his team recently developed the first mouse model of PD-1 resistance to investigate the mechanisms how cancer cells adapt to evade the immune system.

Dr. John Thompson, M.D. is the Medical Director of the Phase 1 Clinical Trials Program and Co-Director of the Melanoma Clinic at the Seattle Cancer Care Alliance. He also serves as a Professor in the Medical Oncology Division at the University of Washington School of Medicine and is a member of the Clinical Research Division at the Fred Hutchinson Cancer Research Center. Dr. Thompson is a member of several medical societies, including the American Society of Clinical Oncology, the American Association for Cancer Research, the Society for Immunotherapy of Cancer, and the National Kidney Cancer Association. He has authored or co-authored more than 150 articles, appearing in the *Journal of Immunology*, *Blood Leukemia*, *Journal of Clinical Oncology*, and *Clinical Cancer Research*, among others.

About Alpine Immune Sciences, Inc.

Alpine Immune Sciences, Inc. is committed to leading a new wave of functional immune therapeutics. Alpine is employing directed evolution to create potentially powerful multifunctional immunotherapies to improve patients’ lives. Supported by promising preclinical data, we aim to have two programs in the clinic in 2019. The first, ALPN-101 for autoimmune/inflammatory diseases, is a dual ICOS/CD28 antagonist, engineered to reduce pathogenic immune responses. The second, ALPN-202 for cancer, is a dual PD-L1/CTLA-4 antagonist and PD-L1-dependent CD28 T cell costimulator intended to combine checkpoint inhibition with a necessary costimulation signal – an approach currently absent from approved checkpoint therapies. Alpine is backed by world-class research capabilities, a highly-productive scientific platform, and a proven management team. For more information, visit www.alpineimmunesciences.com.

Forward-Looking Statements

This release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. These forward-looking statements are not based on historical fact, and include statements regarding Alpine’s platform technology and potential therapies. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as “may,” “will,” “should,” “would,” “expect,” “plan,” “intend,” and other similar expressions among others. These forward-looking statements are based on current assumptions that involve risks, uncertainties and other factors that may cause actual results, events or developments to be materially different from those expressed or implied by such forward-looking statements. These risks and uncertainties, many of which are beyond our control, include, but are not limited to: Alpine’s discovery-stage and pre-clinical programs may not advance into the clinic or result in approved products on a timely or cost-effective basis or at all; Alpine may not achieve additional milestone payments pursuant to its collaborations; the impact of competition; adverse conditions in the general domestic and global economic markets; as well as the other risks identified in Alpine’s filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and Alpine undertakes no obligation to update forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements.

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