Alpine Immune Sciences Showcases Key Preclinical Data at 60th American Society of Hematology Annual Meeting and Exposition

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Company's Lead Program, ALPN-101, Demonstrates Activity in Animal Models of Graft Versus Host Disease and Hemophagocytic Lymphohistiocytosis

Alpine Also Highlights Potential for Transmembrane and Secreted Immunomodulatory Proteins to Enhance Activity of Engineered T Cells

Company Adds Distinguished Investigator to Scientific Advisory Board

SEATTLE--(BUSINESS WIRE)--Dec. 3, 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 positive results from multiple preclinical studies which were presented at the American Society of Hematology's (ASH) 60 th Annual Meeting & Exposition in San Diego, CA. Oral and poster presentations described promising efficacy of ALPN-101 in preclinical models of acute graft versus host disease (GvHD) and hemophagocytic lymphohistiocytosis (HLH), while a poster presentation described the company's transmembrane and secreted immunomodulatory protein (TIP/SIP) platform to enhance the activity of engineered T cell therapies for cancer. Additionally, Alpine strengthened its Scientific Advisory Board with the addition of Anne Davidson, MBBS, Professor, Center for Autoimmune, Musculoskeletal, and Hematopoietic Diseases, Feinstein Institute for Medical Research.

ALPN-101 Preclinical Study Results

Djamilatou Adom, PhD, from the Indiana University School of Medicine laboratory of Sophie Paczesny, MD PhD, and one of Alpine's collaborators, presented an oral abstract titled, "ICOSL+ Plasmacytoid Dendritic Cells as Biomarker and Inducer of Graft-Versus-Host Disease" (publication #355), highlighting the novel role ICOS ligand (ICOSL) plays in acute GvHD and describing a strong correlation between ICOSL-positive plasmacytoid dendritic cells and the gastrointestinal manifestations of GvHD. In the investigators' model of GvHD, ALPN-101 significantly improved survival.

"I'm excited about the potential of ALPN-101 in GvHD given its dual CD28/ICOS mechanism of action," said Dr. Paczesny, Professor of Immunology and Pediatrics at Indiana University School of Medicine and lead of the Biomarkers Stem Cell Transplantation Program. "Early biomarker development could identify patients at risk, specifically early quantification of ICOSL+ Plasmacytoid Dendritic Cells frequency may allow for identification of patients at risk of gastrointestinal and support ALPN-101 as an early intervention in this patient population."

In a poster titled, "Therapeutic Candidate ALPN-101, a Dual ICOS/CD28 Antagonist, Potently Suppresses Human/NSG Mouse Xenograft Graft vs. Host Disease (GvHD) in a Dose Ranging Study and Reduces Disease Activity in a Mouse Model of Hemophagocytic Lymphohistiocytosis (HLH)" (publication #2037), ALPN-101 was evaluated in a humanized model of GvHD and an experimental model of HLH. GvHD is a life-threatening disease reflecting immune-mediated attack of recipient tissue by donor T cells and is one of the leading causes of death following allogeneic stem cell transplantation. HLH is a rare, life-threatening inflammatory disease characterized by excessive T cell and macrophage activation. Results showed ALPN-101:

Humanized GvHD Model

- Enhanced survival and suppressed disease activity in GvHD, even after administration of only a single dose.
- Demonstrated superior efficacy to belatacept, an approved CD28 pathway inhibitor, in survival and disease activity, correlating with better suppression of activated T cells and circulating cytokines.

HLH Model

- Reduced CD4+ T cell activation and liver inflammation
- Did not appear to affect the activity of viral-specific T cells directed against lymphocytic choriomeningitis virus (LCMV), the virus used to induce the model.

The HLH data were generated in collaboration with the laboratory of Kim Nichols, MD, Director of the Cancer Predisposition Division at St. Jude Children's Research Hospital. Dr. Nichols noted, "ALPN-101 clearly reduces inflammation in these models, but importantly the activity of viral-specific T cells was preserved, suggesting ALPN-101 may reduce pathogenic, but spare desired, immune responses."

"These results reinforce our confidence in ALPN-101 as a promising therapeutic candidate, not only in GvHD but multiple other autoimmune and/or inflammatory diseases," said Stanford Peng, M.D., Ph.D., Executive Vice President of Research and Development and Chief Medical Officer of Alpine. "We remain on track to initiate a Phase 1 study in the first quarter of 2019."

Transmembrane and Secreted Immunomodulatory Protein (TIP/SIP) Data Presented

A second poster, titled "'Switch' Transmembrane Immunomodulatory Proteins (TIPs) Consisting of High-Affinity PD-1 Extracellular Domains (PD-1 vIgDs) and Costimulatory Intracellular Domains Potently Enhance the Activity of TCR-Engineered T Cells" (publication #2052), described for the first time an application of Alpine's variant immunoglobulin domain (vIgD) platform to enhance the activity of engineered T cells (ECTs). Multiple formats

were demonstrated, in which vIgDs expressed by TCR and/or CAR-T cells in either transmembrane or secreted forms enhanced their activity as determined by T cell proliferation, cytokine production, and/or target cell killing. Examples included CD86 costimulatory TIPs, PD-L2 checkpoint inhibitory SIPs, and PD-1 “switch” TIPs incorporating costimulatory intracellular signaling domains, using HPV-specific TCRs, as well as HER2- and CD19-specific CARs. Importantly, the success of this work relied upon Alpine’s development of a proprietary transduction vector to achieve high T cell transduction efficiencies.

Dr. Peng added, “Engineered T cell therapies continue to hold great promise but have seemed so far to demonstrate only modest efficacy in solid tumors, possibly due to an immunosuppressive and/or insufficiently immuno-stimulatory tumor environment. These data suggest Alpine’s TIPs and SIPs may represent a next-generation strategy to overcome such obstacles. We look forward to continuing to develop this potential.”

Scientific Advisory Board Appointment

Dr. Anne Davidson, MBBS, Professor, Center for Autoimmune, Musculoskeletal and Hematopoietic Diseases and Investigator at the Feinstein Institute for Medical Research, has been appointed to the Alpine Immune Sciences Scientific Advisory Board.

“We are pleased to have Anne join our ranks and lend her considerable expertise to the Alpine Scientific Advisory Board,” said Andy Scharenberg, M.D., Chair of the Scientific Advisory Board. “She is a distinguished researcher and investigator, and her deep expertise in autoimmune disease processes will be valuable as Alpine works to advance its novel molecules in its autoimmune and inflammatory programs.”

Dr. Davidson is a practicing rheumatologist at North Shore University Hospital and serves as program director of the Rheumatology Fellowship at Northwell Health. She has served on the medical advisory board for the S.L.E. Lupus Foundation and co-chairs a grant review committee for the Lupus Research Alliance. Her accolades include multiple grants from the National Institutes of Health, the Kirkland Scholar Award, the Dubois Award from the American College of Rheumatology, and the American College of Rheumatology Distinguished Investigator Award.

“I am pleased to join the Scientific Advisory Board at this pivotal time as Alpine advances its programs toward the clinic,” said Dr. Davidson. “In particular, I am excited by what the ALPN-101 preclinical data has demonstrated to date, and I look forward to working with the team as Alpine explores this novel molecule’s potential application to a wide array of autoimmune disorders.”

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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