Alpine Immune Sciences Presents ALPN-101 Phase 1 Healthy Volunteer Study Data and Details of Upcoming Phase I/II BALANCE GVHD Study at the 61st American Society of Hematology Annual Meeting

December 9, 2019

ALPN-101 demonstrates ability to potently inhibit both T and B cell responses in first-in-human study

Human experience supports both IV and SQ dosing regimens

SEATTLE--(BUSINESS WIRE)--Dec. 9, 2019-- Alpine Immune Sciences, Inc. (NASDAQ:ALPN), a leading clinical-stage immunotherapy company focused on developing innovative treatments for cancer and autoimmune/inflammatory diseases, presented Phase 1 data yesterday from the healthy volunteer study of ALPN-101, a first-in-class dual CD28/ICOS antagonist, and details on its upcoming Phase 1/2 BALANCE study of ALPN-101 in steroid-resistant or steroid-refractory acute graft-versus-host disease (GVHD) at the 61st American Society of Hematology Annual Meeting (ASH) in Orlando, FL.

Jan Hillson, MD, Senior Vice President of Clinical Development at Alpine, presented “An Open Label Study of ALPN-101, a First-in-Class Dual CD28/ICOS Antagonist, in Subjects with Steroid-Resistant or Steroid-Refractory Acute Graft Versus Host Disease (BALANCE)” as part of the oral session, “Chemical Biology and Experimental Therapeutics: Novel Compounds and Mechanisms of Action.”

Highlights included:

- T cell costimulation via the CD28 and ICOS pathways is critical to the pathogenesis of GVHD. Available therapies blocking the CD28 – CD80/86 pathway, such as abatacept and belatacept (CTLA4-Ig), may be at least partially beneficial in acute GVHD, but based on models they appear also to permit escape of ICOS+ T cells, which correlate with disease activity.
- ALPN-101 is a dual inhibitor of CD28 and ICOS and demonstrates potent efficacy in preclinical models. It exhibits a potent, unique activity superior to combinations of biologics individually antagonizing the CD28 – CD80/86 and ICOS – ICOSL pathways.
- In adult healthy volunteers, ALPN-101 has been well tolerated as single intravenous or subcutaneous doses, without cytokine release, infusion-related reactions, hypersensitivity, or other signs of agonist activity.
- Dose-dependent pharmacodynamic activity was observed, including inhibition of T cell activation, assessed *ex vivo* based on inhibition of staphylococcal entereotoxin B (SEB)-induced cytokine production, and inhibition of antibody responses, assessed following immunization with keyhole limpet hemocyanin (KLH).
- Based on activity in models, together with favorable tolerability and pharmacodynamics in healthy volunteers, ALPN-101 has the potential to be a clinically meaningful immunomodulator for the treatment of inflammatory diseases such as GVHD.
- BALANCE is a Phase 1/2, first-in-disease dose escalation and expansion study of ALPN-101 in patients with active, steroid-refractory or steroid-resistant acute GVHD. It will explore the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of ALPN-101.

“Despite decades of intense research, GVHD remains a major cause of morbidity and mortality after hematopoietic stem cell transplantation,” commented Sophie Paczesny, MD, PhD, Professor of Immunology and Pediatrics at Indiana University School of Medicine and lead of the Biomarkers Stem Cell Transplantation Program and one of Alpine's research collaborators. “Current therapies are associated with significant toxicities or are simply insufficient to control the disease. CD28 and ICOS appear to be key pathways in the pathogenesis of GVHD, and the presented data with ALPN-101 appear uniquely strong. I look forward to the BALANCE study, which may demonstrate the therapeutic potential of ALPN-101.”

About Graft Versus Host Disease (GVHD)

Graft versus host disease (GVHD) is the most common life-threatening complication of a hematopoietic cell transplant. It occurs when donor cells see recipient cells as foreign and attack them. Acute GVHD typically occurs within the early weeks and months after transplant, usually involving the skin, liver, and gastrointestinal tract. GVHD patients remain at risk of organ system damage and increased mortality due to the disease and to high dose glucocorticoids.

About ALPN-101

ALPN-101 is a novel Fc fusion protein of a human inducible T cell costimulator ligand (ICOSL) variant immunoglobulin domain (vIgD™), and a first-in-class therapeutic designed to inhibit simultaneously the CD28 and ICOS inflammation pathways. CD28 and ICOS are closely-related costimulatory molecules with partially overlapping roles in T cell activation likely playing a role in multiple autoimmune and inflammatory diseases. In preclinical models of graft versus host disease, inflammatory arthritis, connective tissue disease, and multiple sclerosis, ALPN-101 demonstrates efficacy superior to agents blocking the CD28 – CD80/86 or ICOS - ICOSL pathways alone.

About Alpine Immune Sciences, Inc.

Alpine Immune Sciences, Inc. is committed to leading a new wave of immune therapeutics, creating potentially powerful multifunctional immunotherapies to improve patients' lives via unique protein engineering technologies. Alpine has two lead programs. The first, ALPN-101 for autoimmune/inflammatory diseases, is a selective dual T cell costimulation blocker engineered to reduce pathogenic T and B cell immune responses by blocking ICOS and CD28. ALPN-101 has recently completed enrollment in a Phase 1 healthy volunteer trial. The second, ALPN-202 for cancer, is a conditional CD28 costimulator and dual checkpoint inhibitor. Alpine is backed by world-class research and development 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 our platform technology and potential therapies, the timing of and results from clinical trials and pre-clinical development activities, clinical and regulatory objectives and the timing thereof, expectations regarding the sufficiency of cash to fund operations, the potential efficacy, safety profile, future development plans, addressable market, regulatory success, and commercial potential of our product candidates, the timing of our public presentations and potential publication of future clinical data, the efficacy of our clinical trial designs, expectations regarding our ongoing collaborations, and our ability to successfully develop and achieve milestones in our development programs. 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: clinical trials may not demonstrate safety and efficacy of any of our product candidates; our ongoing discovery and pre-clinical efforts may not yield additional product candidates; our discovery-stage and pre-clinical programs may not advance into the clinic or result in approved products; any of our product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; we may not achieve additional milestones in our proprietary or partnered programs; the impact of competition; adverse conditions in the general domestic and global economic markets; as well as the other risks identified in our filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and we undertake no obligation to update forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements.

"Secreted Immunomodulatory Proteins", "SIP", "Transmembrane Immunomodulatory Protein," "TIP," "Variant Ig Domain," "vIgD" and the Alpine logo are registered trademarks or trademarks of Alpine Immune Sciences, Inc. in various jurisdictions.

View source version on businesswire.com: https://www.businesswire.com/news/home/20191209005130/en/

Source: Alpine Immune Sciences, Inc.

Investor Relations:
Pure Communications
Courtney Dugan, 212-257-6723
cdugan@purecommunications.com

Media Relations:
Pure Communications
Sheryl Seapy, 213-262-9390
sseapy@w2ogroup.com