Alpine Immune Sciences to Highlight Clinical Updates on Autoimmune and Immuno-Oncology Programs at Inaugural R&D Day

September 12, 2022

- ALPN-303 well-tolerated in a Phase 1 healthy volunteer study with on-target effects on key biomarkers, supporting a highly competitive, potentially best in class profile -

- Davoceticept (ALPN-202) demonstrates encouraging outcomes, especially in renal cell carcinoma, as monotherapy and in combination with pembrolizumab in ongoing NEON-1 and NEON-2 studies respectively -

- Alpine management and leading experts to conduct webcast at 5:00 pm ET/2:00 pm PT today -

SEATTLE--(BUSINESS WIRE)--Sep. 12, 2022-- Alpine Immune Sciences, Inc. (NASDAQ: ALPN), a leading clinical-stage immunotherapy company focused on developing innovative treatments for cancer and autoimmune and inflammatory diseases, today announced clinical updates from two wholly owned programs, ALPN-303 and davoceticept. A broad development plan for ALPN-303 will be presented, including a proof-of-concept phase 2 study in systemic lupus erythematosus (SLE) and basket studies in renal, hematologic, and dermatologic autoimmune diseases, with initial clinical data from the baskets expected in the second half of 2023.

“We are pleased to share these important updates which we believe strongly support and frame the next phase of development for these two programs,” said Stanford Peng, MD, PhD, Alpine’s President and Head of R&D. “The initial healthy volunteer data with ALPN-303 suggest a differentiated and potentially best-in-class development profile, which we anticipate could have a meaningful impact on clinical outcomes in SLE and also potentially a wide range of autoantibody-related inflammatory diseases. Davoceticept, our lead Immuno-oncology program, continues to show encouraging signs of meaningful clinical activity with an acceptable safety profile. Renal cell carcinoma has emerged as a particular area of interest given the preliminary experience in both ongoing studies which correlates with existing translational data in the literature, supporting the importance of CD28 costimulation in this particular tumor type.”

Mitchell H. Gold, MD, Alpine’s Executive Chairman and Chief Executive Officer, added, “Since our founding, we’ve made tremendous progress in advancing our platform and clinical pipeline. With these new data, we have set a clear path for the company with the goal of achieving proof-of-concept for all three development programs and of advancing each to pivotal and/or registrational studies, which will be transformational for the company.”

In addition to Alpine management reviewing these data and planned clinical development plans, the R&D Day will also feature presentations by two leading experts, Vibeke Strand, MD, Biopharmaceutical Consultant and Adjunct Clinical Professor, Division of Immunology/Rheumatology, Stanford University School of Medicine, and Katy E. Beckermann, MD, PhD, Assistant Professor of Medicine, Division of Hematology/Oncology, Vanderbilt University Medical Center, who will review the current treatment landscape as well as the potential role for new treatment options in lupus and renal cell carcinoma (RCC), respectively.

R&D Day Program Highlights

ALPN-303

- Well tolerated in healthy adults when administered intravenously or subcutaneously (SQ) at doses up to 960 mg.
- Encouraging preliminary pharmacodynamic analyses, including reductions in circulating immunoglobulins and antibody-secreting cells ($CD38^{hi}$ plasmablasts/plasma cells) – the latter not previously reported with inhibitors of BAFF and/or APRIL in healthy adults, to the best of the Company’s knowledge.
- Pharmacodynamic analyses further support the feasibility of convenient subcutaneous therapeutic dosing every four weeks, suggesting potential for more robust activity and greater convenience over related inhibitors of BAFF and/or APRIL.

  - Doses selected for the next studies include 80 mg and 240 mg SQ every four weeks

- The Company believes these encouraging data support a broad development plan including:

  - A randomized, placebo-controlled phase 2 proof-of-concept study in SLE; and

  - Open-label basket studies in renal, hematologic, and dermatologic autoimmune diseases with initial data anticipated in the second half of 2023.

“ALPN-303 is particularly exciting because it may be the first truly dual inhibitor of both BAFF and APRIL – a clinically validated target space for complex diseases like lupus,” said Dr. Vibeke Strand. “This early human data suggest that ALPN-303 is in fact more potent and should be able to be more conveniently administered than existing candidates like the wild-type TACIs, which have already shown proof-of-concept in these diseases. Together with ALPN-303’s excellent initial tolerability, these findings strongly encourage further clinical development, and I look forward to continuing to work with this team and seeing the results of the planned studies.”

Davoceticept (ALPN-202)

- Engineered to provide PD-L1-dependent CD28 costimulation along with dual PD-L1/CTLA-4 checkpoint inhibition

- Preliminary analyses of the ongoing dose escalation in NEON-2, the study of davoceticept in combination with pembrolizumab, show encouraging outcomes. These include evidence of tumor reduction in two subjects: a 37.8% reduction in prostate-specific antigen (PSA; 622.9 to 387.7 ng/mL) in a subject with castrate-resistant prostate cancer, and a 25.5% tumor volume reduction in a subject with poorly differentiated renal cell carcinoma (RCC) with prior **primary** resistance to pembrolizumab and axitinib. A third subject, with clear cell RCC including with prior **primary** resistance to nivolumab, achieved a durable confirmed partial response (-30%).
- Across both the NEON-1 davoceticept monotherapy and NEON-2 studies, 2/5 (40%) and 3/5 (60%) of subjects have achieved a confirmed partial response or stable disease, respectively.
- Dose escalation in NEON-2 is ongoing. In NEON-1, expansion cohorts in RCC, melanoma, and PD-L1-positive tumors are also ongoing.

“These initial data are compelling given the responses observed in PD-1 refractory RCC,” remarked Dr. Beckermann. “Such findings are highly consistent with our own translational data demonstrating that the CD28 pathway may be relevant to the biology of treatment resistance -- and strongly support further development of davoceticept, particularly in RCC.”

Alpine R&D Day Conference Call and Webcast Information

A live webcast of the event will be available in the investor relations section of the company’s website at https://ir.alpineimmunesciences.com/events. A replay will be available on the Company's website for 90 days following the live event.

About ALPN-303 and the Phase 1 (RUBY-1) Study

ALPN-303 is a dual B cell cytokine antagonist being developed for multiple autoimmune and/or inflammatory diseases. Based upon an engineered TACI (transmembrane activator and CAML interactor) domain, ALPN-303 in preclinical studies shows robust inhibition of B cell activating factor/B lymphocyte stimulator (BAFF, BLyS) and a proliferation inducing ligand (APRIL). These two pleiotropic B cell cytokines play key roles in B cell development, differentiation, and survival, and together contribute to the pathogenesis of multiple autoimmune diseases like systemic lupus erythematosus (SLE) and many other autoantibody-related inflammatory diseases. By simultaneously blocking these two cytokines, ALPN-303 has the potential to improve outcomes in patients suffering from severe autoimmune and/or inflammatory diseases. Alpine plans to conduct a phase 2 proof-of-concept study in SLE and open-label basket studies in renal, hematologic, and dermatologic autoimmune diseases, with the first of these anticipated to begin in the first half of 2023.

RUBY-1 (NCT05034484) is a phase 1, randomized, placebo-controlled study in healthy adult volunteers that has been designed to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of intravenously and subcutaneously administered ALPN-303.

About Davoceticept and the NEON Studies

Davoceticept (ALPN-202) is a first-in-class, conditional CD28 costimulator and dual checkpoint inhibitor intended for the treatment of cancer. Preclinical studies of davoceticept have successfully demonstrated superior efficacy in tumor models compared to checkpoint inhibition alone. NEON-1 (NCT04186637), a phase 1 monotherapy dose escalation and expansion study in patients with advanced malignancies, has completed dose escalation and is currently enrolling its expansion cohorts. NEON-2 (NCT04920383), a combination study of davoceticept (ALPN-202) and pembrolizumab, was initiated in June 2021.

About Alpine Immune Sciences

Alpine Immune Sciences is committed to leading a new wave of immune therapeutics. With world-class research and development capabilities, a highly productive scientific platform, and a proven management team, Alpine is seeking to create first- or best-in-class multifunctional immunotherapies via unique protein engineering technologies to improve patients’ lives. Alpine has entered into strategic collaborations with leading global biopharmaceutical companies and has a diverse pipeline of clinical and preclinical candidates in development. For more information, visit www.alpineimmunesciences.com. Follow @AlpineImmuneSci on Twitter and LinkedIn.

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 preclinical development activities; clinical and regulatory objectives and the timing thereof; the potential efficacy, safety profile, future research and development plans, addressable market, regulatory success, and commercial potential of our product candidates; our ability to achieve additional milestones in our collaborations; the progress and potential of our other ongoing development programs; the timing of our public presentations and potential publication of future clinical data; the efficacy of our clinical trial designs; anticipated enrollment in our clinical trials and the timing thereof; 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 preclinical efforts may not yield additional product candidates; our discovery-stage and preclinical 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; the impact of the COVID-19 pandemic on our business, research and clinical development plans and timelines and results of operations, including the impact on our clinical trial sites, collaborators, and contractors who act for or on our behalf, may be more severe and prolonged than currently anticipated; 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.

“NEON-1,” “NEON-2,” "Synergy," “RUBY” and the Alpine logo are registered trademarks or trademarks of Alpine Immune Sciences, Inc. in various jurisdictions.

ALPN-202, NEON-2 study is being conducted in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA

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