UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 12, 2022

ALPINE IMMUNE SCIENCES, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-37449**	**20-8969493**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

188 East Blaine Street, Suite 200
Seattle, Washington 98102
(Address of principal executive offices, including zip code)

(206) 788-4545

(Registrant's telephone number, including area code)
N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value $0.001 per share	ALPN	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).
Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On September 12, 2022, Alpine Immune Sciences, Inc. (the Company) provided clinical updates for its two wholly owned programs, ALPN-303 and davoceticept, at the Company's inaugural research and development day. Key highlights from the announcement include:

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 (CD38hi 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.

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.

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. The Company 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.

Forward-Looking Statements

This Current Report on Form 8-K 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 the Company's 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 the Company's product candidates; the Company's ability to achieve additional milestones in the Company's collaborations; the progress and potential of the Company's other ongoing development programs; the timing of the Company's public presentations and potential publication of future clinical data; the efficacy of the Company's clinical trial designs; anticipated enrollment in the Company's clinical trials and the timing thereof; expectations regarding the Company's ongoing collaborations; and the Company's ability to successfully develop and achieve milestones in the Company's 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 the Company's control, include, but are not limited to: clinical trials may not demonstrate safety and efficacy of any of the Company's product candidates; the Company's ongoing discovery and preclinical efforts may not yield additional product candidates; the Company's discovery-stage and preclinical programs may not advance into the clinic or result in approved products; any of the Company's 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; the Company may not achieve additional milestones in the Company's 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 the Company's business, research and clinical development plans and timelines and results of operations, including the impact on the Company's clinical trial sites, collaborators, and contractors who act for or on the Company's behalf, may be more severe and prolonged than currently anticipated; as well as the other risks identified in the Company's filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and the Company undertakes no obligation to update forward-looking statements, and readers are cautioned not to place undue reliance on such forward-looking statements.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 12, 2022

ALPINE IMMUNE SCIENCES, INC.

By: /s/ Paul Rickey
Name: Paul Rickey
Title: Senior Vice President and Chief Financial Officer