Alumis Initiates ONWARD Phase 3 Clinical Program Evaluating ESK-001, an Oral TYK2 Inhibitor, in Moderate-to-Severe Plaque Psoriasis

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– Co-primary endpoint of PASI 75 and sPGA 0/1 score at 24 weeks to serve as basis for U.S. regulatory submission –

– Pivotal Phase 3 program supported by positive Phase 2 STRIDE clinical data as well as ongoing open-label extension (OLE) study –

– Topline data anticipated in 2026 –

SOUTH SAN FRANCISCO, Calif., July 29, 2024 (GLOBE NEWSWIRE) -- Alumis Inc. (Nasdaq: ALMS), a clinical-stage biopharmaceutical company developing oral therapies using a precision approach to optimize clinical outcomes and significantly improve the lives of patients with immune-mediated diseases, today announced that patient dosing has commenced in the ONWARD Phase 3 clinical program. This Phase 3 program consists of two identical 24-week global Phase 3 clinical trials (ONWARD1 and ONWARD2) designed to evaluate the efficacy and safety of ESK-001 in adult patients with moderate-to-severe plaque psoriasis and includes a long-term extension (LTE) trial, ONWARD3, that will evaluate durability and maintenance of response and long-term safety.

“For people suffering from moderate-to-severe plaque psoriasis, there remains a significant unmet need for an oral treatment that can deliver high efficacy without compromising safety. ESK-001’s ability to maximally inhibit the TYK2 target offers the potential to deliver a differentiated profile to address this critical need,” said Dr. Jörn Drappa, Alumis’ Chief Medical Officer. “The ONWARD Phase 3 program is designed to mirror the Phase 2 program, building on the positive Phase 2 data in which ESK-001 was generally well tolerated and showed significant therapeutic effect, particularly in the ongoing OLE that shows increasing and durable responses over time with longer treatment. We look forward to generating the Phase 3 data that will support global regulatory submissions to potentially bring ESK-001 to patients.”

“Initiating the ONWARD Phase 3 clinical program for ESK-001 is an important milestone for Alumis as it brings us one step closer to our goal of delivering improved clinical outcomes for patients with immune-mediated diseases,” said Martin Babler, President and Chief Executive Officer of Alumis. “We believe this Phase 3 clinical program will further establish the ESK-001 profile we have seen to date as potentially the first and only oral allosteric TYK2 inhibitor that is well tolerated at doses that deliver maximal target inhibition for the treatment of moderate-to-severe plaque psoriasis.”

ESK-001 is also being evaluated in LUMUS, a Phase 2b clinical trial of ESK-001 for the treatment of patients with systemic lupus erythematosus. In addition, Alumis continues to leverage its precision

data analytics platform to explore ESK-001's potential application in other autoimmune indications.

About the ONWARD Phase 3 Clinical Program
The ONWARD Phase 3 clinical program consists of two identical global Phase 3, multi-center, randomized, double-blind placebo-controlled 24-week clinical trials, ONWARD1 and ONWARD2, designed to evaluate the efficacy and safety of ESK-001 in adult patients with moderate-to-severe plaque psoriasis. Comparators will include placebo, through Week 16, and apremilast, a widely used oral drug for the treatment of psoriasis, through Week 24. Each trial will enroll approximately 840 patients randomized 2:1:1 to receive either ESK-001 40 mg twice-daily, placebo or apremilast. The co-primary efficacy endpoints will be the proportion of patients with moderate-to-severe plaque psoriasis achieving greater than or equal to 75% reduction in Psoriasis Area and Severity Index (PASI 75) and static Physician's Global Assessment (sPGA) score 0/1 of ESK-001 compared to placebo at Week 16. Key secondary endpoints will include PASI 90, PASI 100 and sPGA 0 measured at Weeks 16 and 24, and safety and tolerability. Additionally, patient-reported outcomes including quality of life measures and pruritus will be captured. Patients completing Week 24 will have the opportunity to participate in a long-term extension (LTE) trial, ONWARD3, that will evaluate durability and maintenance of response and long-term safety. PASI is an instrument used to score, assess and grade the severity of psoriatic lesions and the patient's response to treatment. sPGA evaluates the severity of disease at a given point in time; an sPGA score of 1 indicates almost clear skin and 0 indicates totally clear skin.

In parallel with the Phase 3 clinical program, Alumis is developing a once-daily modified release (MR) oral formulation of ESK-001 that can replace the current immediate release (IR) oral formulation that is dosed twice daily.

About Psoriasis
Psoriasis is a chronic autoimmune inflammatory skin condition that can affect any part of the body. Plaque psoriasis, the most common type of psoriasis, causes red, dry and scaly thickened skin patches (plaques) that are itchy and may be painful. Disease severity can vary depending on intensity of symptoms. Moderate-to-severe disease has a greater negative impact on quality of life, with nearly one-quarter of psoriasis patients considered to have moderate-to-severe disease.

About ESK-001
Alumis' lead clinical candidate, ESK-001, is a potent, highly selective allosteric tyrosine kinase 2 (TYK2) inhibitor that reduces signaling through several cytokine receptors including receptors for interleukin (IL)-12, IL-23, and interferon (IFN)-a. The ongoing Phase 3 clinical program is supported by positive data from the Phase 2 STRIDE clinical trial in which 228 patients were randomized to one of five ESK-001 dose cohorts, or placebo. The trial met its primary endpoint, the proportion of patients achieving a PASI 75 at week 12 compared to placebo, and key secondary efficacy endpoints at all clinically relevant doses tested. Clear dose-dependent responses were observed with maximal efficacy and TYK2 inhibition achieved at the highest dose of 40 mg twice daily. ESK-001 was found to be generally well tolerated at all dose levels.

Upon completion of the STRIDE clinical trial, patients were eligible to be enrolled in an OLE study evaluating two ESK-001 doses (40 mg once daily and 40 mg twice daily). Preliminary data as of March 1, 2024 from the OLE study at 28 weeks of treatment showed significant increases in PASI endpoint responses over time, with the majority of patients (93% of evaluable patients (n=71), 82.7% using non-responder imputation (n=81)) achieving PASI 75 at the 40 mg twice-daily dose and ESK-001 continuing to be well tolerated. Data from the OLE study confirms the dose-dependence

relationship observed in the Phase 2 STRIDE trial, with the highest response rates and maximal TYK2 inhibition achieved at the highest dose of 40 mg BID. Beyond the March 1, 2024 data cut, patients in the OLE who were receiving the 40 mg QD dose will switch to the 40 mg BID dose, as the 40 mg BID dose was determined to represent the optimal risk benefit. Additional data cuts will be generated in the future as the study progresses, with anticipated updates in the second half of 2024 as well as in 2025.

About Alumis

Alumis is a clinical-stage biopharmaceutical company developing oral therapies using a precision approach to optimize clinical outcomes and significantly improve the lives of patients with immune-mediated diseases. Leveraging its proprietary precision data analytics platform, Alumis is building a pipeline of molecules with the potential to address a broad range of immune-mediated diseases as monotherapy or combination therapies. Alumis' most advanced product candidate, ESK-001, is an oral, highly selective, small molecule, allosteric inhibitor of tyrosine kinase 2 that is currently being evaluated for the treatment of patients with moderate-to-severe plaque psoriasis and systemic lupus erythematosus. Alumis is also developing A-005, a CNS-penetrant, allosteric TYK2 inhibitor for the treatment of neuroinflammatory and neurodegenerative diseases. Beyond TYK2, Alumis' proprietary precision data analytics platform and drug discovery expertise have led to the identification of additional preclinical programs that exemplify its precision approach. Incubated by Foresite Labs and led by a team of industry veterans experienced in small-molecule compound drug development for immune-mediated diseases, the Company is pioneering a precision approach to drug development to potentially produce the next generation of treatment to address immune dysfunction.

Forward-Looking Statements

This press release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will" and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this press release that are not statements of historical fact may be deemed to be forward-looking statements. These forward-looking statements include, without limitation, statements regarding Alumis' future plans and prospects, the potential for ESK-001 to become the first and only oral allosteric TYK2 inhibitor that is well tolerated at doses that deliver maximal target inhibition for the treatment of moderate-to-severe plaque psoriasis, any expectations regarding the safety, efficacy or tolerability of ESK-001, including based on the clinical update from Alumis' Phase 2 STRIDE clinical trial and ongoing OLE study, the ability of ESK-001 to treat moderate-to-severe plaque psoriasis and the planned initiation and number of expected patients of Alumis' ONWARD Phase 3 program and the timing thereof. Any forward-looking statements in this press release are based on Alumis' current expectations, estimates and projections only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Readers are cautioned that actual results, levels of activity, safety, efficacy, performance or events and circumstances could differ materially from those expressed or implied in Alumis' forward-looking statements due to a variety of risks and uncertainties, which include, without limitation, risks and uncertainties related to Alumis' ability to advance ESK-001 and its other clinical candidates and to obtain regulatory approval of and ultimately commercialize Alumis' clinical candidates, the timing and results of preclinical and clinical trials, Alumis' ability to fund development activities and achieve

development goals, Alumis' ability to protect its intellectual property and other risks and uncertainties described in Alumis' filings with the Securities and Exchange Commission (SEC), including any future reports Alumis may file with the SEC from time to time. Alumis explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

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