Alumis Presents Positive Data from Phase 2 Clinical Trial of ESK-001, an Oral Allosteric TYK2 Inhibitor for the Treatment of Plaque Psoriasis, at AAD Annual Meeting

March 9, 2024

– STRIDE Phase 2 primary endpoint of PASI 75 and key secondary endpoints met at all clinically relevant doses tested; sustained maximal target inhibition safely achieved at top dose –

– Open label extension (OLE) study data to date demonstrate increasing PASI responses over time, with high efficacy responses of 80-90% PASI 75 at top dose and continued favorable safety profile supporting potential for best-in-class profile –

– Initiation of Phase 3 clinical trials of ESK-001 planned in 2H 2024 –

– Alumis to host webcast on March 9 at 5:00 p.m. PT/8:00 p.m. ET –

SOUTH SAN FRANCISCO, Calif., March 9, 2024 – Alumis Inc., a clinical-stage biopharmaceutical company developing oral therapies using a precision approach to transform the lives of patients with immune-mediated diseases, today announced the presentation of positive clinical data from a Phase 2 clinical trial of ESK-001, a highly selective allosteric tyrosine kinase 2 (TYK2) inhibitor, for the treatment of patients with moderate-to-severe plaque psoriasis. These data were presented during a late-breaking session at the American Academy of Dermatology (AAD) Annual Meeting being held March 8-12 in San Diego, California.

The STRIDE trial enrolled 228 patients who were randomized to one of five ESK-001 dose cohorts, or placebo. The trial met its primary endpoint, the proportion of patients achieving a 75% improvement in the Psoriasis Area and Severity Score (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.

In the ongoing open label extension (OLE) study evaluating two ESK-001 doses (40 mg once daily and 40 mg twice daily), preliminary data from 16 weeks of treatment show significant increases in PASI endpoint responses over time, with the majority of patients (90% of evaluable patients, 80% using non-responder imputation) achieving PASI 75 at the 40 mg twice-daily dose, as well as a continued favorable safety profile. These data support the planned initiation of Phase 3 clinical trials of ESK-001 in moderate-to-severe plaque psoriasis in the second half of 2024.

“The Phase 2 clinical program was designed to evaluate the effect of different degrees of target inhibition on safety and clinical efficacy in psoriasis. We were pleased to see that ESK-001 was able to maximally inhibit the target safely, and this translated to a high degree of clinical improvement at week 12 that continued to increase over time,” said Dr. Jörn Drappa, Alumis’ Chief Medical Officer. “We are very excited about the risk-benefit profile observed in our Phase 2 program. These highly promising data support the potential for a best-in-class profile of ESK-001 in psoriasis.”

“Since starting my clinical practice years ago, I have witnessed the challenges faced by psoriasis patients. I see, and I feel, the very negative impact psoriasis has on their quality of life. Well tolerated and safe oral treatments with biologic-like efficacy would represent a true innovation in the treatment of psoriasis. I am excited about the possibility of TYK2 inhibitors achieving that goal,” said Dr. Kim Papp, Founder and President of Probity Medical Research and clinical investigator in the STRIDE clinical trial. “These Phase 2 results for ESK-001 support its potential as a new treatment option in moderate-to-severe psoriasis. I am thrilled to see how this treatment may offer hope and relief for my patients who need more effective options.”

Martin Babler, President and Chief Executive Officer of Alumis, added, “Importantly, in the Phase 2 study, the ESK-001 dose cohorts explored the full range of TYK2 target inhibition and its translation to efficacy as confirmed by RNA sequencing. We observed that maximal target inhibition through the 24-hour dosing period, achieved by our top dose, is required for high biologic-range efficacy. Doses that did not achieve maximum target inhibition led to a significant reduction in long-term efficacy. This gives us confidence as we prepare to initiate Phase 3 trials with the goal of offering an oral treatment with greater efficacy as compared to existing treatments, not only for patients with psoriasis but for other immune-mediated diseases as well."

Data from the STRIDE Phase 2 clinical trial are summarized as follows:

- The trial met its primary endpoint of 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 consistent with increasing levels of target inhibition.

ESK-001 STRIDE – PASI Responses at Week 12

	PASI 75 (%)	PASI 90 (%)	PASI 100 (%)
40 mg BID	64.1***	38.5***	15.4*
20 mg BID	56.4***	25.6***	10.3*
40 mg QD	56.4***	25.6***	7.7
20 mg QD	33.3***	11.1*	0
10 mg QD	19.4**	0	0
Placebo	0	0	0

*p<0.05; **p< 0.005; ***p<0.001; *BID = twice daily, QD = once daily*

- ESK-001 treatment response continued to improve over time with maximum efficacy reached at week 24 and beyond, consistent with PASI 75 outcomes for psoriasis treatments irrespective of mechanism.

- Treatment with ESK-001 was well tolerated with no treatment-related serious adverse events. The incidence of treatment-related AEs was similar between ESK-001 and placebo and the majority of treatment-emergent adverse events were mild or moderate in severity. There was no evidence of adverse events associated with JAK inhibition. There was a low (<3%) discontinuation rate due to AEs. Most common AEs were headache, upper respiratory tract infection and nasopharyngitis.
- At the 40 mg twice-daily dose, ESK-001 RNA sequencing data showed maximal target inhibition in both plasma and skin biopsies.

Data from the ongoing OLE study as of December 8, 2023, are summarized as follows:

- Data show significant increases in PASI endpoint responses and that ESK-001 continues to be well tolerated with up to 28 weeks of treatment.
- At 16 weeks, at the 40 mg twice-daily dose, the majority of patients (90% of evaluable patients, 80% using non-responder imputation) achieved PASI 75.

ESK-001 OLE – PASI Responses at Week 16, 40 mg BID

	PASI 75 (%)	PASI 90 (%)	PASI 100 (%)
As Observed	90	57	35
NRI*	80	51	31

**NRI: non responder imputation*

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 (SLE), and in OPTYK-1, a proof-of-concept Phase 2 clinical trial in non-infectious uveitis. In addition, Alumis continues to leverage its precision data analytics and a multi-platform approach to explore ESK-001's potential application in other autoimmune indications. Alumis is also developing a once-daily tablet for ESK-001.

Webcast Details

Alumis will be hosting an investor event webcast to discuss these data at 5:00 p.m. PT on March 9, 2024. To access the webcast, register on the Events page of the Alumis website.

About the STRIDE Clinical Trial and Open-Label Extension Study

The STRIDE trial (NCT05600036) is a randomized, double-blind, placebo-controlled Phase 2 dose-ranging clinical trial designed to evaluate the efficacy, safety, pharmacokinetics and pharmacodynamics of ESK-001 in patients with moderate to severe plaque psoriasis. The trial enrolled 228 patients across five doses of ESK-001 (10 mg QD, 20 mg QD, 40 mg QD, 20 mg BID, 40 mg BID). Patients received ESK-001 or placebo over a 12-week period, with a 4-week treatment withdrawal follow-up period. The primary endpoint of the trial is the proportion of patients with moderate to severe plaque psoriasis achieving greater than or equal to 75% reduction in PASI (PASI 75) across doses of ESK-001 compared to placebo. PASI, or Psoriasis Area and Severity Index, is an instrument used to score, assess and grade the severity of psoriatic lesions and the patient's response to treatment. Key secondary endpoints include safety and tolerability, PASI 90, PASI 100 and static Physician's Global Assessment (sPGA) score. sPGA evaluates the severity of diseases at a given point in time; an sPGA score of 1 indicates almost clear skin and 0 indicates totally clear skin. Upon completion of the clinical trial, including the 4-week treatment withdrawal follow-up period, patients are eligible to enroll in an open-label extension (OLE) study (NCT05739435) evaluating two doses of ESK-001. In the ongoing OLE, 164 patients were randomized to receive 40 mg once daily or 40 mg twice daily; the primary endpoint is safety and tolerability, and secondary endpoints include PASI and DLQI scores, as well as pharmacokinetic measures.

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 highly-selective and potentially best-in-class 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. In Alumis' Phase 1 studies, ESK-001 demonstrated maximal inhibition of the pharmacodynamic assay over the dosing schedule of 24 hours, with no observed Janus kinase (JAK)-related safety events to date. ESK-001 was well-tolerated in these studies, with no serious adverse events observed.

About Alumis

Alumis is a clinical-stage biopharmaceutical company developing oral therapies using a precision approach to optimize outcomes and transform the lives of patients with immune-mediated diseases. Leveraging its precision data analytics and a multi-platform approach, Alumis is advancing a pipeline of oral therapies designed to address immune dysfunction. Alumis' lead candidate ESK-001 is a highly selective and potentially best-in-class allosteric tyrosine kinase 2 (TYK2) inhibitor that is currently being evaluated for the treatment of patients with moderate to severe plaque psoriasis, systemic lupus erythematosus (SLE), and non-infectious uveitis. Alumis is also developing A-005, a potential first-in-class brain-penetrant allosteric TYK2 inhibitor for the treatment of neuroinflammatory and neurodegenerative diseases that is anticipated to enter a Phase 1 clinical trial in the first half of 2024. Alumis also has discovery efforts in undisclosed immune-mediated diseases and targets identified by its data analytics platform. Incubated by Foresite Labs and led by a team of experts with deep experience and proven track records in drug discovery, development and immunology, Alumis is developing transformative therapies that aim to reimagine the lives of people with immune-mediated diseases. For more information, please visit alumis.com.

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