Alumis Announces Positive Phase 1 Data for CNS Penetrant TYK2 Inhibitor, A-005

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– A-005 was well tolerated and demonstrated ability to cross blood-brain barrier –

– Maximal TYK2 inhibition achieved with favorable pharmacokinetic profile in CNS and periphery –

– Data support advancement to Phase 2 clinical trial in multiple sclerosis, anticipated in 2H 2025 –

SOUTH SAN FRANCISCO, Calif., Dec. 19, 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 positive data from a Phase 1 clinical trial evaluating the safety, tolerability, and pharmacokinetics (PK) of single- and multiple-ascending doses of A-005, a potent, selective, central nervous system (CNS) penetrant TYK2 inhibitor, in healthy participants.

“A-005 is the first reported allosteric TYK2 inhibitor that has demonstrated the ability to cross the human blood-brain barrier to address inflammation within the central nervous system (CNS). Based on these data, we expect to begin a Phase 2 clinical trial in patients with multiple sclerosis (MS) in the second half of 2025,” said Jörn Drappa, M.D., Alumis’ Chief Medical Officer. “Our Phase 2 clinical trial of ESK-001 in psoriasis demonstrated that maximal TYK2 inhibition was critical for increased clinical responses. Similarly, we hope to demonstrate that potent and selective target engagement of A-005 in the CNS leads to clinical benefit in MS, our first indication, and potentially in other neuroinflammatory and neurodegenerative conditions in the future.”

In the clinical trial, A-005 was well tolerated with no serious adverse events reported. A-005 demonstrated the ability to penetrate into the CNS with significant and prolonged exposure in the cerebral spinal fluid (CSF). A-005 levels in the CSF were comparable to or exceeded the free drug exposure in plasma and exceeded IC_{90} levels in cell-based assays. In the single-ascending dose cohorts, drug exposures generally increased in a dose proportional manner, rapidly reaching peak drug concentration (Tmax) and half-lives of up to 12 hours. A PK/PD relationship was established showing prolonged and maximal TYK2 inhibition in the periphery, as assessed by levels of phosphorylated STAT proteins.

Alumis plans to present data from the Phase 1 clinical trial at the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum 2025 taking place February 27- March 1, 2025, in West Palm Beach, Florida.

About the Phase 1 Clinical Trial
The Phase 1 clinical trial evaluated the safety, tolerability, and pharmacokinetics (PK) of single- and multiple-ascending doses of A-005 in 135 healthy participants. The trial included a single-ascending

dose (SAD) portion which evaluated ten dose cohorts, a 14-day multiple-ascending (MAD) dose portion which evaluated five dose cohorts (n=8, 6 active, 2 placebo) and a single dose cohort which included a lumbar puncture to assess A-005 concentrations in the CSF. For the SAD and MAD portions of the study, pharmacodynamic (PD) markers (including pSTAT levels) were measured to establish a PK/PD relationship.

About A-005
A-005 is a potential first-in-class CNS penetrant allosteric tyrosine kinase 2 (TYK2) inhibitor being developed for the treatment of neuroinflammatory and neurodegenerative diseases such as multiple sclerosis and Parkinson's Disease. A-005 is designed to achieve maximal TYK2 inhibition and to cross the blood brain barrier for localized treatment both within the CNS and in the periphery, supporting its potential across multiple TYK2-mediated indications. TYK2 is a protein that plays a role in mediating signaling responses to key proinflammatory cytokines, including interleukin (IL)-23, IL-12 and interferon-alpha (IFNα). TYK2 inhibition has been clinically validated in autoimmune conditions, and Alumis' data analytics support a genetic rationale for TYK2 inhibition as a novel approach in diseases of the central nervous system.

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, with multiple sclerosis (MS) as its initial indication. With two clinical-stage TYK2 inhibitors that have the ability to achieve maximal target inhibition, Alumis' TYK2 franchise enables the company to pursue the broad range of immune-mediated diseases identified by TYK2 genetics in a strategically thoughtful way. 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, Alumis is pioneering a precision approach to drug development to potentially produce the next generation of treatment to address immune dysfunction. For more information, visit https://www.alumis.com.

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 cost and timing of its product candidate development activities and current and future clinical trials and studies, including its strategy in pursuing immune-mediated diseases, trial design and commencement, any expectations

regarding the safety, efficacy, or tolerability of A-005, and the ability of A-005 to treat MS and other neuroinflammatory and neurodegenerative diseases, and Alumis' participation at upcoming conferences. 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 A-005 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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