Alkermes Announces Positive Phase 1b Results Demonstrating Clinical Proof-of-Concept for ALKS 7290 in Adults With Attention-Deficit Hyperactivity Disorder (ADHD)

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— ALKS 7290 is the First Orexin 2 Receptor Agonist to Demonstrate Clinically Meaningful Improvements in ADHD Symptoms in Adults —

— ALKS 7290 Was Generally Well Tolerated at All Doses Tested in Healthy Volunteers and Adults With ADHD —

— Phase 2 Study of ALKS 7290 in Adults With ADHD is Enrolling, Data Expected in 2027 —

DUBLIN--(BUSINESS WIRE)--Sep. 21, 2026-- Alkermes plc (Nasdaq: ALKS) today announced positive topline results from a phase 1 proof-of-concept study evaluating ALKS 7290, the company's novel, investigational orexin 2 receptor (OX2R) agonist in development for the treatment of attention-deficit hyperactivity disorder (ADHD). The study evaluated the safety and tolerability (primary objective) and pharmacokinetics (PK) and pharmacodynamics (PD) of ALKS 7290 in healthy volunteers (n=88) and in adults with ADHD (n=50). In the phase 1 study, ALKS 7290 was generally well tolerated at all doses tested in healthy volunteers and adults with ADHD. In adult participants with ADHD, ALKS 7290 demonstrated dose-dependent, clinically meaningful improvements on exploratory endpoints evaluating change from baseline on established clinical scales, the Adult ADHD Investigator Symptom Rating Scale (AISRS) and Clinical Global Impression-Severity Scale (CGI-S), at day 14 of treatment. These findings represent the first clinical evidence of the effects of an orexin receptor agonist in the treatment of ADHD and further support the dose range selected for the ongoing phase 2 study evaluating the efficacy and safety of ALKS 7290 in adults with ADHD.

"ADHD is a common mental health condition that can have profound effects on multiple aspects of daily life, including academic achievement, career success, relationships and overall physical and emotional well-being. For many patients today, there remains a critical need for differentiated therapies that provide strong, well-tolerated efficacy," said Greg Mattingly, M.D., Founding Partner of St. Charles Psychiatric Associates, President at Midwest Research Group and Associate Clinical Professor in the Department of Psychiatry at the Washington University School of Medicine. "These data provide early evidence supporting the potential of the orexin pathway to influence the brain's neural networks that are linked to ADHD and suggest that ALKS 7290 could represent a meaningful new therapeutic approach for patients."

The phase 1b study enrolled 50 adults with ADHD in a double-blind, placebo-controlled, parallel-group trial with two cohorts. Following a two-week washout of existing ADHD medications, participants were randomized (4:1, active:placebo) within each cohort to receive ALKS 7290 (total daily dose of 20 mg (n=20) or 50 mg (n=20), administered in split doses) or placebo (n=10) for 14 days of inpatient treatment. In addition to safety, tolerability and PK and PD effects, the study evaluated change from baseline across a range of exploratory endpoints to begin to characterize the effects of ALKS 7290 on symptoms of ADHD. The study was not designed or powered to detect statistically significant differences between treatment groups.

Topline results from the study include:

Clinical Endpoints

- AISRS [1]: ALKS 7290 demonstrated clinically meaningful[2] improvements from baseline in ADHD symptoms as measured by the AISRS, a 54-point, clinician-administered, validated measure of ADHD symptom severity. At baseline, participants had a median AISRS total score of approximately 39, consistent with substantial ADHD symptom burden. Clinically meaningful improvements were observed as early as day 6, the first post-baseline AISRS assessment. At day 14, treatment with ALKS 7290 demonstrated median reductions from baseline in AISRS total scores of 14.0 points for the 20 mg dose and 19.0 points for the 50 mg dose. Clinically meaningful improvements were observed across AISRS Inattentive and Hyperactivity/Impulsivity subscales.

- CGI-S [3]: ALKS 7290 demonstrated clinically meaningful[2] improvements from baseline in overall ADHD disease severity as measured on the CGI-S scale. At baseline, participants had median CGI-S scores of 4.0 and 5.0 in the 20 mg and 50 mg dose groups, respectively. Clinically meaningful improvements were observed as early as day 6, the first post-baseline CGI-S assessment. At day 14, treatment with ALKS 7290 demonstrated median reductions from baseline in CGI-S scores of 1.0 for the 20 mg dose and 2.0 for the 50 mg dose, representing a shift in disease severity from markedly or moderately ill to mildly ill.

CNS Biomarkers and Objective Cognitive Performance Tests

- The phase 1b study included multiple EEG-based biomarkers and performance-based cognitive tests designed to measure dose-related central activity and domains underlying ADHD symptoms. Findings from these assessments support our dosing decisions for phase 2 and showed treatment effects of ALKS 7290 across important cognitive domains, including processing speed, information processing, working memory and attention.

Topline Safety

- ALKS 7290 was generally well tolerated across all doses tested in participants with ADHD. No serious treatment-emergent adverse events (TEAEs) were reported.
- Most TEAEs were mild in severity. The most common TEAEs[4] were insomnia, pollakiuria, dizziness, change in sustained attention, micturition urgency, and constipation.
- There were no clinically significant findings observed in hepatic or renal parameters, vital signs or ECGs.
- Two participants in the placebo group discontinued the study; there were no discontinuations among participants receiving ALKS 7290.

In healthy volunteers (n=88), single- and multiple-ascending doses of ALKS 7290 were evaluated for up to 10 days. ALKS 7290 was generally well tolerated across all doses tested and the maximum tolerated dose was not reached. ALKS 7290 was observed to be centrally active and to have a PK and PD profile that supports oral dosing with a wide therapeutic index.

"Results from this phase 1 study of ALKS 7290 represent an important milestone in the advancement of our orexin portfolio and support our strategy to explore the potential of orexin biology beyond hypersomnolence disorders," said Craig Hopkinson, M.D. (MBChB), Chief Medical Officer and Executive Vice President of Research & Development at Alkermes. "This exploratory, first-in-patient study was designed to provide early insights into the potential of orexin 2 receptor agonism as a novel treatment for adults with ADHD, and we are excited to see the emerging clinical profile of ALKS 7290. The results begin to build the foundation of our understanding of ALKS 7290, and we look forward to further evaluating its safety and efficacy in our ongoing well-powered phase 2 study."

A phase 2 study evaluating the safety and efficacy of once-daily and split doses of ALKS 7290 compared to placebo in adults with ADHD is currently enrolling (NCT07755410). Following a two-week washout period of existing ADHD medications, participants will be randomized to receive one of three dosing regimens of ALKS 7290 or placebo. The study will evaluate the primary endpoint of change from baseline in AISRS total score at week four compared to placebo. The study is expected to enroll approximately 312 participants with ADHD. The first participant was dosed in September 2026.

About the ALKS 7290 Phase 1 Study

The phase 1 study for ALKS 7290 consisted of three parts: single-ascending dose and multiple-ascending dose evaluations in healthy volunteers (parts 1 and 2), and a phase 1b, proof-of-concept study in adults with attention-deficit hyperactivity disorder (ADHD) (part 3).

In the healthy volunteer portion of the study, each cohort included eight participants, six of whom were randomized to receive ALKS 7290 and two of whom received placebo. In the multiple-ascending dose portion, participants received doses of ALKS 7290 for up to 10 days. The objectives of parts 1 and 2 of the study were to assess ALKS 7290's safety, tolerability, pharmacokinetics and pharmacodynamics.

The phase 1b proof-of-concept portion of the study (part 3) enrolled 50 adults with ADHD in a double-blind, placebo-controlled, parallel-group study. Following a two-week washout period of existing ADHD medications, participants within each cohort were randomized in a 4:1 (active:placebo) ratio to receive split doses of ALKS 7290 (total daily dose of 20 mg or 50 mg) or matching placebo for 14 days of inpatient treatment. The primary objective was to evaluate the safety and tolerability of ALKS 7290. Changes from baseline on established clinical ADHD scales, including the ADHD Investigator Symptom Rating Scale (AISRS) and the Clinical Global Impression-Severity Scale (CGI-S), were assessed as an exploratory objective. The study was not designed or powered to detect statistically significant differences between treatment groups; findings disclosed are not in reference to any other study group. The study also included exploratory translational and neuropsychological performance measures to characterize the effects of treatment in a short duration study.

About ALKS 7290

ALKS 7290 is a novel, investigational, oral orexin 2 receptor (OX2R) agonist in development for the treatment of attention-deficit hyperactivity disorder (ADHD). Orexin, a neuropeptide produced in the lateral hypothalamus, plays a crucial role in regulating wakefulness, and engages multiple downstream pathways and neural circuits relevant to attention, cognition and mood.[5] By targeting the orexin system, ALKS 7290 has the potential to address symptoms relevant to a broad range of disorders characterized by impairments in these domains. ALKS 7290 has been evaluated in a phase 1 study in healthy volunteers and adults with ADHD, and is currently being evaluated in a phase 2 study in adults with ADHD.

About Alkermes plc

Alkermes plc (Nasdaq: ALKS), a mid-cap growth and value equity, is a global biopharmaceutical company that seeks to develop innovative medicines in the field of neuroscience. The company has a portfolio of proprietary commercial products for the treatment of alcohol dependence, opioid dependence, schizophrenia, bipolar I disorder and narcolepsy. Alkermes' pipeline includes late-stage clinical candidates in development for narcolepsy and idiopathic hypersomnia, and orexin 2 receptor agonists in early clinical development for other neurological disorders, including attention-deficit hyperactivity disorder (ADHD) and fatigue associated with multiple sclerosis and Parkinson's disease. Headquartered in Ireland, Alkermes also has a corporate office and research and development center in Massachusetts and a manufacturing facility in Ohio. For more information, please visit Alkermes' website at www.alkermes.com.

Note Regarding Forward-Looking Statements

Certain statements set forth in this press release constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the potential therapeutic and commercial value of ALKS 7290, and the company's expectations, including timelines, related to the ALKS 7290 development program. The company cautions that forward-looking statements are inherently uncertain. Although the company believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those expressed or implied in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: clinical study results for ALKS 7290 may not be predictive of results of future stages of ongoing clinical studies, future clinical studies or real-world results; clinical studies for ALKS 7290 may not be initiated or completed on expected timelines or at all; ALKS 7290 may be shown to be ineffective or unsafe; the FDA may not agree with the company's regulatory strategies or components of its development program for ALKS 7290, including clinical trial designs, conduct and methodologies; potential changes in the cost, scope and duration of the ALKS 7290 development program; and those risks and uncertainties described under the heading "Risk Factors" in the company's Annual Report on Form 10-K for the year ended Dec. 31, 2025 and in subsequent filings made by the company with the U.S. Securities and Exchange Commission (SEC), which are available on the SEC's website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof.

Except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release.

[1] AISRS: 18-item clinician-administered rating scale (score: 0-54) used to assess the severity of inattentive and hyperactive/impulsive ADHD symptoms in adults, with higher scores reflecting greater symptom severity.

[2] Spencer TJ, Adler LA, Qiao M, et al. Validation of the Adult ADHD Investigator Symptom Rating Scale (AISRS). *J Atten Disord*. 2010;14(1):57-68. doi:10.1177/1087054709347435.

[3] CGI-S: Clinician-rated, single item scale assessing severity of illness on a 7-point Likert-type rating scale (1 = normal, no signs of illness to 7 = among the most extremely ill patients).

[4] TEAEs in ≥10% of participants treated with ALKS 7290.

[5] Katzman MA, Katzman MP. Neurobiology of the Orexin System and Its Potential Role in the Regulation of Hedonic Tone. *Brain Sciences*. 2022; 12(2):150. https://doi.org/10.3390/brainsci12020150

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