Nuvalent Presents Preliminary Data for Neladalkib in Advanced ALK-positive Solid Tumors Beyond NSCLC at ESMO 2025

Encouraging preliminary activity observed across diverse set of advanced ALK-positive solid tumors

Global enrollment ongoing for adult and adolescent patients with advanced ALK-positive solid tumors beyond NSCLC in a Phase 2 cohort of the ALKOVE-1 trial

CAMBRIDGE, Mass., Oct. 18, 2025 /PRNewswire/ -- Nuvalent, Inc. (Nasdaq: NUVL), a clinical-stage biopharmaceutical company focused on creating *precisely* targeted therapies for clinically proven kinase targets in cancer, today announced preliminary data from the ongoing ALKOVE-1 Phase 1/2 clinical trial of neladalkib, an investigational ALK-selective inhibitor, in patients with advanced ALK-positive solid tumors outside of non-small cell lung cancer (NSCLC). These data will be presented during a poster session at the European Society for Medical Oncology (ESMO) Congress 2025, taking place October 17-21, 2025, in Berlin, Germany, and are available on Nuvalent's website atwww.nuvalent.com.

"Neladalkib was designed with the goal of being a best-in-class ALK-selective inhibitor, and initial clinical safety and efficacy data have been reported in TKI pre-treated ALK-positive NSCLC with topline pivotal data expected by the end of this year. Today, we're excited to share the first report of neladalkib's encouraging preliminary activity beyond NSCLC, which continue to demonstrate its target characteristics of activity against ALK and ALK resistance mutations, brain penetrance, and avoidance of TRK inhibition associated with off-target CNS adverse events," **said Christopher Turner, M.D., Chief Medical Officer of Nuvalent.** "These data highlight the potential for an ALK-selective inhibitor to broadly address medical needs for patients with ALK-positive solid tumors, and the importance of widespread genomic testing. We continue to enroll adult and adolescent TKI naïve and TKI pre-treated patients with advanced ALK-positive solid tumors beyond NSCLC in the global Phase 2 portion of our ALKOVE-1 study, and look forward to providing additional updates as these data mature."

Preliminary data are reported for 34 response-evaluable patients enrolled across 14 solid tumor types outside of NSCLC in the Phase 1 and Phase 2 portions of the ALKOVE-1 clinical trial as of a data cutoff date of August 7, 2025. The majority (32/34) of patients received the recommended Phase 2 dose of 150 mg once daily. Patients were ALK TKI-naïve (38%, 13/34) or ALK TKI pre-treated (62%, 21/34), and 62% (21/34) of patients had received prior chemotherapy.

Among all patients with advanced ALK-positive solid tumors treated with neladalkib, an objective response rate of 44% (15/34) was observed, including 9/13 patients who were ALK TKI-naïve and 6/21 who were ALK TKI pre-treated. 80% (12/15) of

responders remained on treatment without disease progression as of the data cutoff date. Three case studies support neladalkib's potential to induce deep and durable responses in a range of treatment settings:

- Treatment ongoing for approximately 12 months with partial response in a TKI-naïve patient with an inflammatory myofibroblastic tumor previously treated with standard of care chemotherapy;
- Treatment ongoing for approximately 16 months with partial response in a TKI and chemotherapy pre-treated patient with peritoneal mesothelioma; and,
- Treatment ongoing for approximately 10 months with confirmed intracranial complete response in a TKI pre-treated patient with adenocarcinoma of unknown origin with baseline brain metastasis and ALK V1180L resistance mutation.

Among these 34 patients, neladalkib was generally well-tolerated with low rates of dose reduction (8.8%) and no discontinuations due to treatment-related adverse events as of the data cutoff date. The preliminary overall safety profile was consistent with its ALK-selective, TRK-sparing design, and with previously reported data.

Enrollment is ongoing in the global Phase 2 cohort of the ALKOVE-1 trial for adult and adolescent patients with advanced ALK-positive solid tumors other than NSCLC.

The company remains on track to report topline data for patients with TKI pre-treated ALK-positive NSCLC from the ALKOVE-1 trial by the end of 2025. Neladalkib is also being evaluated in ALKAZAR, a global Phase 3 randomized, controlled trial for the treatment of patients with TKI-naïve ALK-positive NSCLC.

About Neladalkib

Neladalkib is an investigational brain-penetrant ALK-selective inhibitor created with the aim to overcome limitations observed with currently available ALK inhibitors. Neladalkib is designed to remain active in tumors that have developed resistance to first-, second-, and third-generation ALK inhibitors, including tumors with single or compound treatment-emergent ALK mutations such as G1202R. In addition, neladalkib is designed for central nervous system (CNS) penetrance to improve treatment options for patients with brain metastases, and to avoid inhibition of the structurally related tropomyosin receptor kinase (TRK) family. Together, these characteristics have the potential to avoid TRK-related CNS adverse events seen with dual TRK/ALK inhibitors and to drive deep, durable responses for patients across all lines of therapy. Neladalkib has received breakthrough therapy designation for the treatment of patients with locally advanced or metastatic ALK-positive non-small cell lung cancer (NSCLC) who have been previously treated with 2 or more ALK tyrosine kinase inhibitors and orphan drug designation for ALK-positive NSCLC.

About Nuvalent

Nuvalent, Inc. (Nasdaq: NUVL) is a clinical-stage biopharmaceutical company focused on creating *precisely* targeted therapies for patients with cancer, designed to overcome the limitations of existing therapies for clinically proven kinase targets. Leveraging deep expertise in chemistry and structure-based drug design, we develop innovative small molecules that have the potential to overcome resistance, minimize adverse events, address brain metastases, and drive more durable responses. Nuvalent is advancing a robust pipeline with investigational candidates for ROS1-positive, ALK-positive, and HER2-altered non-small cell lung cancer, and multiple discovery-stage research programs.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding Nuvalent's strategy, business plans, and focus; the expected timing of data announcements; the clinical development programs for neladalkib; the potential benefits and effects of Nuvalent's product development candidates; the design and enrollment of the ALKOVE-1 trial; the potential of Nuvalent's pipeline programs, including neladalkib; the implications of data readouts and presentations; Nuvalent's research and development programs for the treatment of cancer; and risks and uncertainties associated with drug development. The words "may," "might," "will," "could," "would," "should," "plan," "anticipate," "aim," "goal," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" or the negative of these terms and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. You should not place undue reliance on these statements or the scientific data presented.

Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties, and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation: risks that Nuvalent may not fully enroll its clinical trials or that enrollment will take longer than expected; unexpected concerns that may arise from additional data, analysis, or results obtained during preclinical studies or clinical trials; the risk that results of earlier clinical trials may not be predictive of the results of later-stage clinical trials; the risk that data from our clinical trials may not be sufficient to support registration and that Nuvalent may be required to conduct one or more additional studies or trials prior to seeking registration of our product candidates; the occurrence of adverse safety events; risks that the FDA may not

approve our potential products on the timelines we expect, or at all; risks of unexpected costs, delays, or other unexpected hurdles; risks that Nuvalent may not be able to nominate drug candidates from its discovery programs; the direct or indirect impact of public health emergencies or global geopolitical circumstances on the timing and anticipated timing and results of Nuvalent's clinical trials, strategy, and future operations; the timing and outcome of Nuvalent's planned interactions with regulatory authorities; and risks related to obtaining, maintaining, and protecting Nuvalent's intellectual property. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Nuvalent's Quarterly Report on Form 10-Q for the quarter ended June 30, 2025, as well as any prior and subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent Nuvalent's views only as of today and should not be relied upon as representing its views as of any subsequent date. Nuvalent explicitly disclaims any obligation to update any forward-looking statements.

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