# Nuvalent Details Strategy to Seek First Potential Approval in 2026 and Outlines Key Anticipated 2025 Milestones

## Strategy prioritizes most accelerated path to first potential approval

## Initial NDA submission expected by mid-year for zidesamtinib in TKI pre-treated ROS1-positive NSCLC population, with topline pivotal data anticipated in the first

# half of 2025

# Topline pivotal data for neladalkib (NVL-655) in TKI pre-treated ALK-positive NSCLC population anticipated by year-end 2025

# Company to present at 43rd Annual J.P. Morgan Healthcare Conference on Tuesday, January 14th at 9:00 a.m. PT

CAMBRIDGE, Mass., Jan. 13, 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 highlighted pipeline progress and outlined key anticipated milestones towards its first potential U.S. Food and Drug Administration (FDA) approval under its "OnTarget 2026" operating plan.

As part of this plan, Nuvalent anticipates the following 2025 milestones:

- Report pivotal data for tyrosine kinase inhibitor (TKI) pre-treated patients with advanced ROS1-positive non-small cell lung cancer (NSCLC) from its ARROS-1 Phase 1/2 trial of zidesamtinib in the first half of 2025;
- Submit a New Drug Application (NDA) for zidesamtinib with initial target indication of TKI pre-treated patients with advanced ROS1-positive NSCLC by mid-year 2025;
- Report pivotal data for TKI pre-treated patients with advanced ALK-positive NSCLC from its ALKOVE-1 Phase 1/2 trial of neladalkib (NVL-655) by year-end 2025;
- Initiate the ALKAZAR Phase 3 randomized, controlled trial of neladalkib for TKI-naïve patients with ALK-positive NSCLC in the first half of 2025; and

- Progress the HEROEX-1 Phase 1a/1b trial of NVL-330 for patients with advanced HER2-altered NSCLC.

With the achievement of these milestones, the company anticipates that the first potential approval from its pipeline of novel kinase inhibitors will be for zidesamtinib for the treatment of TKI pre-treated ROS1-positive NSCLC in 2026.

"2025 marks our opportunity to transition to becoming a fully integrated commercial-stage biopharmaceutical company. Throughout this period of growth and evolution, our strategy remains rooted in our commitment to our core value of Patient Impact, and our responsibility to the patients and treating physicians who continue to support our clinical trials," said **James Porter, Ph.D., Chief Executive Officer at Nuvalent.**"Enrollment momentum in the Phase 2 portions of our ARROS-1 and ALKOVE-1 clinical trials has further accelerated following our presentation of updated Phase 1 data at ESMO 2024, reinforcing our plan to report pivotal data from both programs this year. We believe this enthusiasm is a clear demonstration of the medical need for patients with ROS1- and ALK-positive NSCLC, and of our responsibility to bring new treatment options to TKI pre-treated patients as quickly as possible."

"Parallel development paths are in place towards our ultimate goal to provide new, potential best-in-class treatment options to *all* patients with ROS1- or ALK-positive NSCLC,"**said Darlene Noci, A.L.M., Chief Development Officer at Nuvalent.**"For zidesamtinib, we plan to submit an NDA this year with an initial target indication for TKI pre-treated patients with ROS1-positive NSCLC, where we believe zidesamtinib has demonstrated the potential to address a medical need. We expect to report topline pivotal data from this population in the first half of 2025. In parallel, we continue a collaborative dialogue with the FDA on accelerated opportunities towards a potential line-agnostic indication supported by our ongoing TKI-naïve cohort in the Phase 2 portion of our ARROS-1 trial."

**Ms. Noci continued**, "Similarly for neladalkib, we expect our initial NDA submission to be for TKI pre-treated patients with ALK-positive NSCLC, supported by topline pivotal data from the ALKOVE-1 trial that we expect to report by year-end 2025. Additionally, we remain on-track to initiate the Phase 3 randomized, controlled ALKAZAR trial for TKI-naïve patients in the first half of this year, a critical step towards our ultimate goal of moving neladalkib up the treatment paradigm."

"We believe we have the right team in place and are well resourced with cash runway into 2028 to support the advancement of our clinical programs and ongoing buildout of a commercial infrastructure," said **Alexandra Balcom, Chief Financial Officer at Nuvalent.** "Beyond our parallel-lead programs, we remain committed to advancement of our HEROEX-1 Phase 1a/1b trial and robust discovery pipeline for sustainable long-term growth."

**Enrollment Updates for ARROS-1 and ALKOVE-1**

*ARROS-1 for ROS1-positive NSCLC*

- As of December 31, 2024, a total of 430 Phase 1 and Phase 2 patients had been enrolled in the ongoing ARROS-1 Phase 1/2 trial of zidesamtinib for patients with advanced ROS1-positive NSCLC and other solid tumors, which is designed with registrational intent for TKI pre-treated and TKI-naïve patients with advanced ROS1-positive NSCLC. Updated Phase 1 data were presented in September 2024 at the ESMO Congress.

*ALKOVE-1 for ALK-positive NSCLC*

- As of December 31, 2024, a total of 596 Phase 1 and Phase 2 patients had been enrolled in the ongoing ALKOVE-1 Phase 1/2 trial of neladalkib for patients with advanced ALK-positive NSCLC and other solid tumors, which is designed with registrational intent for TKI pre-treated patients. Updated Phase 1 data were presented in September 2024 at the ESMO Congress.

**Presentation at 43rd Annual J.P. Morgan Healthcare Conference**

Dr. Porter will present at the 43rd Annual J.P. Morgan Healthcare Conference in San Francisco on Tuesday, January 14, 2025 at 9:00 a.m. PT. A live webcast will be available in the Investors section of Nuvalent's website at www.nuvalent.com, and will be archived for 30 days following the conference.

**About Zidesamtinib**

Zidesamtinib is a novel brain-penetrant ROS1-selective inhibitor created with the aim to overcome limitations observed with currently available ROS1 inhibitors. Zidesamtinib is designed to remain active in tumors that have developed resistance to currently available ROS1 inhibitors, including tumors with treatment-emergent ROS1 mutations such as G2032R. In addition, zidesamtinib 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/ROS1 inhibitors and to drive deep, durable responses for patients across all lines of therapy. Zidesamtinib has received breakthrough therapy designation for the treatment of patients with ROS1-positive metastatic non-small cell lung cancer (NSCLC) who have been previously treated with 2 or more ROS1 tyrosine kinase inhibitors and orphan drug designation for ROS1-positive NSCLC.

**About Neladalkib (NVL-655)**

Neladalkib is a novel 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 NVL-330**

NVL-330 is a novel brain-penetrant HER2-selective tyrosine kinase inhibitor designed to address the combined medical need of treating HER2-mutant tumors, including those with HER2 exon 20 insertion mutations, avoiding treatment related adverse events due to off-target inhibition of wild-type EGFR, and treating brain metastases.

**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; Nuvalent's estimated cash runway; the expected timing of data announcements, clinical trial initiations, FDA submissions and potential product approval, including the projections in our OnTarget 2026 operating plan; the clinical development programs for zidesamtinib, neladalkib and NVL-330; the timing of the ALKAZAR trial; the potential clinical effects of Nuvalent's product development candidates; the design and enrollment of Nuvalent's clinical trials, including for ARROS-1 and ALKOVE-1 their intended pivotal registration-directed design; the potential of Nuvalent's pipeline programs, including zidesamtinib, neladalkib and NVL-330; the implications of data readouts and presentations; timing and content of potential discussions with FDA regarding potential accelerated approval pathways; Nuvalent's potential buildout of a commercial infrastructure; 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," "expect," "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 and 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 zidesamtinib or neladalkib product candidates; risks that Nuvalent may not achieve the goals and milestones set forth in its OnTarget 2026 operating plan; 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, including the ARROS-1, ALKOVE-1, ALKAZAR and HEROEX-1 trials; 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 quarterly period ended September 30, 2024, 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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