Nuvalent to Present Trial in Progress Posters for the ALKAZAR Trial of Neladalkib and HEROEX-1 Trial of NVL-330 at the 2025 American Society of Clinical Oncology Annual Meeting

CAMBRIDGE, Mass., April 23, 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 two "Trial in Progress" poster presentations for its novel ALK-selective inhibitor, neladalkib, and novel HER2-selective inhibitor, NVL-330, at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting from May 30 – June 5, 2025, in Chicago. Posters will be archived on the Nuvalent website at www.nuvalent.com.

The first "Trial in Progress" poster will include background and study design for ALKAZAR NCT06765109), a global, randomized, controlled Phase 3 trial designed to evaluate neladalkib versus the current standard of care for the treatment of patients with TKI-naïve ALK-positive non-small cell lung cancer (NSCLC). Patients will be randomized 1:1 to receive neladalkib monotherapy or ALECENSA® (alectinib) monotherapy. The company plans to initiate the ALKAZAR trial in the first half of 2025.

The second poster will include background and study design for the ongoing HEROEX-1 Phase 1a/1b clinical trial (NCT06521554) evaluating the overall safety and tolerability of NVL-330 for pre-treated patients with HER2-altered NSCLC. Additional objectives include determination of the recommended Phase 2 dose, characterization of NVL-330's pharmacokinetic profile, and preliminary evaluation of anti-tumor activity.

Details of the poster presentations are as follows:

Title: Neladalkib (NVL-655), a highly selective anaplastic lymphoma kinase (ALK) inhibitor, compared to alectinib in first-line treatment of patients with ALK-positive advanced non-small cell lung cancer: The Phase 3 ALKAZAR study

Authors: Sanjay Popat*[1], Benjamin J. Solomon[2], Thomas E. Stinchcombe[3], Geoffrey Liu[4], Gilberto Lopes[5], Melissa Johnson[6], Misako Nagasaka[7], Ece Cali Daylan[8], Christina Baik[9], James D'Olimpio[10], Tzu-Chuan Huang[11], Alexander Spira[12], Daniel Haggstrom[13], Benjamin Creelan[14], Tina Kehrig[15], Junwu Shen[15], Rachel DeLaRosa[15], Viola W. Zhu[15], Alexander Drilon[16], Alice T. Shaw[17]
Abstract Number: TPS8666
Session Title: Lung Cancer—Non-Small Cell Metastatic
Session Date and Time: May 31, 2025, from 1:30 p.m.–4:30 p.m. CDT
Poster Board Number: 136b

**Presenter, corresponding author; [1]Royal Marsden Hospital NHS Foundation Trust and The Institute of Cancer Research, London, UK; [2]Peter MacCallum Cancer Centre, Melbourne, Australia; [3]Duke Cancer Center, Durham, NC, USA; [4]Princess Margaret Hospital, Toronto, ON, Canada; [5]Sylvester Comprehensive Cancer Center, Miami, FL, USA; [6]Sarah Cannon Research Institute Oncology Partners, Nashville, TN, USA; [7]University of California Irvine School of Medicine, Orange, CA, USA; [8]Washington University School of Medicine, St. Louis, MO, USA; [9]Fred Hutchinson Cancer Center, Seattle, WA, USA; [10]Clinical Research Alliance Inc., Westbury, NY, USA; [11]University Cancer and Blood Center, LLC, Athens, GA, USA; [12]Virginia Cancer Specialists (Fairfax) - USOR, Fairfax, VA, USA; [13]Carolinas Medical Center, Charlotte, NC, USA; [14]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [15]Nuvalent, Inc., Cambridge, MA, USA; [16]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [17]Dana-Farber Cancer Institute, Boston, MA, USA*

Title: NVL-330, a selective HER2 tyrosine kinase inhibitor, in patients with advanced or metastatic HER2-altered non-small cell lung cancer: The Phase 1 HEROEX-1 study

Authors: Xiuning Le*[1], Zofia Piotrowska[2], Alexander Spira[3], Christina Baik[4], Maria Q. Baggstrom[5], Gerald Falchook[6], Joel Neal[7], Shirish Gadgeel[8], Gilberto Lopes[9], Melissa Johnson[10], Jonathan W. Riess[11], Danny Nguyen[12], Lisa Morelli[13], Danieska Sandino[13], Steven Margossian[13], Vivek Upadhyay[13], Fernando C. Santini[14]
Abstract Number: TPS8665
Session Title: Lung Cancer—Non-Small Cell Metastatic
Session Date and Time: May 31, 2025, from 1:30 p.m.–4:30 p.m. CDT
Poster Board Number: 136a

**Presenter, corresponding author; [1]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Massachusetts General Hospital, Boston, MA, USA; [3]NEXT Oncology, Fairfax, VA, USA; [4]Fred Hutchinson Cancer Center, Seattle, WA, USA; [5]Washington University School of Medicine, St. Louis, MO, USA; [6]Sarah Cannon Research Institute at HealthONE, Denver, CO, USA; [7]Stanford Cancer Institute, Stanford, CA, USA; [8]Henry Ford Cancer Institute, Detroit, MI, USA; [9]Sylvester Comprehensive Cancer Center, Miami, FL, USA; [10]Sarah Cannon Research Institute Oncology Partners, Nashville, TN, USA; [11]University of California Davis, Davis Comprehensive Cancer Center, Sacramento CA, USA; [12]City of Hope-Lennar, Irvine, CA, USA; [13]Nuvalent, Inc., Cambridge, MA, USA; [14]Memorial Sloan Kettering Cancer Center, New York, NY, USA*

About Neladalkib
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; the expected timing of presentations; the potential benefits and effects of Nuvalent's product development candidates; the potential of Nuvalent's pipeline programs, including zidesamtinib, neladalkib and NVL-330; 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: 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 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 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 Annual Report on Form 10-K for the fiscal year ended December 31, 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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