Nuvalent Outlines Pipeline and Business Progress, Reiterates Key Anticipated Milestones, and Reports Fourth Quarter and Full Year 2024 Financial Results

Topline pivotal data expected in 2025 for both TKI pre-treated ROS1-positive and TKI pre-treated ALK-positive NSCLC populations

First NDA submission planned for mid-year 2025 towards potential first approval in 2026 for zidesamtinib in TKI pre-treated ROS1-positive NSCLC population

Development strategies in place for TKI-naïve populations, including planned initiation of ALKAZAR Phase 3 randomized, controlled trial of neladalkib for front-line ALK-positive NSCLC in first half of 2025

Implemented global Expanded Access Programs for zidesamtinib and neladalkib, in line with goal of prioritizing patient access

CAMBRIDGE, Mass., Feb. 27, 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 outlined pipeline and business progress, reiterated key anticipated milestones, and reported fourth quarter and full year 2024 financial results.

"The efficient execution by the Nuvalent team to date reflects a shared sense of urgency driven by patient need for additional treatment options – a need that we believe has been clearly demonstrated by the robust enrollment momentum in our ARROS-1 and ALKOVE-1 trials," said **Darlene Noci, A.L.M., Chief Development Officer at Nuvalent** "We believe we are on track to report pivotal data for TKI pre-treated patients from both trials this year and to submit our first NDA by mid-year 2025."

Ms. Noci continued, "In parallel to advancing initial registration paths for zidesamtinib and neladalkib for TKI pre-treated patients, we continue to work with regulators towards our goal of bringing new therapies to all patients with ROS1-positive or ALK-positive NSCLC. Development programs for TKI-naïve patients are underway for both our ROS1 and ALK programs. To ensure patient access to these therapies, we are also pleased to announce the recent launch of global Expanded Access Programs for patients who are eligible and have no other treatment options outside of a clinical trial."

"As we transition towards becoming a fully integrated commercial-stage biopharmaceutical company, we reiterate our commitment to meeting the medical needs of patients by advancing our programs as quickly as possible," said **James Porter, Ph.D., Chief Executive Officer at Nuvalent.** "This is an important time for Nuvalent and with a steady cadence of anticipated milestones across our pipeline this year, a strong balance sheet and a dedicated and proven team at the helm, we believe we are well-positioned to deliver on our near-, mid- and long-term goals."

Recent Pipeline Progress and Anticipated Milestones

ROS1 Program

- Nuvalent has implemented a global Expanded Access Program (EAP) for zidesamtinib for eligible patients with locally advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC) who have previously received at least one prior ROS1 tyrosine kinase inhibitor (TKI) and lack satisfactory therapeutic alternatives and are unable to access zidesamtinib through a clinical trial.
- As of December 31, 2024, a total of 430 patients had been enrolled in the Phase 1 and Phase 2 portions of 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. The company expects to report pivotal data for TKI pre-treated patients with advanced ROS1-positive NSCLC in the first half of 2025 in support of an anticipated New Drug Application (NDA) submission by mid-year 2025, with an initial target indication of TKI pre-treated patients with advanced ROS1-positive NSCLC. The company plans to continue engagement with the U.S. Food and Drug Administration (FDA) on accelerated opportunities towards a potential line-agnostic indication supported by the ongoing TKI-naïve cohort in the Phase 2 portion of the ARROS-1 trial.

ALK Program

- Nuvalent has implemented a global EAP for neladalkib for eligible patients with locally advanced or metastatic ALK-positive NSCLC who have previously received lorlatinib or a second-generation ALK TKI and lack satisfactory therapeutic alternatives and are unable to access neladalkib through a clinical trial.
- As of December 31, 2024, a total of 596 patients had been enrolled in the Phase 1 and Phase 2 portions of 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. The company expects to report pivotal data for TKI pre-treated patients with advanced ALK-positive NSCLC by year-end 2025.
- Nuvalent plans to initiate the ALKAZAR Phase 3 trial, its front-line development strategy for the company's ALK program, in the first half of 2025. The Phase 3 ALKAZAR trial will be a global, randomized, controlled trial designed to evaluate neladalkib versus the current standard of care for the treatment of patients with TKI-naïve ALK-positive NSCLC. Patients will be randomized 1:1 to receive neladalkib monotherapy or ALECENSA® (alectinib) monotherapy, reflecting input from collaborating physician-scientists and alignment with the FDA.

HER2 Program

- Enrollment is ongoing in the HEROEX-1 Phase 1a/1b clinical trial 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. The company expects to continue to progress the HEROEX-1 trial throughout 2025.

Business Updates

- **Appointed Grant Bogle to Board of Directors:** As previously announced, Nuvalent appointed Grant Bogle to its board of directors in December 2024. Mr. Bogle brings nearly four decades of proven leadership in building and growing biotechnology companies to the Nuvalent board. Throughout his career, he has served in senior leadership roles at several specialty pharmaceutical and biotechnology companies and worked alongside oncologists as part of the leadership of U.S. Oncology, the largest network of community oncology practices in the United States. He has a proven track record of success in the field of oncology and has guided numerous products from early-stage development to commercialization. Most recently, Mr. Bogle was the Chief Executive Officer at Epizyme, Inc., and oversaw the 2022 acquisition of the company by Ipsen. Prior to that, Mr. Bogle was Senior Vice President and Chief Commercial Officer of TESARO, which was acquired by GlaxoSmithKline in 2018. Earlier, he served as Senior Vice President of Pharmaceutical and Biotech Solutions at McKesson Specialty Health (formerly U.S. Oncology).

Fourth Quarter and Full Year 2024 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $1.1 billion as of December 31, 2024. Nuvalent continues to believe that its existing cash, cash equivalents and marketable securities will be sufficient to fund its current operating plan into 2028.
- **R&D Expenses:** Research and development (R&D) expenses were $69.4 million for the fourth quarter of 2024 and $217.8 million for the year ended December 31, 2024.
- **G&A Expenses:** General and administrative (G&A) expenses were $16.9 million for the fourth quarter of 2024 and $62.6 million for the year ended December 31, 2024.
- **Net Loss:** Net loss was $74.8 million for the fourth quarter of 2024 and $260.8 million for the year ended December 31, 2024.

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; 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.

CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share amounts)
(Unaudited)

	Three Months Ended December 31,		Year ended December	
	2024	2023	2024	2
Operating expenses				
Research and development	$ 69,423	$ 35,585	$ 217,774	$
General and administrative	16,876	10,852	62,594	
Total operating expenses	86,299	46,437	280,368	
Loss from operations	(86,299)	(46,437)	(280,368)	
Other income (expense)				
Change in fair value of related party revenue share liability	(1,340)	—	(17,940)	
Interest income and other income (expense), net	13,047	8,145	38,316	

Total other income (expense), net	11,707	8,145	20,376	
Loss before income taxes	(74,592)	(38,292)	(259,992)	
Income tax provision	171	—	764	
Net loss	$ (74,763)	$ (38,292)	$ (260,756)	$
Net loss per share attributable to common stockholders, basic and diluted	$ (1.05)	$ (0.62)	$ (3.93)	$
Weighted average shares of common stock outstanding, basic and diluted	71,156,489	62,183,325	66,408,807	5

SELECTED BALANCE SHEET DATA
(In thousands)
(Unaudited)

	December 31,	
	2024	**2023**
Cash, cash equivalents and marketable securities	$ 1,118,302	$ 719,905
Working capital	$ 1,078,428	$ 694,665
Total assets	$ 1,141,752	$ 732,384
Total liabilities	$ 71,960	$ 31,823
Total stockholders' equity	$ 1,069,792	$ 700,561

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