Nuvalent Highlights Corporate and Pipeline Achievements, Reiterates Key Anticipated Milestones, and Reports Third Quarter 2024 Financial Results

Achievement of all anticipated 2024 milestones and accelerated development timelines reinforce progress on OnTarget 2026 operating plan towards first approved product in 2026

Leading medical oncologist Alice Shaw, M.D., Ph.D. appointed to

Scientific Advisory Board

Strong cash position of $1.2 billion, including proceeds from upsized $575 million public offering, expected to extend operating runway into 2028

CAMBRIDGE, Mass., Nov. 12, 2024 /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, reiterated key anticipated milestones, and reported third quarter 2024 financial results.

"Throughout 2024, the Nuvalent team has made significant strides in advancing our pipeline of novel kinase inhibitors, exemplified by the achievement of all of the 2024 milestones originally laid out in our OnTarget 2026 operating plan. We believe our recent upsized public offering reflects the shared excitement around these achievements and the potential for multiple value-creating catalysts ahead," **said Alexandra Balcom, Chief Financial Officer at Nuvalent. "**We believe we are well-positioned to execute on our mid- and long-term goals and remain sharply focused on moving our programs forward as efficiently as possible for patients."

"Our portfolio achievements and the acceleration of our development timelines have stemmed from a foundational tenet of our approach to drug discovery and development: collaboration with leading physician-scientists from the outset of each program," said **James Porter, Ph.D., Chief Executive Officer at Nuvalent.** "Today, we are thrilled to welcome Dr.Alice Shaw, Chief of Strategic Partnerships at Dana-Farber Cancer Institute, to our Scientific Advisory Board in recognition of her invaluable contributions to our ROS1 and ALK programs since our company's formation. A leading expert in targeted oncology, Dr. Shaw's research has deepened the scientific understanding of oncogene-driven lung cancers and their mechanisms of resistance, and contributed to numerous new therapeutic options for patients. We look forward to continuing to leverage her insights and expertise as we advance our clinical programs and discovery pipeline."

"Targeted kinase inhibitors are important treatment options for cancer patients, but key challenges, including drug resistance and off-target side effects, can limit their therapeutic impact," **said Dr. Shaw.** "I am excited by Nuvalent's pursuit of new therapeutic approaches to overcome the limitations of existing therapies. The clinical proof-of-concept data from both the ROS1 and ALK programs are encouraging and support the approach of designing highly selective and brain-penetrant inhibitors that retain potency against known resistance mutations. I look forward to working with the team to advance the current pipeline of novel therapeutic candidates and identify additional areas of medical need where Nuvalent could potentially make a meaningful impact for patients."

Recent Pipeline Progress and Anticipated Milestones

ROS1 Program

- Nuvalent recently reported updated data from the fully enrolled Phase 1 portionof its ongoing ARROS-1 Phase 1/2 clinical trial in patients with advanced ROS1-positive NSCLC during an oral presentation at the European Society for Medical Oncology (ESMO) Congress 2024. Data presented showed that treatment with zidesamtinib resulted in durable clinical responses in heavily pre-treated patients with ROS1-positive NSCLC, including in subgroups of patients who had likely exhausted all available therapies including lorlatinib and/or repotrectinib, had a history of brain metastases, or had the G2032R resistance mutation. Additionally, zidesamtinib was well-tolerated with a preliminary safety profile that was favorable and consistent with its ROS1-selective, TRK-sparing design.
- Additionally, during a poster session at the ESMO Congress 2024, the company presented new preclinical data further characterizing the intracranial activity of zidesamtinib.
- Enrollment is ongoing in the Phase 2 portion of the ARROS-1 Phase 1/2 trial of zidesamtinib for patients with advanced ROS1-

positive NSCLC and other solid tumors. Between September 2023 and September 1, 2024, 227 patients were enrolled in the ongoing single-arm, multi-cohort Phase 2 portion of the ARROS-1 trial, which is designed with registrational intent. The company expects to report pivotal data from this trial in 2025.

ALK Program

- Nuvalent recently reported updated data from the fully enrolled Phase 1 portion of its ongoing ALKOVE-1 Phase 1/2 clinical trial in patients with advanced ALK-positive NSCLC during an oral presentation at the ESMO Congress 2024. Data presented showed that treatment with NVL-655 resulted in durable clinical responses in heavily pre-treated patients with ALK-positive NSCLC, including in subgroups of patients who had likely exhausted all available therapies including lorlatinib, had a history of brain metastases, or had single or compound ALK resistance mutations. Additionally, NVL-655 demonstrated a favorable preliminary safety profile consistent with its ALK-selective, TRK-sparing design.
- Enrollment is ongoing in the Phase 2 portion of the ALKOVE-1 Phase 1/2 trial of NVL-655 for patients with advanced ALK-positive NSCLC and other solid tumors. Between February 2024 and September 1, 2024, 229 patients were enrolled in the ongoing single-arm, multi-cohort Phase 2 portion of the ALKOVE-1 trial, which is designed with registrational intent for TKI pre-treated patients. The company expects to report pivotal data from this trial in 2025.
- Nuvalent recently announced the ALKAZAR Phase 3 trial, its front-line development strategy for the company's ALK program. The Phase 3 ALKAZAR trial will be a global, randomized, controlled trial designed to evaluate NVL-655 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 NVL-655 monotherapy or ALECENSA® (alectinib) monotherapy, reflecting input from collaborating physician-scientists and alignment with the U.S. Food and Drug Administration (FDA). The company plans to initiate the ALKAZAR study in the first half of 2025.
- A manuscript describing the design and characterization of NVL-655 and detailing Nuvalent's approach to rationally targeting ALK, was published in *Cancer Discovery*, a journal of the American Association for Cancer Research. The publication, Nuvalent's second in *Cancer Discovery*, provides a comprehensive assessment of NVL-655's preclinical activity and includes preliminary clinical case studies.

HER2 Program

- Enrollment is ongoing in the HEROEX-1 Phase 1a/1b clinical trial evaluating NVL-330 for pre-treated patients with HER2-altered NSCLC. The trial will evaluate the overall safety and tolerability of NVL-330. Additional objectives include determination of the recommended Phase 2 dose (RP2D), characterization of the pharmacokinetic profile, and preliminary evaluation of anti-tumor activity.

Corporate Highlight

- Nuvalent has appointed leading medical oncologist Alice T. Shaw, M.D., Ph.D., to its Scientific Advisory Board. Dr. Shaw is the Chief of Strategic Partnerships at Dana-Farber Cancer Institute and oversees the collaborative efforts between researchers and the life sciences industry to help accelerate the development of new and innovative therapies for patients with cancer. Dr. Shaw was previously Vice President and Global Head of Translational Clinical Oncology at Novartis Institutes for BioMedical Research (NIBR) where she led early drug development in oncology for almost five years. Prior to Novartis, Dr. Shaw was the Director of the Center for Thoracic Cancers at Massachusetts General Hospital (MGH), the Paula O'Keeffe Endowed Chair of Thoracic Oncology at MGH, Co-Leader of the Dana-Farber/Harvard Cancer Center Thoracic Oncology Program, and Professor of Medicine at Harvard Medical School. During her time at MGH, Dr. Shaw studied resistance to targeted therapies in the lab and the clinic, and helped develop numerous targeted therapies for patients with oncogene-driven lung cancer. She was the overall principal investigator of multiple Phase 1, 2 and 3 studies, including registrational trials leading to FDA approval of crizotinib for ALK and ROS1-positive NSCLC, ceritinib, alectinib, and lorlatinib. Dr. Shaw was recently elected to the American Association for Cancer Research (AACR) Board of Directors. She was previously Co-Leader of the SU2C Lung Cancer Dream Team and a standing member of the US FDA Oncologic Drug Advisory Committee (ODAC).

Financing Highlight

- On September 18, 2024, Nuvalent closed an upsized underwritten public offering of 5,750,000 shares of Class A common stock, which included 750,000 shares of Class A common stock sold pursuant to the exercise in full by the underwriters of their option to purchase additional shares, at a price to the public of $100.00 per share. The gross proceeds of the offering were approximately $575.0 million, before deducting underwriting discounts and commissions and other offering expenses.

Upcoming Events

- **Guggenheim's Inaugural Healthcare Innovation Conference:** Management will be participating in a fireside chat on Wednesday, November 13, 2024, at 9:00 a.m. ET in Boston.
- **Stifel 2024 Healthcare Conference:** Management will be participating in a fireside chat on Tuesday, November 19, 2024, at 3:35 p.m. ET in NYC.

A live webcast of each fireside chat 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.

Third Quarter 2024 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $1.2 billion as of September 30, 2024. The company's cash, cash equivalents and marketable securities as of September 30, 2024, inclusive of the proceeds from the $575 million public

offering, are expected to extend the company's operating runway into 2028.
- **R&D Expenses:** Research and development (R&D) expenses were $60.6 million for the third quarter of 2024.
- **G&A Expenses:** General and administrative (G&A) expenses were $15.8 million for the third quarter of 2024.
- **Net Loss:** Net loss was $84.3 million for the third quarter of 2024.

About OnTarget 2026

OnTarget 2026 delineates Nuvalent's 3-year operating plan towards bringing new, potential best-in-class medicines to patients with cancer. As part of this plan announced in January 2024, Nuvalent outlined the following anticipated milestones throughout 2024, leading to the company's first potential pivotal data in 2025 and first potential approved product in 2026:

- ***2024: Execute on Global Registrational Strategies***
    - Progress the Phase 2 portion of its ARROS-1 trial of zidesamtinib in patients with advanced ROS1-positive NSCLC with registrational intent;
    - Initiate the Phase 2 portion of its ALKOVE-1 trial of NVL-655 in patients with advanced ALK-positive NSCLC with registrational intent;
    - Launch the front-line development strategy for its ALK program;
    - Present interim data from its ongoing ARROS-1 and ALKOVE-1 clinical trials at medical meetings; and,
    - Initiate the Phase 1 trial for its HER2 program.
- ***2025: First Pivotal Data***
- ***2026: First Approved Product***

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 period over which Nuvalent estimates its cash, cash equivalents and marketable securities will be sufficient to fund its future operating expenses and capital expenditure requirements; the expected timing of data announcements, clinical trial initiations and FDA product approvals, including the projections in our OnTarget 2026 operating plan; the clinical development programs for zidesamtinib, NVL-655 and NVL-330; the design and timing of the ALKAZAR trial, including alignment with the FDA regarding the design of the 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, NVL-655 and NVL-330; 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," "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 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 NVL-655 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 June 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 September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Operating expenses				
Research and development	$ 60,551	$ 29,611	$ 148,351	$ 77,658
General and administrative	15,780	9,172	45,718	25,397
Total operating expenses	76,331	38,783	194,069	103,055
Loss from operations	(76,331)	(38,783)	(194,069)	(103,055)
Other income (expense)				
Change in fair value of related party revenue share liability	(16,600)	—	(16,600)	—
Interest income and other income (expense), net	8,626	5,138	25,269	15,128
Total other income (expense), net	(7,974)	5,138	8,669	15,128
Loss before income taxes	(84,305)	(33,645)	(185,400)	(87,927)
Income tax provision	40	—	593	—
Net loss	$ (84,345)	$ (33,645)	$ (185,993)	$ (87,927)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.28)	$ (0.59)	$ (2.87)	$ (1.55)

Weighted average shares of common stock outstanding, basic and diluted	65,678,693	57,091,394	64,814,695	56,888,839

SELECTED BALANCE SHEET DATA
(In thousands)
(Unaudited)

	September 30, 2024	December 31, 2023
Cash, cash equivalents and marketable securities	$ 1,168,309	$ 719,905
Working capital	$ 1,128,543	$ 694,665
Total assets	$ 1,188,858	$ 732,384
Total liabilities	$ 67,732	$ 31,823
Total stockholders' equity	$ 1,121,126	$ 700,561

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https://investors.nuvalent.com/2024-11-12-Nuvalent-Highlights-Corporate-and-Pipeline-Achievements,-Reiterates-Key-Anticipated-Milestones,-and-Reports-Third-Quarter-2024-Financial-Results