Nuvalent Reviews Corporate and Pipeline Achievements and Reports Third Quarter 2022 Financial Results

Preliminary Phase 1 clinical data from ARROS-1 Study presented at the 2022 EORTC-NCI-AACR Symposium supports best-in-class potential of NVL-520 for patients with ROS1-positive NSCLC

Enrollment progressing in ALKOVE-1 Phase 1/2 trial with parallel-lead candidate, NVL-655, for ALK-positive NSCLC

NVL-330 demonstrates potency and selectivity for HER2 Exon 20 insertion mutations, and brain penetration in preclinical studies

$264.5 million upsized public offering along with cash, cash equivalents, and marketable securities as of September 30, 2022 expected to extend operating runway into second half of 2025

CAMBRIDGE, Mass., Nov. 10, 2022 /PRNewswire/ -- Nuvalent, Inc. (Nasdaq: NUVL), a clinical-stage biopharmaceutical company focused on creating *precisely* targeted therapies for clinically proven kinase targets in cancer, today reported recent business and pipeline progress and third quarter 2022 financial results.

"This has been a transformational year for Nuvalent, exemplified by the totality of the data presented at EORTC-NCI-AACR (ENA) which showcased the rapid and meaningful progress our team has made towards our mission of delivering a portfolio of *precisely* targeted therapies for patients with cancer," said James Porter, Ph.D., Chief Executive Officer at Nuvalent. "Importantly, we reported preliminary data from the Phase 1 portion of our ARROS-1 study for NVL-520 in heavily pre-treated patients with ROS1-positive non-small cell lung cancer (NSCLC), representing the first clinical proof-of-concept data from our portfolio. We believe these data support the planned investigation of NVL-520 in the treatment-naïve setting as part of the next phase of our study and continue to support the best-in-class potential of NVL-520 for the treatment of patients with ROS1-positive NSCLC. We look forward to engaging with regulators to discuss the recommended Phase 2 dose and beginning the Phase 2 portion of the ARROS-1 trial."

Dr. Porter continued, "Furthermore, the learnings from our work on NVL-520 and the ARROS-1 trial have directly informed our parallel lead program, NVL-655, and the design of the ALKOVE-1 trial for patients with ALK-positive NSCLC, as well as our earlier-stage pipeline including our third development candidate, NVL-330. Data supporting the differentiated preclinical profiles of NVL-655 and NVL-330 were presented at ENA. Enrollment in the Phase 1 portion of the ALKOVE-1 study continues, and we look forward to updating on each of these programs in the future."

"In just a few years from the company's creation, we have brought forward three potential best-in-class molecules and delivered clinical proof-of-concept data from our first program, which is a testament to the strength of our team and our ability to execute," added Alexandra Balcom, Chief Financial Officer at Nuvalent. "This execution enabled us to complete an upsized public offering of our common stock that meaningfully extends our expected operating runway and fuels the continued advancement of our clinical-stage pipeline with NVL-520 and NVL-655, as well as our early research and development pipeline, led by NVL-330. With a founding scientific thesis that we have started to see play out in the clinic, this is an energizing time for Nuvalent and we are excited to carry this momentum forward."

Pipeline Progress

- **Preliminary Dose-Escalation Data from Ongoing ARROS-1 Trial Demonstrates Proof-of-Concept for NVL-520's Potential Best-in-Class Clinical Profile:** Initial data from the Phase 1 dose-escalation portion of Nuvalent's ongoing ARROS-1 Phase 1/2 clinical trial of NVL-520, its novel, brain-penetrant, ROS1-selective inhibitor, as a potential treatment for patients with advanced ROS1-positive NSCLC and other solid tumors were presented during the "New Drugs on the Horizon" plenary session at ENA 2022. Data presented showed that a favorable preliminary safety profile was observed with NVL-520 treatment with no dose-limiting toxicities, treatment-related serious adverse events, treatment-related dizziness, or adverse events leading to treatment reductions or discontinuations. Additionally, treatment with NVL-520 resulted in encouraging preliminary signs of activity observed across all dose levels in heavily pre-treated patients with ROS1-positive NSCLC, including in subgroups of patients with G2032R resistance mutation or with brain metastases.

  The ARROS-1 clinical trial is continuing to enroll patients in the Phase 1 portion of the study and is focused on further characterizing the safety profile of NVL-520, its pharmacokinetic profile, and determining the recommended Phase 2 dose.

- **New Data in Patient-Derived Models Continues to Support Best-in-Class Preclinical Profile of Parallel Lead Candidate, NVL-655:** A poster presented at ENA 2022 included new preclinical data on NVL-655, Nuvalent's brain penetrant, ALK-selective inhibitor, in additional patient derived models harboring single and compound ALK resistance mutations. Notably, NVL-655 induced regression in an in vivo model derived from a patient with ALK fusion-positive NSCLC harboring G1202R/L1196M compound mutation after disease progression on sequential crizotinib, alectinib and lorlatinib treatment. Among all inhibitors tested, NVL-655 showed the broadest preclinical activity across ALK fusion partners and resistance mutations while maintaining a wide selectivity window over TRKB.

  Clinical investigation of NVL-655 is ongoing and enrollment is progressing in the Phase 1 portion of the ALKOVE-1 Phase 1/2 study of NVL-655 for patients with advanced ALK-positive NSCLC and other solid tumors. The Phase 1 portion of the ALKOVE-1 trial is focused on characterizing the safety profile of NVL-655, its pharmacokinetic profile, and determining the recommended Phase 2 dose.

- **Preclinical Profile of NVL-330 Demonstrates Achievement of Target Characteristics of Potency and Selectivity for HER2 Exon 20 Insertion Mutations, and Brain Penetration:** Nuvalent presented preclinical data characterizing its third development candidate, NVL-330, a novel, brain-penetrant HER2-selective tyrosine kinase inhibitor targeting HER2 exon 20 insertion mutations (HER2ex20) during a poster session at ENA 2022. Preclinical data demonstrated that NVL-330 potently inhibited HER2ex20 in cell-based assays and was highly selective for HER2ex20 as opposed to the structurally related wild-type EGFR and other off-target kinases – a critical aspect of NVL-330's design given that off-target inhibition of EGFR results in dose-limiting side effects including skin rash and gastrointestinal toxicity. In addition, given its demonstrated preclinical brain penetrance and intracranial activity, NVL-330 has the potential to treat or prevent brain metastasis as a potential best-in-class molecule.

Financing Highlight

- **Completed Upsized Public Offering of Common Stock Raising $264.5 Million in Gross Proceeds:** On November 3, 2022, Nuvalent closed an upsized underwritten public offering of 7,895,522 shares of Class A common stock at a price to the public of $33.50 per share. The gross proceeds from the offering were approximately $264.5 million, before deducting underwriting discounts, commissions and other offering expenses, which when combined with the company's existing cash, cash equivalents and marketable securities as of September 30, 2022, is expected to extend the company's operating runway into the second half of 2025.

Upcoming Events

- **Evercore ISI HealthCONx Conference 2022:** Management will be participating in a fireside chat during the Evercore ISI HealthCONx Conference 2022 on Wednesday, November 30, 2022, at 8:50 a.m. ET.
- **The Piper Sandler 34th Annual Healthcare Conference:** Management will be participating in a fireside chat during The Piper Sandler 34th Annual Healthcare Conference on Thursday, December 1, 2022, at 9:00 a.m. ET.

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 2022 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $240.1 million as of September 30, 2022. The company's cash, cash equivalents and marketable securities as of September 30, 2022, in combination with the proceeds from the follow-on offering, are expected to be sufficient to fund the company's current operating plan into the second half of 2025.
- **R&D Expenses:** Research and development (R&D) expenses were $14.6 million for the third quarter of 2022.
- **G&A Expenses:** General and administrative (G&A) expenses were $5.8 million for the third quarter of 2022.
- **Net Loss:** Net loss for the third quarter of 2022 was $19.7 million, or $0.41 per share.

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 parallel lead programs in ROS1-positive and ALK-positive non-small cell lung cancer (NSCLC), a program in HER2 Exon 20 insertion-positive cancers, and multiple discovery-stage research programs. We routinely post information that may be important to investors on our website at www.nuvalent.com. Follow us on Twitter (@nuvalent) and LinkedIn.

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 and the proceeds from its follow-on public offering will be sufficient to fund its future operating expenses and capital expenditure requirements; the preclinical and clinical development programs for NVL-520, NVL-655 and NVL-330; the potential clinical effect of NVL-520 and NVL-655; the potential benefits of NVL-330; the design and enrollment of the ARROS-1 and ALKOVE-1 studies; the potential of Nuvalent's pipeline programs, including NVL-520, NVL-655 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: risks that Nuvalent may not fully enroll the ARROS-1 or ALKOVE-1 studies 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 occurrence of adverse safety events; risks of unexpected costs, delays, or other unexpected hurdles; risks that Nuvalent may not be able to nominate drug candidates from its ALK IXDN and other discovery programs; the direct or indirect impact of COVID-19 or other global geopolitical circumstances on the timing and anticipated timing and results of Nuvalent's clinical trials, strategy, and future operations, including the ARROS-1 and ALKOVE-1 studies; the timing and outcome of Nuvalent's planned interactions with regulatory authorities; and obtaining, maintaining, and protecting its intellectual property. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2022, 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.

SELECTED STATEMENTS OF OPERATIONS DATA
(In thousands, except share and per share data)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Operating expenses:				
Research and development	$ 14,625	$ 9,055	$ 40,876	$ 22,365
General and administrative	5,763	3,372	15,933	6,074
Total operating expenses	20,388	12,427	56,809	28,439
Loss from operations	(20,388)	(12,427)	(56,809)	(28,439)
Other income (expense):				
Change in fair value of preferred stock tranche rights	—	—	—	(635)
Other income, net	672	1	1,078	25
Total other income (expense), net	672	1	1,078	(610)
Net loss	$ (19,716)	$ (12,426)	$ (55,731)	$ (29,049)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.41)	$ (0.39)	$ (1.15)	$ (2.26)
Weighted average shares of common stock outstanding, basic and diluted	48,410,514	32,066,089	48,338,580	12,858,574

SELECTED BALANCE SHEET DATA
(In thousands)
(Unaudited)

	September 30, 2022	December 31, 2021
Cash, cash equivalents and marketable securities	$ 240,064	$ 288,111
Working capital	$ 232,270	$ 281,841
Total assets	$ 249,558	$ 293,824
Total liabilities	$ 12,975	$ 8,787
Total stockholders' equity	$ 236,583	$ 285,037

SOURCE Nuvalent, Inc.

Investor Contact:
Chelcie Lister
THRUST Strategic Communications
chelcie@thrustsc.com

Media Contact:
Amanda Sellers
Verge Scientific Communications
asellers@vergescientific.com