Nuvalent Announces First Patient Dosed in HEROEX-1 Phase 1a/1b Clinical Trial of NVL-330, its Novel HER2-selective Inhibitor

CAMBRIDGE, Mass., July 22, 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 announced the initiation of HEROEX-1, its Phase 1a/1b clinical trial evaluating its novel HER2-selective inhibitor, NVL-330, for pre-treated patients with HER2-altered non-small cell lung cancer (NSCLC).

"HER2 alterations are an important category of oncogenic drivers within NSCLC that includes both HER2 amplification and HER2 mutations, the majority of which are exon 20 mutations. While HER2- targeted therapies have been developed, there are currently no approved TKIs for the HER2-mutant NSCLC patient population," **said Christopher Turner, M.D., Chief Medical Officer of Nuvalent.** "At the outset of our program, physician-scientists outlined the need for a HER2 therapy that maintained activity against HER2 exon 20 mutations, was selective for HER2 versus wild-type EGFR to limit gastrointestinal and skin toxicities associated with EGFR inhibition, and was brain penetrant to address and limit brain metastases. NVL-330's preclinical profile has demonstrated the potential to be differentiated through combining these desired characteristics, and supports its initial clinical investigation in our HEROEX-1 trial for patients with HER2-altered NSCLC."

HEROEX-1 is a Phase 1a/1b, multicenter, open-label, dose-escalation and expansion trial evaluating NVL-330 in pre-treated patients with advanced HER2-altered NSCLC, including those with HER2 exon 20 mutations. 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.

"The initiation of this trial represents a significant milestone for Nuvalent, marking the third program from our novel pipeline to enter clinical development in under three years," **said James Porter, Ph.D., Chief Executive Officer at Nuvalent.**"This rapid execution serves as a testament to our team's dedication to rapid progress and growth across our pipeline, and our unwavering commitment to our goal of bringing *precisely* targeted therapies to patients with cancer."

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-altered 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. NVL-330 is currently being investigated in the HEROEX-1 Phase 1a/1b clinical trial for pre-treated patients with advanced HER2-altered NSCLC.

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 clinical development program for NVL-330; the potential clinical effect of NVL-330; the design of the HEROEX-1 trial; the potential of Nuvalent's pipeline programs, including 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 or 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 future 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 Quarterly Report on Form 10-Q for the quarterly period ended March 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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