Nuvalent Receives U.S. FDA Breakthrough Therapy Designation for NVL-655

CAMBRIDGE, Mass., May 16, 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 that the U.S. Food and Drug Administration (FDA) has granted breakthrough therapy designation (BTD) to NVL-655 for the treatment of patients with locally advanced or metastatic ALK-positive non-small cell lung cancer (NSCLC) who have been previously treated with two or more ALK tyrosine kinase inhibitors (TKIs).

ALK rearrangements occur in up to approximately 5% of metastatic NSCLCs. At the time of diagnosis, up to 40% of these patients present with accompanying brain metastases, and approximately 50% of patients develop resistance mutations following treatment with currently available first- or second-generation ALK TKIs. There remains no clear standard of care for patients who have been previously treated with two or more ALK TKIs.

NVL-655 is a novel brain-penetrant ALK-selective TKI created with the aim to simultaneously overcome the clinical challenges of emergent treatment resistance, brain metastases, and off-target central nervous system (CNS) adverse events associated with inhibition of the structurally-related tropomyosin receptor kinase (TRK) family.

"Today's announcement of FDA breakthrough therapy designation for NVL-655 marks another important milestone for our ALK program and the second breakthrough designation granted to our pipeline of novel kinase inhibitors this year," **said Darlene Noci, A.L.M., Chief Development Officer at Nuvalent** "Our team is committed to expeditiously advancing NVL-655 in recognition of the continued need for innovation for patients with ALK-positive NSCLC who have exhausted available therapies. We expect to provide an update from the ALKOVE-1 trial of NVL-655 at a medical meeting in the second half of this year."

BTD is designed to expedite the development and review of therapies intended to treat a serious or life-threatening condition and whose preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on one or more clinically significant endpoints over existing available therapies. Under the designation, the FDA provides intensive guidance, organizational commitment involving senior managers, and eligibility for rolling review and other actions to expedite review.

The BTD for NVL-655 is based on the preliminary safety and activity of NVL-655 in heavily pretreated patients with advanced ALK-positive NSCLC in the Phase 1 portion of the Phase 1/2 ALKOVE-1 clinical trial. Enrollment in the Phase 2 portion of the trial is ongoing, and the company expects to share updated data from the trial at a medical meeting in the second half of 2024.

About NVL-655
NVL-655 is a novel brain-penetrant ALK-selective inhibitor created with the aim to overcome limitations observed with currently available ALK inhibitors. NVL-655 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, NVL-655 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. NVL-655 has received orphan drug designation for ALK-positive non-small cell lung cancer (NSCLC) and is currently being investigated in the ALKOVE-1 clinical trial (NCT05384626), a first-in-human Phase 1/2 clinical trial for patients with advanced ALK-positive NSCLC and other solid tumors.

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 data announcements; the clinical development program for NVL-655; the potential clinical effect of NVL-655; the design and enrollment of the ALKOVE-1 trial, including its intended pivotal registration-directed design; the potential of Nuvalent's pipeline programs, including NVL-655; Nuvalent's research and development programs for the treatment of cancer; and risks and uncertainties associated with drug development. The words "may," "might," "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 ALKOVE-1 trial 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 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; 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 ALKOVE-1 trial; the timing and outcome of Nuvalent's planned interactions with regulatory authorities; 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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