Nuvalent Announces FDA Acceptance of New Drug Application for Zidesamtinib for the Treatment of TKI Pre-treated Patients with Advanced ROS1-positive NSCLC

NDA based on data from global ARROS-1 Phase 1/2 clinical trial

FDA assigns PDUFA target action date of September 18,

2026

CAMBRIDGE, Mass., Nov. 19, 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 announced the U.S. Food and Drug Administration (FDA) has accepted for filing its New Drug Application (NDA) for zidesamtinib, an investigational ROS1-selective inhibitor, for the treatment of adult patients with locally advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC) who received at least 1 prior ROS1 tyrosine kinase inhibitor (TKI). The application has been assigned a Prescription Drug User Fee Act (PDUFA) target action date of September 18, 2026.

Nuvalent's NDA submission is based on results for TKI pre-treated patients with advanced ROS1-positive NSCLC enrolled in the global registrational ARROS-1 Phase 1/2 clinical trial. These data were reported along with preliminary data from the ongoing Phase 2 TKI-naïve cohort of ARROS-1, and presented as part of the Presidential Symposium at the IASLC 2025 World Conference on Lung Cancer in September 2025.

About Zidesamtinib and the ARROS-1 Phase 1/2 Clinical Trial
Zidesamtinib is an investigational, novel brain-penetrant ROS1-selective inhibitor created with the aim to overcome limitations observed with currently available ROS1 inhibitors. Zidesamtinib is designed to remain active in tumors that have developed resistance to currently available ROS1 inhibitors, including tumors with treatment-emergent ROS1 mutations such as G2032R. In addition, zidesamtinib 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/ROS1 inhibitors and to drive deep, durable responses for patients across all lines of therapy. Zidesamtinib has received breakthrough therapy designation for the treatment of patients with ROS1-positive metastatic non-small cell lung cancer (NSCLC) who have been previously treated with 2 or more ROS1 tyrosine kinase inhibitors and orphan drug designation for ROS1-positive NSCLC.

Zidesamtinib is currently being investigated in the ARROS-1 trial (NCT05118789), a first-in-human Phase 1/2 clinical trial for patients with advanced ROS1-positive NSCLC and other solid tumors. The completed Phase 1 portion enrolled ROS1-positive NSCLC patients who previously received at least one ROS1 TKI, or patients with other ROS1-positive solid tumors who had been previously treated. The Phase 1 portion of the trial was designed to evaluate the overall safety and tolerability of zidesamtinib, with additional objectives including determination of the recommended Phase 2 dose (RP2D), characterization of the pharmacokinetic profile, and evaluation of preliminary anti-tumor activity. The ongoing global, single arm, open label Phase 2 portion is designed with registrational intent for TKI-naïve and TKI pre-treated patients with advanced ROS1-positive 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; its expectations regarding the review and potential regulatory approval of zidesamtinib and the timing thereof; the preclinical and clinical development program for zidesamtinib; the potential benefits and effects of Nuvalent's product development candidates; the potential of Nuvalent's pipeline programs, including zidesamtinib; 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 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 and expected 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 Annual Report on Form 10-Q for the quarter ended September 30, 2025, 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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