Nuvalent to Present New Preclinical Data on ROS1-Selective Inhibitor NVL-520 and ALK-Selective Inhibitor NVL-655 at AACR Annual Meeting 2022

Data supports clinical investigation of NVL-520 and NVL-655 across various ROS1 or ALK fusion partners, resistance mutations, and tumor types

CAMBRIDGE, Mass., March 8, 2022 /PRNewswire/ -- Nuvalent, Inc., (Nasdaq: NUVL) a biotechnology company creating *precisely* targeted therapies for clinically proven kinase targets in cancer, today announced multiple preclinical data presentations supporting advancement of its parallel lead programs including NVL-520 – a ROS1-selective inhibitor – and NVL-655 – an ALK-selective inhibitor. Data will be presented in two poster presentations at the American Association for Cancer Research (AACR) Annual Meeting 2022 from April 8-13 in New Orleans. Posters will be archived on the Nuvalent website at www.nuvalent.com.

The NVL-520 poster presentation will show preclinical data characterizing NVL-520 and other ROS1 inhibitors against a diverse set of ROS1 fusion partners and kinase-domain mutations, both within non-small cell lung cancer (NSCLC) and in a glioblastoma model. NVL-520 is currently under investigation in the Phase 1/2 ARROS-1 study (NCT05118789) for advanced ROS1-positive NSCLC and other solid tumors, including those with resistance mutations.

The second poster characterizes NVL-655 alongside other ALK inhibitors in ALK-driven cancer models beyond NSCLC such as anaplastic large cell lymphoma and neuroblastoma. A Phase 1/2 clinical trial of NVL-655 in patients with advanced ALK-positive NSCLC and other solid tumors is planned for the first half of 2022.

Details for the poster presentations are as follows:

Title: Preclinical Activity of NVL-520 in ROS1-Driven Cancer Models with Diverse Fusion Partners and Kinase-Domain Mutations
Authors: Anupong Tangpeerachaikul*[1], Clare Keddy*[2], Katelyn Nicholson[2], Monika Davare[2], and Henry E. Pelish[1]
Permanent Abstract: 3336
Session Category: Experimental and Molecular Therapeutics
Session Title: Tyrosine Kinase and Phosphatase Inhibitors
Session Date and Time: Tuesday April 12, 2022 from 1:30 – 5:00 p.m. CT
Location: New Orleans Convention Center, Exhibit Halls D-H, Poster Section 26

[1]Nuvalent Inc., Cambridge, MA, USA; [2]Oregon Health and Science University, Portland, OR, USA
**Equal contributions*

Title: Preclinical Activity of NVL-655 in ALK-Driven Cancer Models beyond Non-Small Cell Lung Cancer
Authors: Anupong Tangpeerachaikul[1], Ludovic Bigot[2], Luc Friboulet[2], and Henry E. Pelish[1]
Permanent Abstract: 3337
Session Category: Experimental and Molecular Therapeutics
Session Title: Tyrosine Kinase and Phosphatase Inhibitors
Session Date and Time: Tuesday April 12, 2022 from 1:30 – 5:00 p.m. CT
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[1]Nuvalent Inc., Cambridge, MA, USA; [2]Gustave-Roussy, Villejuif, France

About NVL-520

NVL-520 is a brain-penetrant ROS1-selective inhibitor designed to remain active in tumors that have developed resistance to currently available ROS1 inhibitors, including tumors with the prevalent G2032R resistance mutation and those with the S1986Y/F, L2026M, or D2033N resistance mutations. NVL-520 has been optimized for brain penetrance to potentially improve treatment options for patients with brain metastases. NVL-520 has been observed in preclinical studies to selectively inhibit ROS1 over the structurally related tropomyosin receptor kinase (TRK) family to potentially avoid TRK-related CNS adverse events seen with dual TRK/ROS1 inhibitors and drive more durable responses for patients with ROS1-mutant variants. NVL-520 is currently being investigated in the ARROS-1 study (NCT05118789), a first-in-human Phase 1/2 clinical trial for patients with advanced non-small cell lung cancer (NSCLC) and other solid tumors.

About NVL-655

NVL-655 is a novel brain-penetrant ALK-selective inhibitor created to overcome several limitations observed with currently available therapies. NVL-655 is designed to remain active in tumors that have developed resistance to first-, second-, and third-generation ALK inhibitors, including tumors with the solvent front G1202R mutation or compound mutations G1202R / L1196M ("GRLM"), G1202R / G1269A ("GRGA"), or G1202R/L1198F ("GRLF"). NVL-655 has been optimized for CNS penetrance to improve treatment options for patients with CNS metastases. ALK-selectivity is emphasized to minimize CNS adverse events related to off-target inhibition of the structurally-related tropomyosin receptor kinase (TRK) family. NVL-655 is planned to enter the clinic in the first half of 2022.

About Nuvalent

Nuvalent, Inc. (Nasdaq: NUVL) is a 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), along with 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 clinical development program for NVL-520 and NVL-655 and the timing thereof; the potential clinical effect of NVL-520; the potential benefits of NVL-520 and NVL-655; the design and enrollment of the ARROS-1 study and the timing thereof; the potential of Nuvalent's pipeline programs, including NVL-520 and NVL-655; the design and initiation of the Phase 1/2 clinical trial of NVL-655 and the timing thereof; 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 study or it will take longer than expected; unexpected concerns that may arise from additional data, analysis, or results obtained during the ARROS-1 study; the occurrence of adverse safety events; risks of unexpected costs, delays, or other unexpected hurdles; risks associated with: the impact of COVID-19 on countries or regions in which Nuvalent has operations or does business, as well as on the timing and anticipated timing and results of its clinical trials, strategy, and future operations, including the ARROS-1 study and the planned initiation of the ALKOVE-1 Phase 1/2 study; 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 quarter ended September 30, 2021, as well as any 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.

SOURCE Nuvalent, Inc.

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

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