

Nuvalent to Present New NVL-655 Preclinical Data and ARROS-1 Trial in Progress Poster for NVL-520 at IASLC 2022 World Conference on Lung Cancer Annual Meeting

Preclinical activity of ALK-selective inhibitor NVL-655 in a lorlatinib-resistant model of

NSCLC with a compound resistance mutation continues to support potential for best-in-class profile

CAMBRIDGE, Mass., July 13, 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 announced it will present two posters for its parallel lead programs, NVL-655, an ALK-selective inhibitor and NVL-520, a ROS1-selective inhibitor, at the IASLC 2022 World Conference on Lung Cancer (WCLC) Annual Meeting taking place August 6-9, 2022 in Vienna, Austria. Posters will be archived on the Nuvalent website at www.nuvalent.com.

The first poster characterizes NVL-655 alongside other ALK inhibitors in a patient-derived model of lorlatinib-resistant ALK-positive non-small cell lung cancer (NSCLC) with the treatment-emergent G1202R/T1151M compound resistance mutation. NVL-655 has previously demonstrated differentiation through broad preclinical activity across diverse ALK oncoproteins, resistance mutations, and tumor types while maintaining strong selectivity for ALK over TRKB. Nuvalent [recently announced](#) the first patient has been dosed with NVL-655 in the ALKOVE-1 Phase 1/2 study for patients with advanced ALK-positive NSCLC and other solid tumors.

A "Trial in Progress" poster will also be presented with background and study design for the ongoing ARROS-1 Phase 1/2 study of NVL-520 for patients with advanced ROS1-positive NSCLC and other solid tumors. The multicenter, open-label, dose-escalation and expansion trial is currently evaluating NVL-520 as an oral monotherapy in the Phase 1 portion of the study. Nuvalent plans to share preliminary dose-escalation data from ARROS-1 in the second half of 2022.

Details for the E-poster presentations are as follows:

Title: [Preclinical Activity of NVL-655 in a Patient-Derived NSCLC Model with Lorlatinib-Resistant ALK G1202R/T1151M Mutation](#)

Authors: H. Mizuta¹, L. Bigot¹, A. Tangpeerachaikul², H.E. Pelish², L. Friboulet¹

Abstract Number: EP08.02-020

Session Category: Metastatic Non-small Cell Lung Cancer

Session Title: Molecular Targeted Treatments

Session Date and Time: August 7, 2022, 9:45am – 6:00pm CEST

¹Gustave-Roussy, Villejuif, France; ²Nuvalent, Inc., Cambridge, MA, USA

Title: [NVL-520, a Highly Selective ROS1 Inhibitor, in Patients with Advanced ROS1-Positive Solid Tumors: The Phase 1/2 ARROS-1 Study](#)

Authors: A. Drilon¹, S.-H.I. Ou², S. Gadgeel³, M. Johnson⁴, A. Spira⁵, G. Lopes⁶, B. Besse⁷, E. Felip⁸, A.J. van der Wekken⁹, A. Calles¹⁰, M.J. de Miguel¹¹, D.R. Camidge¹², Y. Elamin¹³, S. Liu¹⁴, J. Bauman¹⁵, D. Haggstrom¹⁶, G. Riley¹⁷, H.E. Pelish¹⁷, V.W. Zhu¹⁷, J.J. Lin¹⁸

Abstract Number: EP08.02-041

Session Category: Metastatic Non-small Cell Lung Cancer

Session Title: Molecular Targeted Treatments

Session Date and Time: August 7, 2022, 9:45am – 6:00pm CEST

¹Memorial Sloan Kettering Cancer Center, New York/NY/USA, ²University Of California Irvine Medical Center, Orange/CA/USA, ³Henry Ford Cancer Institute, Detroit/MI/USA, ⁴Sarah Cannon Research Institute, Nashville/TN/USA, ⁵NEXT Oncology - Virginia Cancer Specialists, Fairfax/VA/USA, ⁶Sylvester Comprehensive Cancer Center at the University of Miami and the Miller School of Medicine, Miami/FL/USA, ⁷Institut Gustave Roussy, Villejuif Cedex/FR, ⁸Hospital Vall d'Hebron, Barcelona/ES, ⁹University of Groningen, University Medical Centre Groningen, Groningen/NL, ¹⁰Hospital Universitario Gregorio Marañón, Madrid/ES, ¹¹START Madrid-HM CIOCC, Madrid/ES, ¹²University of Colorado Cancer Center, Anschutz Medical Campus, Aurora/CO/USA, ¹³MD Anderson Cancer Center, Houston/TX/USA, ¹⁴Georgetown University, Washington/DC/USA, ¹⁵Fox Chase Cancer Center, Philadelphia/PA/USA, ¹⁶Levine Cancer Institute, Atrium Health, Charlotte/NC/USA, ¹⁷Nuvalent, Inc., Cambridge/MA/USA, ¹⁸Massachusetts General Hospital, Boston/MA/USA

About NVL-655

NVL-655 is a novel brain-penetrant ALK-selective inhibitor created 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 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 brain metastases. NVL-655 has been observed in preclinical studies to selectively inhibit wild-type ALK and its resistance variants over the structurally related tropomyosin receptor kinase (TRK) family to potentially avoid TRK-related CNS adverse events seen with dual TRK/ALK inhibitors and drive more durable responses for patients. NVL-655 is currently being investigated in the ALKOVE-1 study ([NCT05384626](#)), a first-in-human Phase 1/2 clinical trial for patients with advanced ALK-positive non-small cell lung cancer (NSCLC) and other solid tumors.

About NVL-520

NVL-520 is a novel 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 wild-type ROS1 and its resistance variants 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. 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 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), 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 programs for NVL-520 and NVL-655 and the timing thereof; the potential clinical effect of NVL-520 and NVL-655; the design and enrollment of the ARROS-1 and ALKOVE-1 studies and the timing thereof; the potential of Nuvalent's pipeline programs, including NVL-520 and NVL-655; Nuvalent's research and development programs for the treatment of cancer; risks and uncertainties associated with drug development; and capital allocation. 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 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 HER2 Exon 20 and ALK IXDN 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 Annual Report on Form 10-K for the year ended December 31, 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.

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<https://investors.nuvalent.com/2022-07-13-Nuvalent-to-Present-New-NVL-655-Preclinical-Data-and-ARROS-1-Trial-in-Progress-Poster-for-NVL-520-at-IASLC-2022-World-Conference-on-Lung-Cancer-Annual-Meeting>