New Clinical and Preclinical Data for Investigational Candidate Zidesamtinib Presented at AACR Annual Meeting 2026

Zidesamtinib demonstrated meaningful clinical activity in subset of TKI pre-treated ROS1-positive NSCLC patients from ARROS-1 trial previously treated with repotrectinib or taletrectinib, including in those with CNS

disease or ROS1 resistance mutations

Preclinical data support differentiated brain penetrance and intracranial activity as compared to repotrectinib and taletrectinib

CAMBRIDGE, Mass., April 17, 2026 /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 new clinical and preclinical data for zidesamtinib, an investigational ROS1-selective inhibitor, to be presented during poster sessions at the American Association for Cancer Research (AACR) Annual Meeting 2026 being held April 17-22 in San Diego.

"The strong patient enrollment in our ARROS-1 trial has reflected meaningful investigator enthusiasm for zidesamtinib's profile and generated a robust data set that enables deep characterization of its activity for patients with ROS1-positive NSCLC beyond our initial pivotal data presentation," said **James Porter, Ph.D., Chief Executive Officer at Nuvalent.** "We're highly encouraged by these clinical data for patients previously treated with repotrectinib or taletrectinib in our ARROS-1 trial, which we believe further reinforce the medical needs that remain for patients with ROS1-positive NSCLC despite the availability of new treatment options."

"Zidesamtinib demonstrated clinically meaningful activity in this heavily pre-treated subgroup, including activity in tumors with the ROS1 G2032R resistance mutation and intracranial complete responses for patients with CNS disease. Importantly, this indicates that ROS1-positive NSCLC tumors may remain ROS1-dependent beyond treatment with repotrectinib or taletrectinib and we believe supports the potential for zidesamtinib, if approved, to provide a clinically meaningful treatment option for patients who have exhausted available therapies," said **Christopher Turner, M.D., Chief Medical Officer at Nuvalent**. "Furthermore, these clinical findings are consistent with the improved preclinical brain penetrance and intracranial ROS1 G2032R antitumor activity of zidesamtinib compared to repotrectinib and taletrectinib, and continue to support the potential for a differentiated clinical profile in earlier lines of therapy."

The U.S. Food and Drug Administration (FDA) has accepted the New Drug Application (NDA) for zidesamtinib for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC who received at least 1 prior ROS1 TKI, and assigned a Prescription Drug User Fee Act (PDUFA) target action date of September 18, 2026. Pending FDA review, Nuvalent anticipates U.S. commercial launch of zidesamtinib in 2026. Additionally, the company plans to submit data to the FDA to support a potential label expansion of zidesamtinib in TKI-naïve patients with advanced ROS1-positive NSCLC in the second half of 2026.

New Clinical Data for Zidesamtinib in Subset of TKI Pre-treated Patients in ARROS-1 Trial

Title: Zidesamtinib in Patients with ROS1+ NSCLC Previously Treated with Repotrectinib or Taletrectinib

Presenting Author: Geoffrey Liu, M.Sc., M.D.[1]
Abstract Number: CT248
Session Title: Phase II Clinical Trials
Session Date and Time: Tuesday, April 21, 2026, 2:00-5:00 p.m. PT
Location: Poster Section 50
Poster Board Number: 13

Zidesamtinib is being evaluated in ARROS-1, a first-in-human, single-arm Phase 1/2 clinical trial in patients with advanced ROS1-positive NSCLC and other solid tumors. Clinical data presented are from a subgroup of patients with advanced ROS1-positive NSCLC in ARROS-1 who had been previously treated with the dual TRK/ROS1 TKIs repotrectinib and/or taletrectinib. No available ROS1 TKIs have demonstrated activity in this heavily pre-treated population.

Patients received at least 1 dose of zidesamtinib at 100 mg QD as of a data cut-off date of September 22, 2025. The population for this analysis was unique and heavily pre-treated:

- 46 efficacy-evaluable patients had received prior repotrectinib, 19 had received prior taletrectinib, and 3 had previously received both;
- 85% (39/46) of repotrectinib-treated patients and 89% (17/19) of taletrectinib-treated patients had received ≥2 prior ROS1 TKIs;
- 63% (29/46) of repotrectinib-treated patients and 53% (10/19) of taletrectinib-treated patients had received prior chemotherapy;
- Active CNS disease was assessed by BICR in 46% (21/46) of repotrectinib-treated patients and 53% (10/19) of taletrectinib-treated patients at baseline; and
- Secondary ROS1 resistance mutations were reported in 35% (16/46) of repotrectinib-treated patients and 42% (8/19) of taletrectinib-treated patients, with a ROS1 G2032R mutation identified in 26% (12/46) and 21% (4/19), respectively.

Treatment with zidesamtinib resulted in clinically meaningful activity in this population, including in patients with the ROS1 G2032R resistance mutation and those with CNS disease. As of the data cut-off date:

Efficacy Parameter (RECIST v1.1, BICR)	**Prior repotrectinib[a]**	**Prior taletrectinib[b]**
ORR, % (n/n) [95% CI]	41% (19/46) [27, 57]	47% (9/19) [24, 71]
CR, n (%)	7% (3/46) [c]	5% (1/19)
mDOR, months [d] [95% CI]	15.7 [5.6, NE]	NR [5.2, NE]
ROS1 G2032R resistance mutation		
ORR, % (n/n) [95% CI]	67% (8/12) [35, 90]	50% (2/4) [e] [7, 93]
CR, n (%)	8% (1/12)	0 %
mDOR, months [d] [95% CI]	15.7 [3.5, NE]	NR [NE, NE]
Intracranial Activity [f]		
IC-ORR, % (n/n) [95% CI]	44% (8/18) [22, 69]	71% (5/7) [29, 96]
IC-CR, n (%)	11% (2/18)	43% (3/7)
mIC-DOR, months [d] [95% CI]	NR [5.2, NE]	NR [5.2, NE]
IC-DOR ≥6 months [d]	86% [33, 98]	80% [20, 97]

BICR, blinded independent central review; CI, confidence interval; CR, complete response; IC, intracranial;
IC-DOR, intracranial duration of response; mDOR, median duration of response; NE, not estimable; NR, not
reached; ORR, objective response rate.

[a] Prior repotrectinib ± other ROS1 TKIs and/or chemotherapy.

[b] Prior taletrectinib ± other ROS1 TKIs and/or chemotherapy.

[c] Includes one single time-point CR pending confirmation in an ongoing patient who previously experienced
confirmed PR.

[d] Kaplan-Meier estimates.

[e] Responses also observed in pts with ROS1 D2033N (n=1) and L2086F (n=1).

[f] Includes patients with measurable (≥5mm) CNS lesions by BICR at baseline.

The safety profile of zidesamtinib in this population was consistent with the previously reported safety results from ARROS-1 for patients with advanced ROS1-positive NSCLC, including low rates of dose reductions and treatment discontinuations, and the avoidance of TRK-related neurologic adverse events.

New Preclinical Data for Zidesamtinib

Title: Zidesamtinib Has Differentiated Preclinical Brain Penetrance and Intracranial Activity Compared to Other ROS1 Inhibitors
Presenting Author: Anupong Tangpeerachaikul, Ph.D.[2]
Abstract Number: LB366
Session Title: Late-Breaking Research: Experimental and Molecular Therapeutics 3
Session Date and Time: Tuesday, April 21, 2026, 2:00-5:00 p.m. PT
Location: Poster Section 53
Poster Board Number: 23

Data presented are from preclinical analyses of the brain penetrance and intracranial ROS1 G2032R antitumor activity of zidesamtinib compared to the dual TRK/ROS1 inhibitors repotrectinib and taletrectinib.[3]

Among the three ROS1 TKIs, all of which have reported activity against the ROS1 G2032R mutation, zidesamtinib demonstrated:

- Highest cell permeability in MDCK-MDR1 cell lines and highest brain-to-plasma partitioning in rats, supporting zidesamtinib's potential for high brain penetrance;
- Most sustained intracranial efficacy in a mouse ROS1 G2032R brain tumor model, with all mice surviving to study end; and,
- Efficacy after progressive disease on earlier-line taletrectinib treatment in a mouse ROS1 G2032R brain tumor model. Data demonstrating that switching from repotrectinib to zidesamtinib resulted in more sustained tumor suppression in the same preclinical model have been previously reported.[4]

[1] Princess Margaret Hospital, Toronto, Ontario, Canada;

[2] Nuvalent, Inc., Cambridge, MA, USA;

[3] Head-to-head clinical studies comparing zidesamtinib with other treatments have not been conducted. Data presented are from preclinical studies, and no clinical conclusions can be drawn.

[4]Tangpeerachaikul et al. Annals of Oncology 2024; 35(2):S217.

About Zidesamtinib
Zidesamtinib is an investigational, 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.

Based on results for tyrosine kinase inhibitor (TKI) pre-treated patients with advanced ROS1-positive non-small cell lung cancer (NSCLC) enrolled in the global registrational ARROS-1 Phase 1/2 clinical trial, the U.S. Food and Drug Administration (FDA) has accepted for filing Nuvalent's NDA submission for zidesamtinib for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC who received at least 1 prior ROS1 TKI. The application has been assigned a Prescription Drug User Fee Act (PDUFA) target action date of September 18, 2026. Zidesamtinib has received breakthrough therapy designation for the treatment of patients with ROS1-positive metastatic NSCLC who have been previously treated with 2 or more ROS1 TKIs and orphan drug designation for 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; the expected timing of data announcements, regulatory submissions, product approvals and commercial launch; the clinical development program for zidesamtinib; the potential benefits and effects of Nuvalent's product development candidates; the design of Nuvalent's clinical trials, including for the ARROS-1 trial its intended pivotal registration-directed design; the potential of Nuvalent's pipeline programs, including zidesamtinib; 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," "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 and 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 zidesamtinib product candidate; 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 Annual Report on Form 10-K for the fiscal year ended December 31, 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.

Investor Contact:
Chelcie Lister
Nuvalent, Inc.
clister@nuvalent.com

Media Contact
Amanda Sellers
Deerfield Group
amanda.sellers@deerfieldgroup.com

SOURCE Nuvalent, Inc.
