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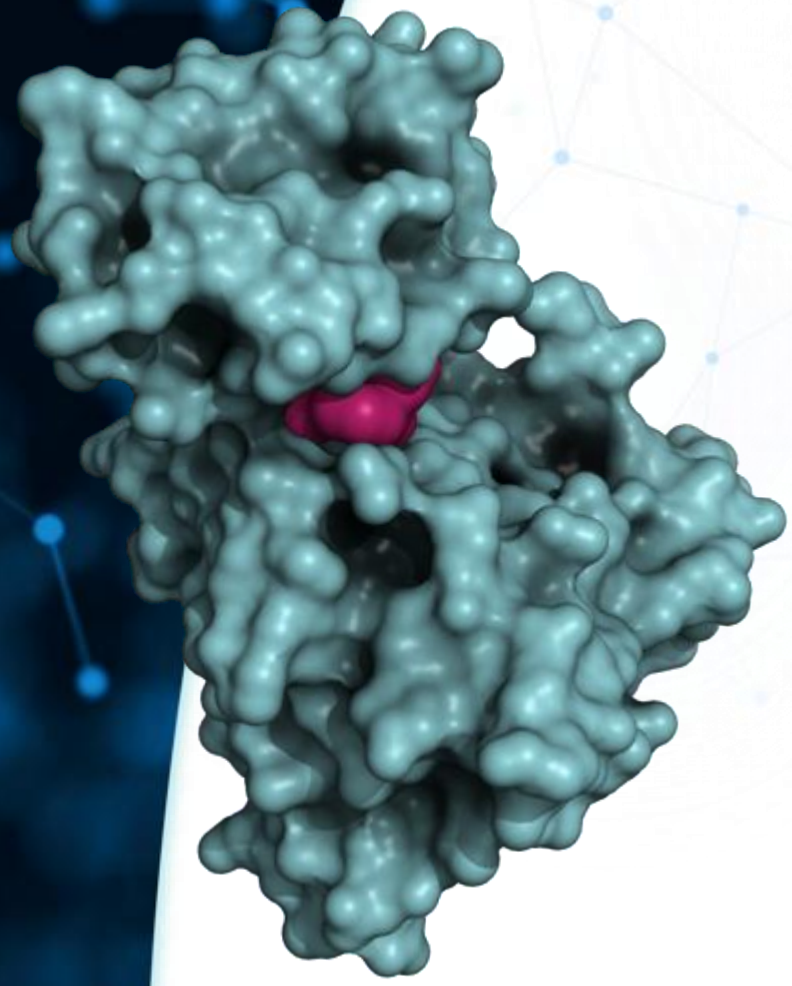
Nuvalent Overview

May 27, 2026



PRECISELY

Targeted Therapies
for patients with cancer

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This presentation 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; Nuvalent's estimated cash runway; the expected timing of potential new product candidate announcements, clinical trial initiations, FDA submissions, product approvals and commercial launch, including the projections in our OnTarget 2026 operating plan; the clinical development programs for zidesamtinib, neladalkib and NVL-330; the potential clinical effects of Nuvalent's product development candidates; the design, timing and enrollment of Nuvalent's clinical trials, including for the ARROS-1, ALKOVE-1 and ALKAZAR trials their intended pivotal registration-directed design; the potential of Nuvalent's pipeline programs, including zidesamtinib, neladalkib and NVL-330 and expectations regarding Nuvalent's discovery pipeline; Nuvalent's potential commercialization of its product candidates, if approved; the implications of data readouts and presentations; timing and content of potential discussions with FDA; 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 presentation 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 presentation, 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 zidesamtinib and neladalkib; risks that Nuvalent may not achieve the goals and milestones set forth in its OnTarget 2026 operating plan; 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, including the ARROS-1, ALKOVE-1, ALKAZAR and HEROEX-1 trials; 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2026, 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.

Nuvalent | AT·A·GLANCE

PRECISELY

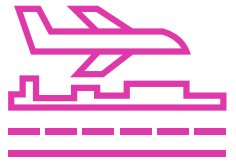
Targeted Therapies *for patients with cancer*

- **Parallel lead programs for ROS1+ and ALK+ NSCLC:** Global clinical development ongoing with potential for first U.S. commercial launch in 2026
- **Proven discovery capabilities:** Third program for HER2-altered NSCLC in Phase 1 investigation & active research pipeline

#NuCrew

Growing team (~300 FTEs)

Hybrid operations with offices in Cambridge, MA



Cash runway expected into 2029

Nasdaq listed

PRECISELY

Targeted Therapies *for patients with cancer*

THE ▪ NUVALENT ▪ APPROACH

Deep Expertise in Chemistry and Structure-based Drug Design

Aim to “thread the needle” between kinase resistance and selectivity

Design of Target Product Profiles in Collaboration with Physician-Scientists

Aim to Compete in 1st Line with Best-in-Class Profiles

GOAL: Maximize Patient Impact

Nuvalent

Meet the #NuCrew

Significant experience in drug discovery, development and company building

BOARD OF DIRECTORS

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VP, Medical Affairs

Josh Horan, PhD
SVP, Chemistry

Jessie Lin
SVP, Corporate Strategy & Portfolio Management

John Soglia, PhD
SVP, Translational Development

Jason Waters
SVP, Commercial

12 Prior FDA Approvals*

mozobil (plerixafor) injection · Cloiar · pyrukynd (mitapivat) tablets · TIBSOYO (ivosidenib) tablets · Fabrazyme (agalsidase beta) · Brukinsa (zanubrutinib) · ALUNBRIG (brigatinib) · ICLUSIG (ponatinib) tablets · BAVENCIO (avelumab) · GAVRETO · Copiktra (duvelisib) · Tivicay (dolutegravir)

* Experience prior to joining Nuvalent

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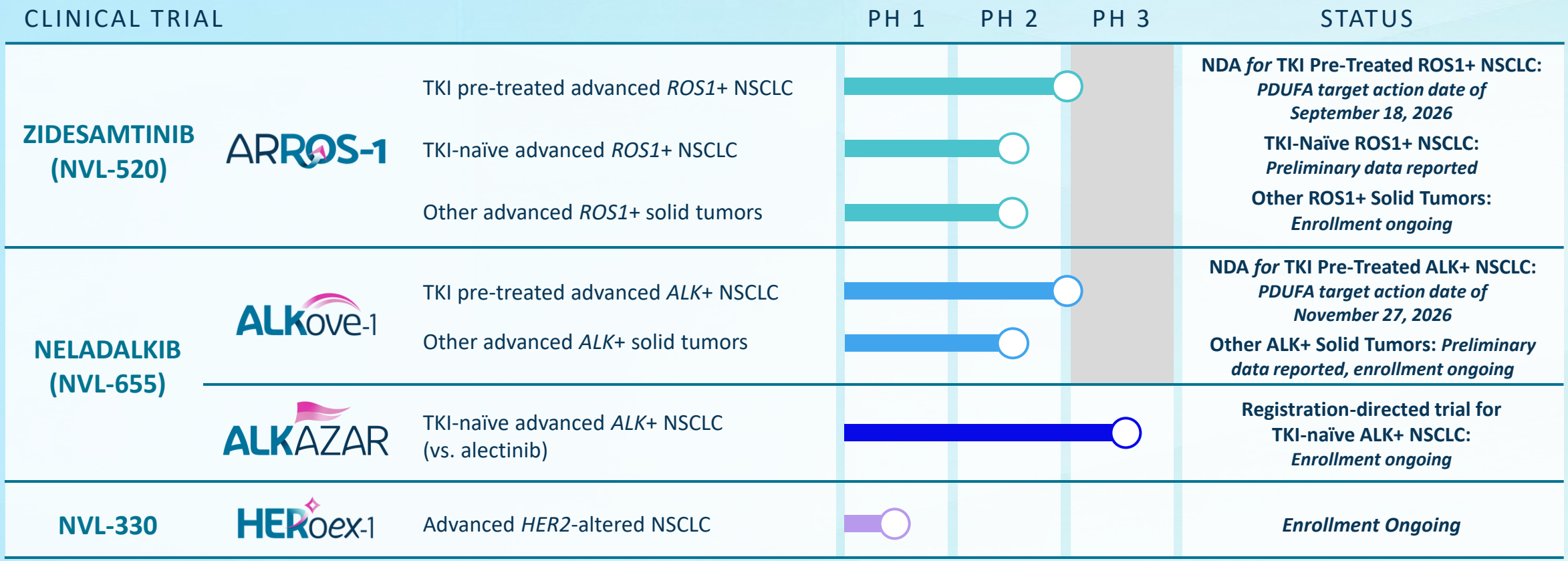
PIPELINE

Advancing a portfolio of potentially best-in-class products, with complementary initial indications in NSCLC



NDA, new drug application; **NSCLC**, non-small cell lung cancer; **PDUFA**, prescription drug user fee act; **TKI**, tyrosine kinase inhibitor.

Additional Discovery Research Programs Ongoing

OnTarget 2026

The Path to Patient Impact

GOAL:

2024	2025	2026
EXECUTE ON GLOBAL REGISTRATIONAL STRATEGIES	FIRST PIVOTAL DATA	FIRST APPROVED PRODUCT

MISSION: Bringing new, potential best-in-class medicines to patients with cancer

Completed & Anticipated 2026 Milestones:

- US commercial launch of zidesamtinib in TKI pre-treated ROS1+ NSCLC in 2H, pending FDA review
- Submit data to FDA for potential label expansion of zidesamtinib in TKI-naïve ROS1+ NSCLC in 2H
- ✓ Submit NDA for neladalkib in TKI pre-treated ALK+ NSCLC in 1H
- Progress ALKAZAR Phase 3 trial for TKI-naïve ALK+ NSCLC
- Progress HEROEX-1 Phase 1a/1b trial for HER2-altered NSCLC
- Disclose new development candidate by year-end

: Planned ✓ : Complete

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Well-positioned to unlock the potential for **Patient Impact** within ROS1+ and ALK+ NSCLC

- Pivotal data demonstrates potential to deliver meaningful durability **and** tolerability
- Growing team (~300 FTEs) building integrated US commercial capabilities
- Well capitalized, with cash runway expected into 2029

NUVALENT VISION

ROS1+ NSCLC

Reimagine what is possible

ALK+ NSCLC

Realize the full potential

NUVALENT VISION

ROS1+ NSCLC

Reimagine what is possible

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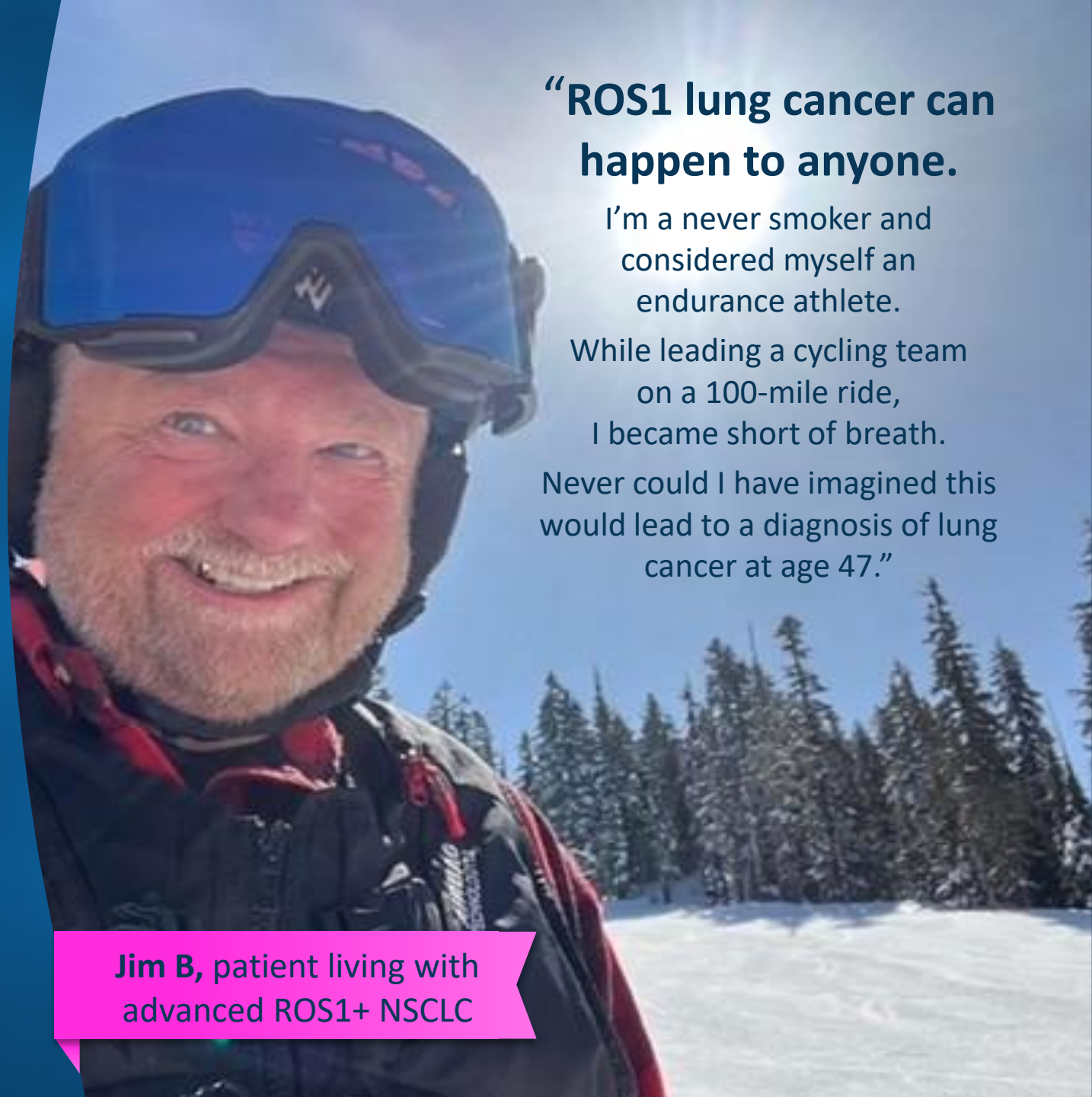

Jim B, patient living with advanced ROS1+ NSCLC

“ROS1 lung cancer can happen to anyone.

I’m a never smoker and considered myself an endurance athlete.

While leading a cycling team on a 100-mile ride, I became short of breath.

Never could I have imagined this would lead to a diagnosis of lung cancer at age 47.”

ROS1+ NSCLC Treatment Paradigm

~1 – 3 % of NSCLC [1,2] | Majority are advanced/metastatic at diagnosis [3]

	STANDARD OF CARE	KEY LIMITATIONS
1L	**Crizotinib** ($374M WW sales, 2023) [4] NCCN guidelines recognize that other ROS1 TKIs may be better for patients with brain metastasis at diagnosis [5]	**Single ROS1 resistance mutations** *ROS1 G2032R mutation observed in ~40% of patients progressing on crizotinib* [6] **Brain penetrance** • *~20 – 40% present with brain metastases at diagnosis* [7,8] • *~30 – 55% have brain metastases at 1L progression* [6,7]
2L	**Evolving standard of care** Patients may consider other approved ROS1 TKIs, clinical trials, or chemotherapy/I-O [5]	**Treatment-limiting off-target adverse events** *CNS adverse events associated with TRK inhibition observed in 77% of patients receiving the dual TRK/ROS1 inhibitor, repotrectinib* [9] *Dose reductions due to adverse reactions occurred in 29 – 38% of patients receiving repotrectinib or taletrectinib* [9,10]
3L+	**No clear standard of care** Patients may consider clinical trials or chemotherapy/I-O [5]	**Activity** *No approved therapies have demonstrated activity after the recently approved dual TRK/ROS1 TKIs, repotrectinib or taletrectinib* [5]

POTENTIAL OPPORTUNITY *for* PATIENT IMPACT

- **Improve 1L durability of response, while also avoiding CNS adverse events**
  - Crizotinib mDOR: **18.3** months [11]
  - Crizotinib mPFS: **19.3** months [12]
- **Improve durability of response after crizotinib or entrectinib, while also avoiding CNS adverse events:**
  - *USPIs for repotrectinib and taletrectinib*:*
  - mDOR: **13.2 – 14.8 months** [9, 10]
- **Demonstrate activity after 2+ prior ROS1 TKIs, including in patients who are repotrectinib and/or taletrectinib experienced**

* Most patients received prior crizotinib only (82% of patients receiving repotrectinib, 79 – 100% of patients receiving taletrectinib).

CNS, central nervous system; **DOR**, duration of response; **m**, median; **ORR**, objective response rate; **TKI**, tyrosine kinase inhibitor; **USPI**, US prescribing information.

Sources: [1] Drilon A. et al., Nat Rev Clin Oncol. 2021. [2] Jordan E.J. et al., Cancer Discovery 2017. [3] Chia P.L. et al., Clin Epidemiol. 2014. [4] Pfizer 2023 Year-end Earnings Report. [5] NCCN Guidelines for NSCLC (version 2.2026). [6] Gainor J et al. JCO Precis Oncol. 2017. [7] Ou S.I. and Zhu V.W., Lung Cancer 2019. [8] Patil T. et al., J Thorac Oncol. 2018. [9] AUGTYRO FDA prescribing information, revised 06/2024. [10] IBTROZI FDA prescribing information, revised 06/2025. [11] XALKORI FDA prescribing information, revised 09/2023. [12] Shaw A. et al., Ann Oncol. 2019.

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NUVALENT VISION

Reimagine what is possible with a ROS1 TKI

Patient Outcomes

BACKGROUND: ROS1 is a proven oncogenic driver, but outcomes today may not be as durable compared to other known targets [1,3,4]

Crizotinib *for* ROS1+ NSCLC	Entrectinib *for* ROS1+ NSCLC
1L mPFS = **19.3** months [1]	1L mPFS = **15.7** months [3]
1st Generation TKI & Global Market Leader [2]	1st Generation TKI & 1L Alternative

INSIGHT: Next generation TKIs that address key drivers of disease progression, including **brain penetrance** and **resistance mutations,** are transforming durability for other known targets

Lorlatinib *for* ALK+ NSCLC (3rd Generation TKI)
1L mPFS = **Not Reached** at 60 months [4]

Market Opportunity

BACKGROUND: Global sales reflect the continued primary use of 1st generation TKIs

Crizotinib WW sales (2023): **$374M** [5,6]
Entrectinib WW sales (2025): **$176M** [6]
Repotrectinib WW sales (2024): **$38M** [6,7]

INSIGHT: Other available TKIs such as repotrectinib are dual TRK/ROS1 inhibitors associated with **risk of CNS adverse events** [8]

For this patient population that is often diagnosed at a younger age, new options are needed to offer both durability **and** tolerability [9]

NUVALENT VISION

Transform the expectation for patient outcomes

Deliver transformative durability **and** tolerability, across lines of therapy, with the first ROS1-selective TKI

&

Unlock the market potential of ROS1+ NSCLC

Build a prevalent population of patients living long-term with ROS1+ NSCLC

Sources: [1] Shaw A. et al., Ann Oncol. 2019. [2] Cortellis, product sales accessed 01/2026. [3] Drilon A. et al., JTO 2022. [4] Solomon B.J. et al., J Clin Oncol. 2024. [5] Crizotinib is FDA approved for ROS1+ NSCLC and ALK+ NSCLC, ALCL, and IMT, but sales are not reported by indication and are no longer separately reported as of 2024; Assumes the large majority of crizotinib sales are for ROS1 following alectinib 1L ALK approval in 2017. [6] Year-end Earnings Reports for Pfizer (2023), Roche (2025), and BMS (2024). [7] Sales of repotrectinib are no longer separately reported as of 2025. [8] AUGTYRO FDA prescribing information, revised 06/2024. [9] Desilets et al., Cancer. 2025.

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NVL-520

Zidesamtinib

A Rationally Designed **ROS1**-selective, TRK-sparing Inhibitor

Potential Best-in-Class Target Product Profile designed in collaboration with physician-scientists to address the limitations of existing agents for ROS1+ NSCLC

DESIGN GOAL *for* ZIDESAMTINIB

ROS1 Activity

- Primary oncogenic driver in ~1 – 3% of NSCLC [1,2]

+

ROS1 Mutant Activity

- ~40% ROS1 G2032R mutation after 1L standard of care, crizotinib [3]

+

CNS Activity

- ~20 – 40% CNS disease at diagnosis [4,5]
- ~30 – 55% CNS disease after 1L standard of care, crizotinib [3,4]

+

Avoiding TRK

- Treatment-limiting neurological adverse events observed with brain-penetrant, dual TRK/ROS1 inhibitors [6]

Zidesamtinib is an investigational candidate and has not been approved by FDA or any other regulatory authority.

CNS, central nervous system; **NSCLC**, non-small cell lung cancer; **TKI**, tyrosine kinase inhibitor; **TRK**, proteins encoded for by the neurotrophic tyrosine receptor kinase (NTRK) family of genes.

Sources: [1] Drilon A. et al., Nat Rev Clin Oncol. 2021. [2] Jordan E.J. et al., Cancer Discovery 2017. [3] Gainor J et al. JCO Precis Oncol. 2017. [4] Ou S.I. and Zhu V.W., Lung Cancer 2019. [5] Patil T. et al., J Thorac Oncol. 2018. [6] AUGTYRO FDA prescribing information, revised 06/2024.

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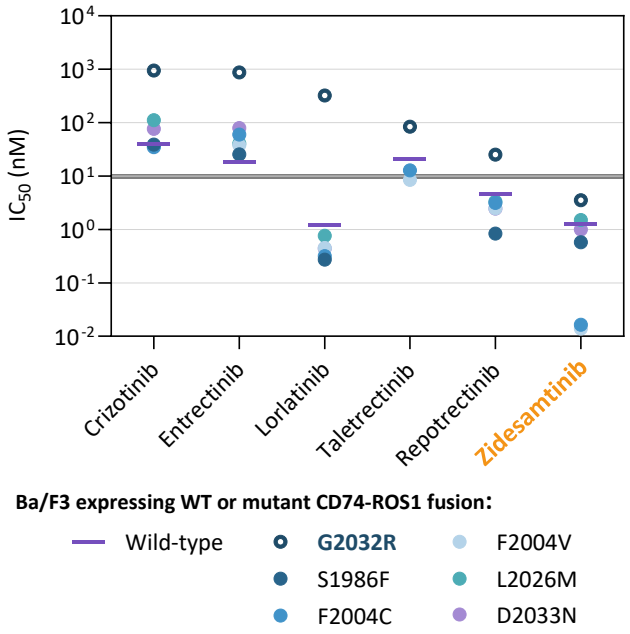
Preclinical Characterization Demonstrates Desired Target Product Profile

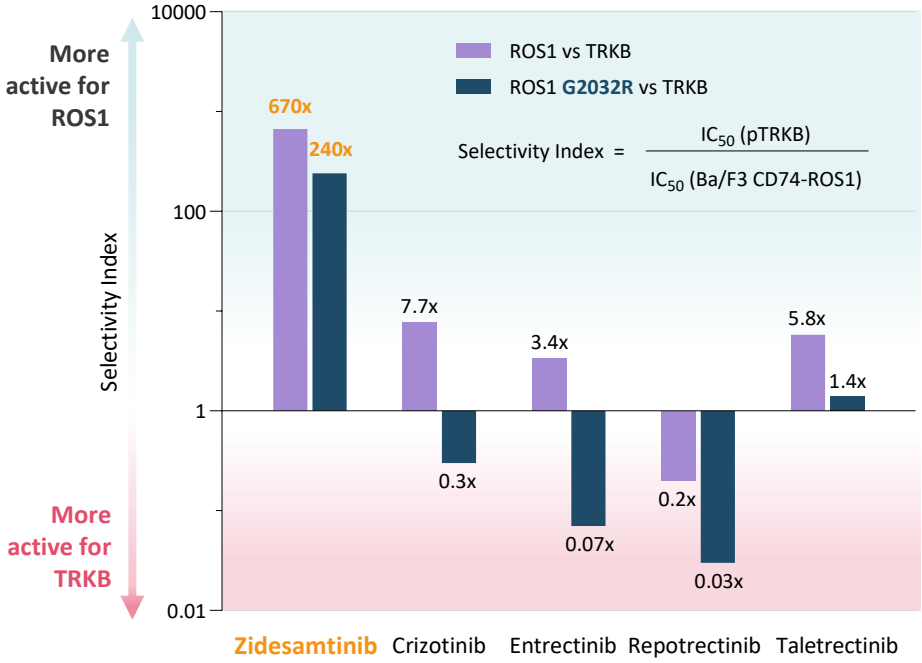
In Vitro Activity, ROS1 Wild-type & Mutant

Sub-10nM activity in 3-day cell viability assays



Avoiding TRK Inhibition

Selectivity for ROS1 and ROS1 G2032R over TRK



Head-to-head clinical studies comparing zidesamtinib (NVL-520) with currently approved or investigational therapies have not been conducted. Above data from preclinical studies and no clinical conclusions can be drawn.

BID, twice daily; **IC50**, half-maximal inhibitory concentration; **PDC**, patient-derived cell line; **PO**, orally; **pTRK**, BDNF-stimulated TRKB phosphorylation.

Sources: Drilon A. et al., Cancer Discov 2023; Tangpeerachaikul, A. et al., AACR 2022; Deshpande, A. et al., EORTC-NCI-AACR 2021; Pelish, H.E. et al., AACR 2021.

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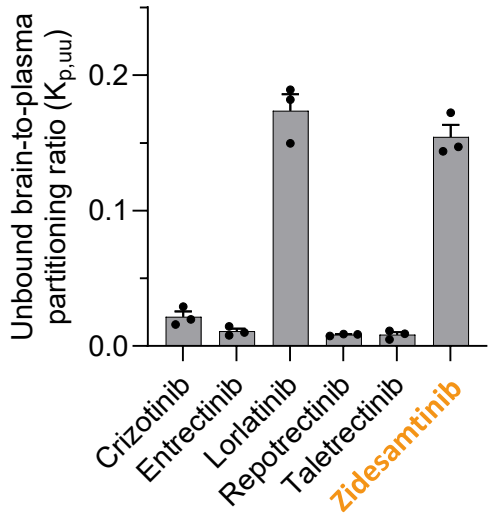
Preclinical Characterization Demonstrates Desired Target Product Profile

Brain Penetrance

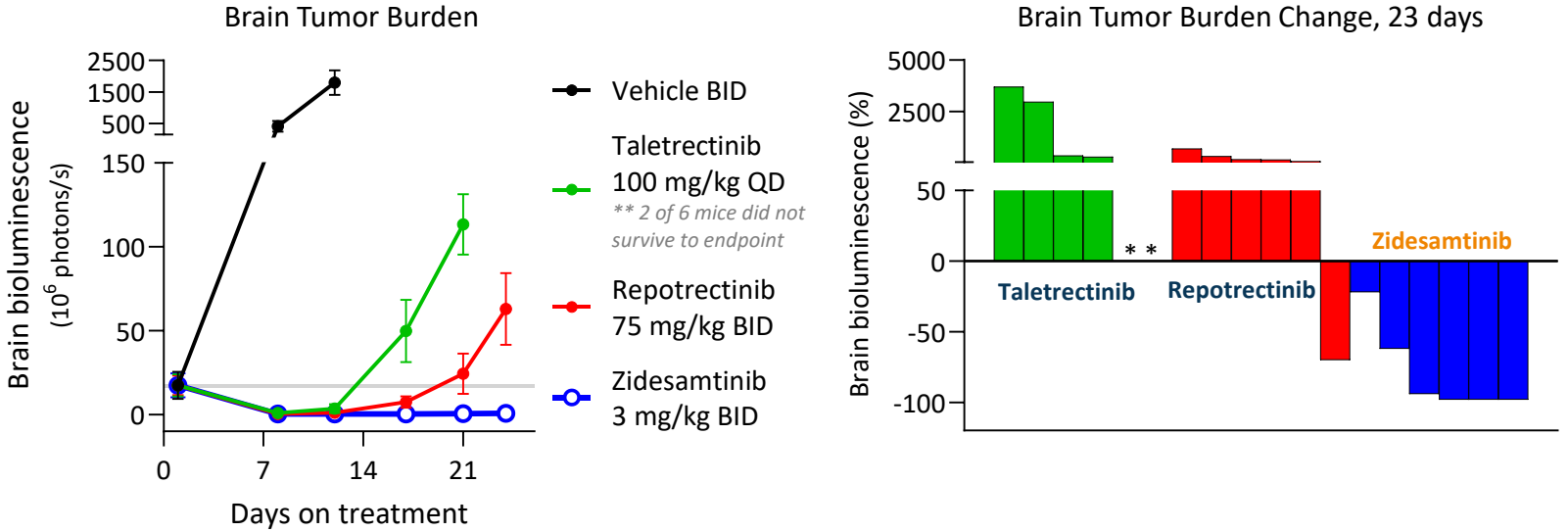
Pharmacokinetic data similar to preclinical observations for lorlatinib



Wistar Han rats
10 mg/kg, single dose PO
1 hour timepoint

Preclinical Intracranial Efficacy

Durable inhibition of intracranially implanted Ba/F3 CD74-ROS1 G2032R luciferase cells



Head-to-head clinical studies comparing zidesamtinib (NVL-520) with currently approved or investigational therapies have not been conducted. Above data from preclinical studies and no clinical conclusions can be drawn.
BID, twice daily; QD, once daily.
Sources: Tangpeerachaikul et al., AACR 2026.; Tangpeerachaikul et al., Mol Cancer Ther 2025.

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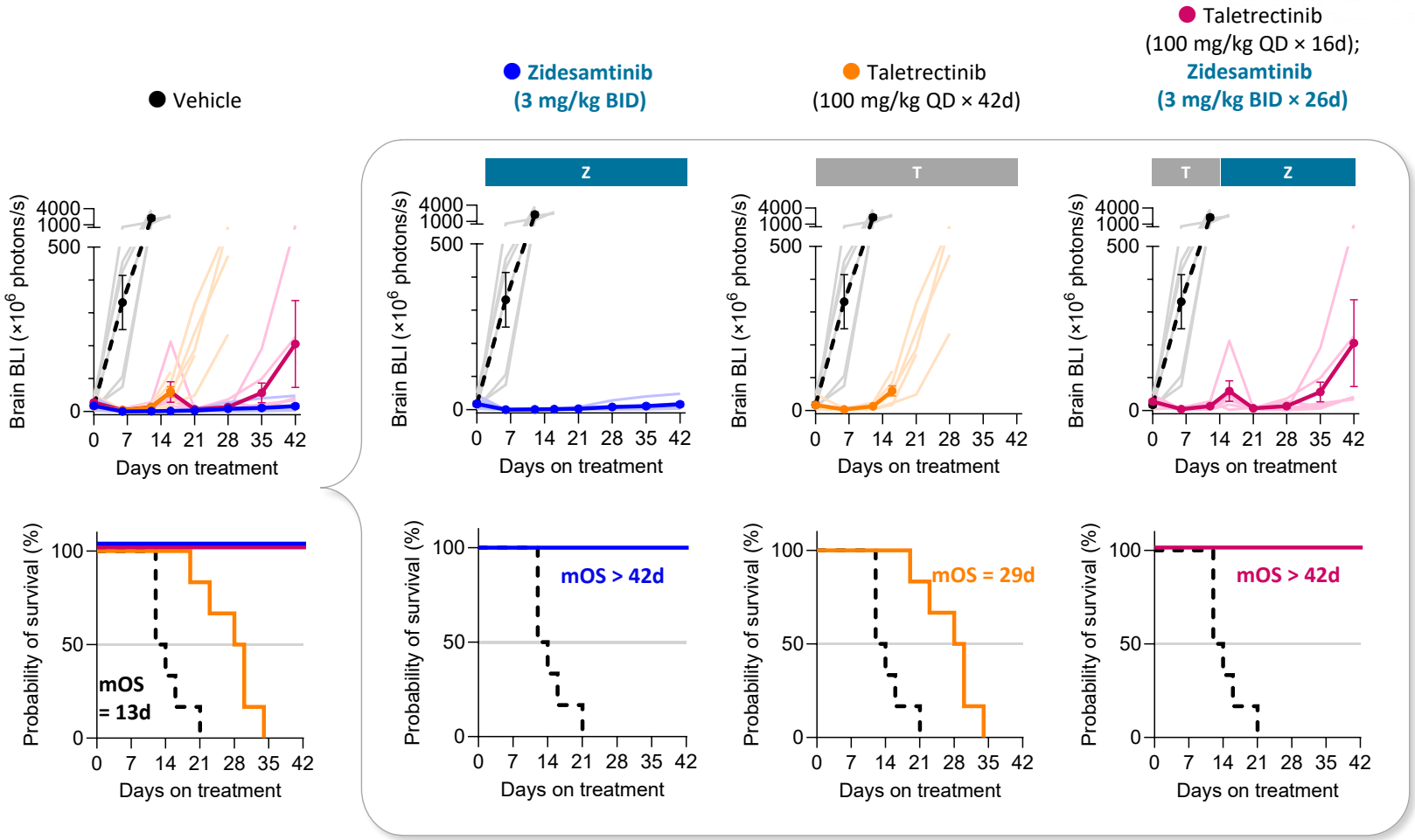
Preclinical Characterization Supports Potential for Intracranial Differentiation

Preclinical Intracranial Efficacy

*Efficacy after progressive disease on earlier-line taletrectinib treatment in a mouse ROS1 G2032R brain tumor model**



Balb/c nude mice. Vehicle: 20% HP-β-CD/water, also used to formulate zidesamtinib.

Head-to-head clinical studies comparing zidesamtinib (NVL-520) with currently approved or investigational therapies have not been conducted. Above data from preclinical studies and no clinical conclusions can be drawn.

*Data demonstrating that switching from repotrectinib to zidesamtinib resulted in more sustained tumor suppression in the same preclinical model have been previously reported (Tangpeerachaikul et al. Annals of Oncology 2024; 35(2):S217).

BID, twice daily; **QD**, once daily.

Sources: Tangpeerachaikul et al., AACR 2026.; Tangpeerachaikul et al., Mol Cancer Ther 2025.; Internal data on file.

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Zidesamtinib | Global Development Strategy

Parallel development paths ongoing to establish zidesamtinib as a best-in-class drug for all patients with ROS1+ NSCLC

ARROS-1 Phase 2: TKI Pre-treated Cohorts

Global enrollment complete

Topline data supports opportunity for broad TKI pre-treated label:

2L+ TKI pre-treated ROS1+ NSCLC receiving zidesamtinib at RP2D (N = 117)

NDA accepted for filing by FDA with PDUFA target action date of September 18, 2026

ARROS-1 Phase 2: TKI-naïve Cohort

Global enrollment complete

Opportunity for single-arm registration path for line-agnostic expansion:

1L No prior ROS1 TKI, ≤ 1 prior line of chemo/I-O

- n = 104 enrolled as of June 16, 2025

Submission of data to FDA planned for 2H'26 for potential label expansion in TKI-naïve ROS1+ NSCLC

ARROS-1

Enrollment ongoing for adult and pediatric patients with other ROS1+ solid tumors

NDA, new drug application; **NSCLC**, non-small cell lung cancer; **RP2D**, recommended phase 2 dose (100 mg QD); **RTOR**, real-time oncology review; **TKI**, tyrosine kinase inhibitor.

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A Global First-in-Human Phase 1/2 Clinical Trial of Zidesamtinib in Advanced **ROS1-Positive** NSCLC and Other Solid Tumors (NCT05118789)

PHASE 1 INITIATED JANUARY 2022

First-in-human dose-escalation in heavily pre-treated ROS1+ NSCLC & other solid tumors

Preliminary data demonstrated clinical proof-of-concept for zidesamtinib's target product profile:

SEPTEMBER 2022

Preliminary Phase 1 Data: Clinical proof-of concept in heavily pre-treated population

Drilon et al., EORTC-NCI-AACR 2022

OCTOBER 2024

Updated Phase 1 Data: Durable responses in heavily pre-treated population

Besse et al., ESMO 2024

PHASE 2 INITIATED SEPTEMBER 2023 (RP2D: 100 mg QD)

Global open-label, multi-cohort design with registrational intent for both TKI pre-treated and TKI-naïve ROS1+ NSCLC

ARROS-1 COHORT	TUMOR TYPE	TREATMENT STATUS	PRIOR ROS1 TKI	PRIOR CHEMO/I-O	DETAIL
2 a	ROS1-positive NSCLC	ROS1 TKI Naive	None	≤ 1	Registrational Intent
2 b	ROS1-positive NSCLC	ROS1 TKI Pre-treated	1[a]	None	
2 c			1[a]	1[b]	
2 d			≥ 2[c]	≤ 1	
2 e	Any ROS1-positive Solid Tumor [d]	Any Prior Therapy	Any	Any	Exploratory Cohort

- Primary Objective: ORR by blinded independent central review
- Secondary Objectives: Additional efficacy measures (DOR, TTR, CBR, PFS, OS), intracranial activity, overall safety and tolerability, confirmation of PK profile, PROs

SEPTEMBER 2025

Pivotal TKI pre-treated (pooled Phase 1/2) & preliminary TKI-naïve data for ROS1+ NSCLC

Drilon et al., WCLC 2025

CBR, clinical benefit rate; **DOR**, duration of response; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression free survival; **PK**, pharmacokinetics; **PRO**, patient reported outcomes; **QD**, once daily; **RP2D**, recommended phase 2 dose; **TKI**, tyrosine kinase inhibitor; **TTR**, time to response.

[a] Either crizotinib or entrectinib; [b] Platinum-based chemotherapy with or without immunotherapy; [c] With initial TKI of either crizotinib or entrectinib; [d] Includes NSCLC who do not qualify for any of the other cohorts.

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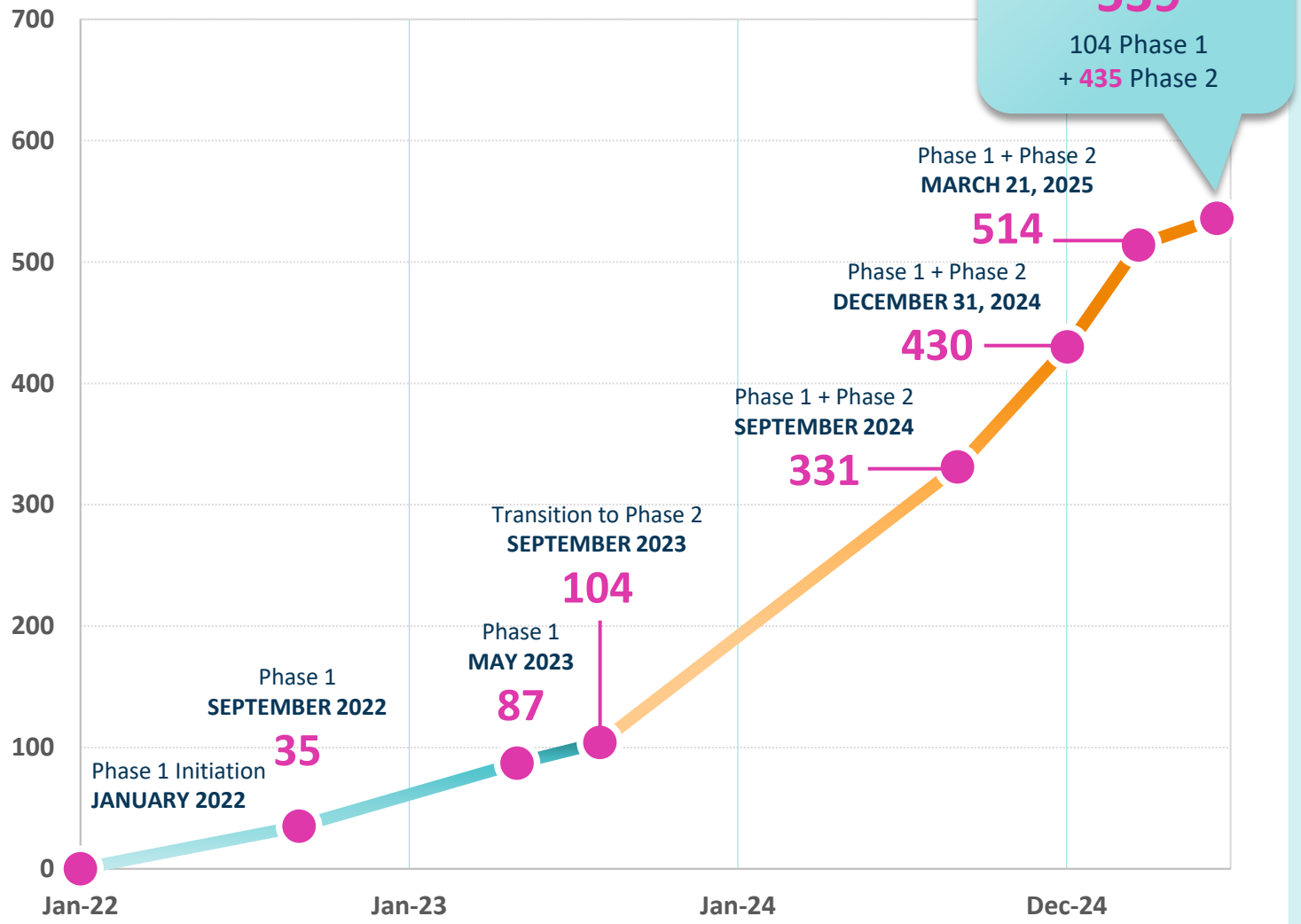
ARROS-1

PHASE 1 + PHASE 2 PATIENT ENROLLMENT

Strong enrollment momentum demonstrates enthusiasm for zidesamtinib & clear medical need for TKI pre-treated patients

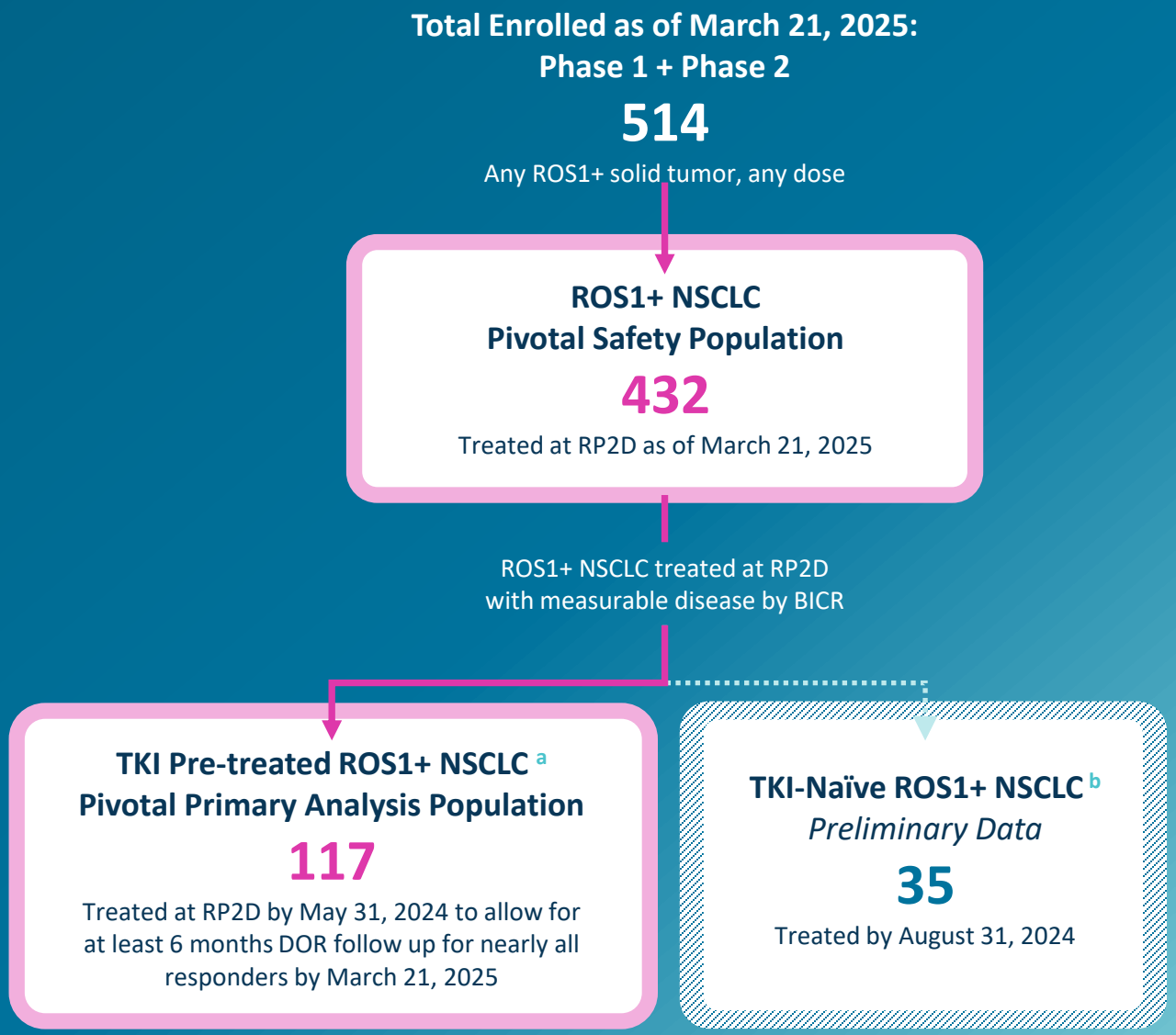


Nuvalent | ARROS-1

ARROS-1

Pivotal Data Populations

- Pivotal ROS1+ NSCLC safety population (n = **432**) and TKI pre-treated efficacy population (n = **117**)
- Preliminary data available from 35 TKI-naïve patients with ROS1+ NSCLC
  - Enrollment continues in ROS1+ solid tumor cohort



BICR, blinded independent central review; DOR, duration of response; NSCLC, non-small cell lung cancer; RP2D, recommended phase 2 dose (100 mg QD); TKI, tyrosine kinase inhibitor.

[a] Includes 4 patients with other oncogenic driver(s) in addition to ROS1.

[b] Includes 1 patient with other oncogenic driver(s) in addition to ROS1.

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Pre-treated ROS1+ NSCLC Population at RP2D

Ability to evaluate activity broadly across TKI pre-treated patients and against key drivers of disease progression:

Patient Characteristic	ROS1 TKI Pre-Treated [a] Pivotal Efficacy Population N = 117
Age, median (range)	57 (31 – 83)
Female	66 (56%)
Never smoker	80 (68%)
Geographic Region	
Asia Pacific	30 (26%)
Europe	38 (32%)
North America	49 (42%)
ECOG PS	
0	45 (38%)
1	72 (62%)
Active CNS disease [b]	**57 (49%)**
Secondary *ROS1* mutation [c]	**42 (36%)**
G2032R	**26 (22%)**

Treatment History	ROS1 TKI Pre-Treated [a] Pivotal Efficacy Population N = 117
Prior anticancer therapy, median (range)	2 (1 – 11)
Prior chemotherapy	62 (53%)
Prior ROS1 TKIs ± chemotherapy	
1 prior (crizotinib or entrectinib)	**55 (47%)**
Crizotinib	*28/55 (51%)*
Entrectinib	*27/55 (49%)*
1 prior (repotrectinib or taletrectinib)	4 (3%)
≥2 prior	**58 (50%)**
Lorlatinib, repotrectinib, or taletrectinib	***54/58 (93%)***
Lorlatinib	*43/58 (74%)*
Repotrectinib	*15/58 (26%)*
Taletrectinib	*5/58 (9%)*

Data cut-off: March 21, 2025. All data shown as n (%) unless otherwise specified. **BICR,** blinded independent central review; **CNS**, central nervous system; **NSCLC**, non-small cell lung cancer; **RP2D**, recommended phase 2 dose (100 mg QD); **TKI**, tyrosine kinase inhibitor.

[a] Includes 4 patients with other oncogenic driver(s) in addition to ROS1.

[b] By BICR; includes patients with untreated CNS lesions and patients with prior disease progression on the brain-penetrant TKIs entrectinib, lorlatinib, repotrectinib, and/or taletrectinib.

[c] ROS1 mutations as per local or central testing of blood (ctDNA) or tissue.

Topline Efficacy: TKI Pre-treated ROS1+ NSCLC

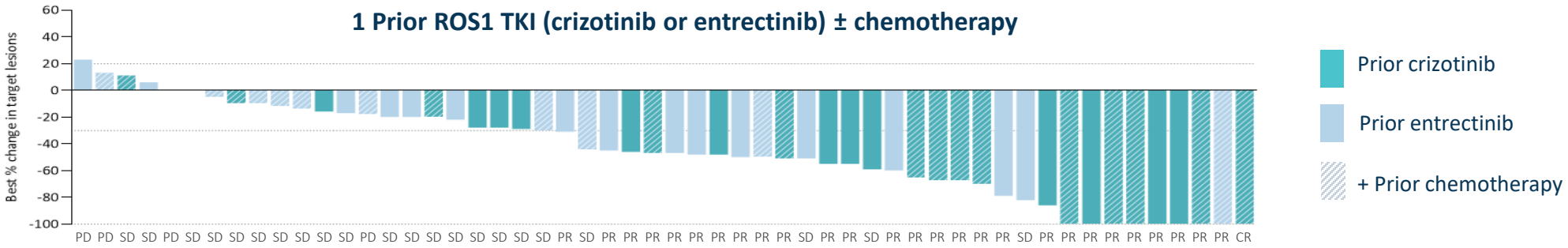
Encouraging overall activity in TKI pre-treated ROS1-positive NSCLC population, and second-line activity following the most commonly used front-line ROS1 TKIs:

Advanced *ROS1*+ NSCLC RECIST 1.1 by BICR	Any prior ROS1 TKI (range 1 – 4) ± chemotherapy	1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy
ORR, % (n/N) [95% CI]	**44%** (51/117) [34, 53]	**51%** (28/55) [a] [37, 65]
CR, % (n/N)	1% (1/117)	2% (1/55)

[a] Prior crizotinib only ± chemotherapy: ORR = 68% (19/28). Prior entrectinib only ± chemotherapy: ORR = 33% (9/27).

Responses were also observed in patients previously treated with:

- **≥2 prior ROS1 TKIs ± chemotherapy**: ORR = 38% (22/58; 95% CI: [26, 52])
- **Prior repotrectinib: ORR = 47% (8/17)**, DOR range 3.5 to 17.2 months
- **Prior taletrectinib: ORR = 43% (3/7)**, DOR range 5.2 to 7.0+ months



*Data pooled for patients treated by May 31, 2024 at RP2D in the Phase 1 or Phase 2 portion of ARROS-1 with a data cut-off of March 21, 2025, allowing for 6 months of follow-up for nearly all responders. Responses were confirmed per RECIST 1.1 as assessed by blinded independent central review (**BICR**).*

CI, confidence interval; **DOR**, duration of response; **m**, median; **NE**, not estimable; **NSCLC**, non-small cell lung cancer; **ORR**, objective response rate; **RP2D**, recommended phase 2 dose (100 mg QD); **TKI**, tyrosine kinase inhibitor.

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Topline Efficacy: TKI Pre-treated ROS1+ NSCLC

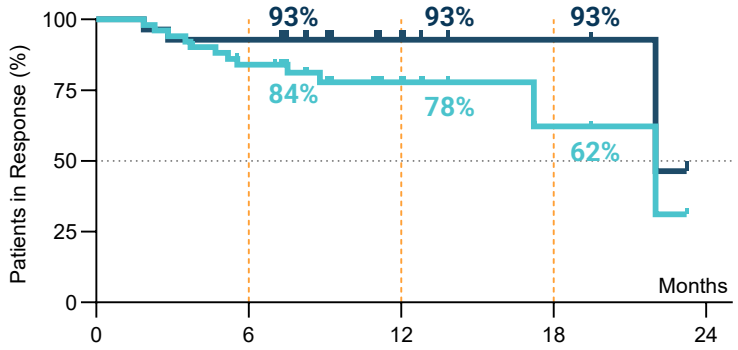
ROS1 ACTIVITY + ROS1 MT ACTIVITY + CNS ACTIVITY + AVOIDING TRK

Advanced *ROS1*+ NSCLC Kaplan-Meier Estimate	Duration of Response		Progression-Free Survival	
	Any prior ROS1 TKIs (range 1-4) ± chemotherapy [a]	1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy [b]	Any prior ROS1 TKIs (range 1-4) ± chemotherapy [a]	1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy [b]
% ≥ 6 months [95% CI]	**84%** [71, 92]	**93%** [74, 98]	**57%** [47, 66]	**70%** [56, 81]
% ≥ 12 months [95% CI]	**78%** [62, 88]	**93%** [74, 98]	**48%** [38, 57]	**68%** [53, 79]
% ≥ 18 months [95% CI]	**62%** [28, 84]	**93%** [74, 98]	**40%** [24, 55]	**68%** [53, 79]

Data cut-off: March 21, 2025

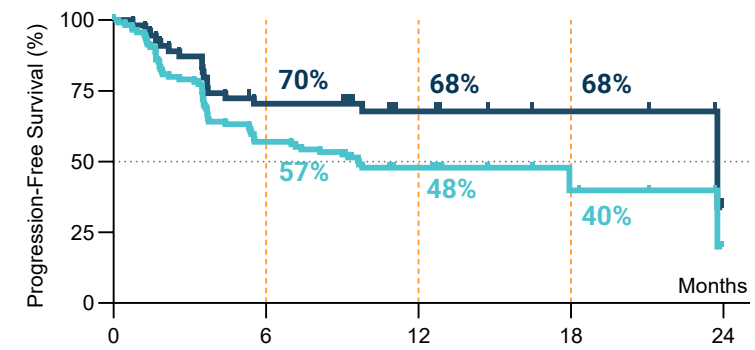
[a] **Any prior ROS1 TKI:** Emerging median DOR of 22 months [95% CI: 17, NE] continues to mature. Median PFS was 9.7 [95% CI: 5.5, NE] months with median follow-up of 11.1 months (range 0.2-25.6).

[b] **1 prior ROS1 TKI (crizotinib [C] or entrectinib [E]):** Emerging median DOR of 22 months [95% CI: 22, NE] and median PFS of 23.8 months [95% CI: 23.8, NE] continue to mature; median follow-up was 11.8 months (range 1.2-25.6).



At Risk

Any prior ROS1 TKIs	51	40	10	3	0
Prior C/E only	28	26	6	3	0



At Risk

Any prior ROS1 TKIs	117	64	27	5	0
Prior C/E only	55	37	14	4	0

- **In patients that received prior crizotinib only, there were no progression events among responders (DOR range: 7.3+ to 23.2+ months). PFS rate was 89% (95% CI: 70, 96) at 6, 12, and 18 months with median not reached.**
- **In patients that received ≥2 prior ROS1 TKIs ± chemotherapy, DOR rate was 71% (95% CI: 46, 86) at 6 months and 56% (95% CI: 29, 76) at 12 months.**

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Demonstrated Ability To Address Key Drivers of Disease Progression

ROS1 ACTIVITY + ROS1 MT ACTIVITY + CNS ACTIVITY + AVOIDING TRK

Zidesamtinib achieved responses in the presence of the ROS1 G2032R resistance mutation

	Any prior ROS1 TKI ± chemotherapy	Prior crizotinib or entrectinib only* ± chemotherapy
ORR, % (n/N)	**54%** (14/26)	**83%** (5/6)
% DOR ≥ 6 months [a] (95% CI)	**79%** (47, 93)	**80% **** (20, 97)
% DOR ≥ 12 months [a] (95% CI)	**60%** (28, 81)	**80% **** (20, 97)

* Patients received zidesamtinib as their first TKI designed with activity against ROS1 G2032R

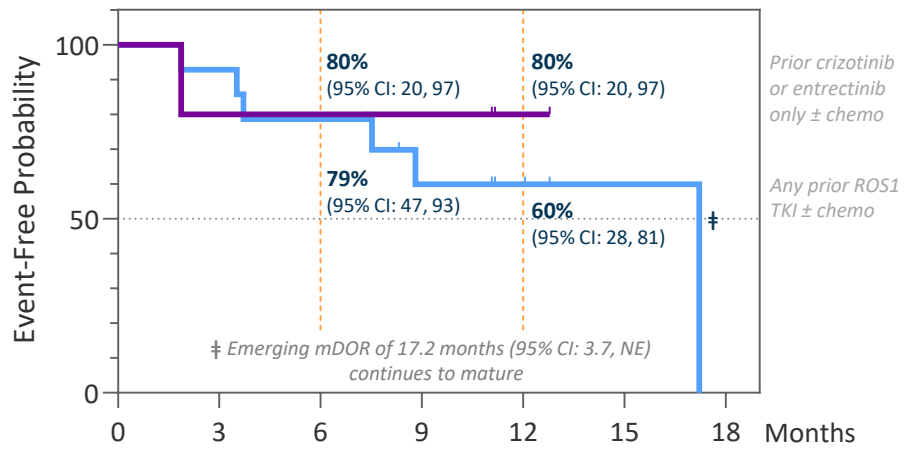
** One progression event among responders

Responses were also observed in patients with:

- **ROS1 G2032R mutation following ≥2 prior ROS1 TKIs ± chemotherapy, including lorlatinib or repotrectinib**
- **Other ROS1 resistance mutations, including G1957A, L1982V, S1986F, F2004C/V, G2032K, and D2033N**

Kaplan-Meier Plot of DOR

ROS1 G2032R



At Risk

Any prior TKI:	14	13	11	6	3	1	0
1 prior TKI (C/E):	5	4	4	4	1	0	

Data pooled for patients treated by May 31, 2024 at RP2D in the Phase 1 or Phase 2 portion of ARROS-1 with a data cut-off of March 21, 2025, allowing for 6 months of follow-up for nearly all responders. Responses were confirmed per RECIST 1.1 as assessed by blinded independent central review (BICR).

C, crizotinib; **CI**, confidence interval; **DOR**, duration of response; **E**, entrectinib; **NE**, not estimable; **ORR**, objective response rate; **RP2D**, recommended phase 2 dose (100 mg QD); **TKI**, tyrosine kinase inhibitor.

[a] Analyses of DOR based on Kaplan-Meier estimates.

Nuvalent

Demonstrated Ability To Address Key Drivers of Disease Progression

ROS1 ACTIVITY + ROS1 MT ACTIVITY + **CNS ACTIVITY** + AVOIDING TRK

Zidesamtinib demonstrated CNS activity

	Any prior ROS1 TKI ± chemotherapy	Prior crizotinib only* ± chemotherapy
IC-ORR, % (n/N)	**48%** (27/56) [a]	**85%** (11/13)
CR, % (n/N)	**20%** (11/56)	**54%** (7/13)
% IC-DOR ≥ 6 months [b] (95% CI)	**79%** (56, 91)	**91%** ** (51, 99)
% IC-DOR ≥ 12 months [b] (95% CI)	**71%** (46, 87)	**91%** ** (51, 99)

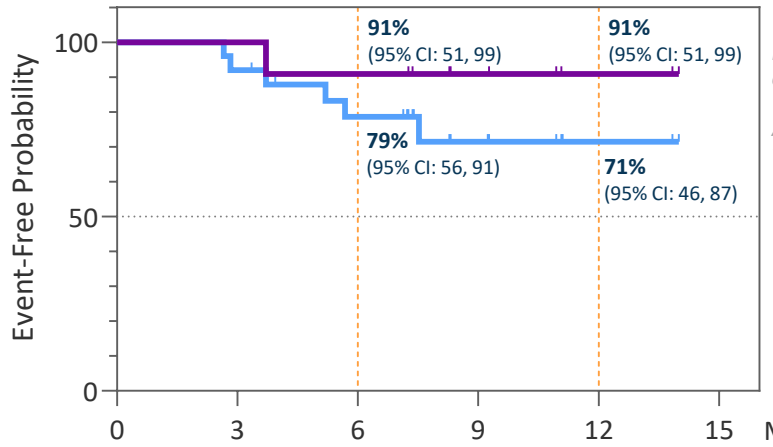
* Limited brain penetrance

** One CNS progression event among CNS responders

- **CNS responses also observed in patients who had received ≥1 prior brain-penetrant TKI, including prior entrectinib, lorlatinib, repotrectinib, or taletrectinib: IC-ORR: 37% (16/43 [a]; [95% CI 23, 53]), including 4 IC-CRs**
- **No CNS progression was observed among patients who entered the study without brain metastases at baseline per BICR**

Kaplan-Meier Plot of IC-DOR

Measurable CNS Lesions at Baseline



# At Risk						
Any prior TKI:	25	23	17	7	2	0
Prior crizotinib:	11	11	10	5	2	0

*Data pooled for patients treated by May 31, 2024 at RP2D in the Phase 1 or Phase 2 portion of ARROS-1 with a data cut-off of March 21, 2025, allowing for 6 months of follow-up for nearly all responders. Responses were confirmed per RECIST 1.1 as assessed by blinded independent central review (**BICR**).*

CI, confidence interval; **CNS**, central nervous system; **CR**, complete response; **DOR**, duration of response; **IC**, intracranial; **ORR**, objective response rate; **RP2D**, recommended phase 2 dose (100 mg QD); **TKI**, tyrosine kinase inhibitor.

[a] Includes 2 unconfirmed intracranial partial responses (**PR**). [b] Analyses of DOR based on Kaplan-Meier estimates.

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Topline Safety Profile

Safety profile of zidesamtinib was generally safe, well tolerated and consistent with its ROS1-selective, TRK-sparing design

- Dose reduction due to TEAE: **10%** (43/432)
  - Most common (>2 patients): peripheral edema (n=8), blood CPK increased (n=4), peripheral sensory neuropathy (n=4), arthralgia (n=3), paresthesia (n=3)
- Discontinuation due to TEAE: **2%** (10/432)
  - Most common (>2 patients): pneumonia (n=3)
- The only treatment-related adverse event in ≥15% of patients was peripheral edema [b] (29%)

Treatment-Emergent Adverse Events (TEAEs) in ≥ 15% of Patients ROS1-positive NSCLC Treated at RP2D (N = 432)

Preferred or Grouped Term	Any Grade	Grade ≥3
Peripheral edema [a]	36%	0.7%
Constipation	17%	0
Blood CPK increased	16%	3.5%
Fatigue [b]	16%	0.7%
Dyspnea [c]	15%	3.0%

[a] Includes terms oedema peripheral, peripheral swelling, oedema, generalized oedema
[b] Includes terms fatigue, asthenia, malaise
[c] Includes terms dyspnea, dyspnoea extertional, orthopnoea

Data pooled for patients in the Phase 1 or Phase 2 portion of ARROS-1 with a data cut-off of March 21, 2025. Patients received at least 1 dose of zidesamtinib at RP2D with median duration of exposure of 5 months (range: 0, 32)
NSCLC, non-small cell lung cancer; **RP2D**, recommended phase 2 dose (100 mg QD); **TEAE**, treatment emergent adverse event; **TRK**, proteins encoded for by the neurotrophic tyrosine receptor kinase (NTRK) family of genes.

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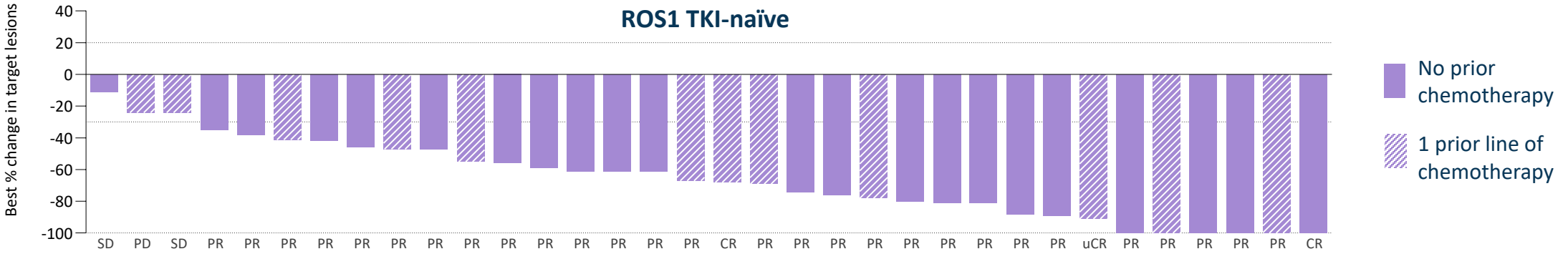
Encouraging Preliminary Data for TKI-naïve Population

TKI-naïve advanced *ROS1*+ NSCLC Analysis by BICR	Response-evaluable n = 35
ORR, % (n/N)	**89%** (31/35)
CR, % (n/N)	**9%** (3/35) [a]
% DOR ≥ 6 months [95% CI] [b]	**96%** [76, 99]
% DOR ≥ 12 months [95% CI] [b]	**96%** [76, 99]
DOR range	1.9+ to 13.9+ months

[a] Includes 1 unconfirmed CR following confirmed partial response (PR).

[b] Analyses of DOR based on Kaplan-Meier estimates.

TKI-naïve advanced *ROS1*+ NSCLC Analysis by BICR	Measurable intracranial lesions n = 6
IC-ORR, % (n/N)	**83%** (5/6)
IC-CR, % (n/N)	**67%** (4/6)
IC-DOR	**No CNS progression events among intracranial responders**
IC-DOR range	4.6+ to 11.1+ months



*Data for patients treated by August 31, 2024 at RP2D in the Phase 2 portion of ARROS-1 with a data cut-off of March 21, 2025. Responses were confirmed per RECIST 1.1 as assessed by blinded independent central review (**BICR**).*

CR, complete response; **DOR**, duration of response; **IC**, intracranial; **NSCLC**, non-small cell lung cancer; **ORR**, objective response rate; **RP2D**, recommended phase 2 dose (100 mg QD); **TKI**, tyrosine kinase inhibitor.

[a] Includes 1 unconfirmed CR following confirmed partial response (**PR**). [b] Analyses of DOR based on Kaplan-Meier estimates.

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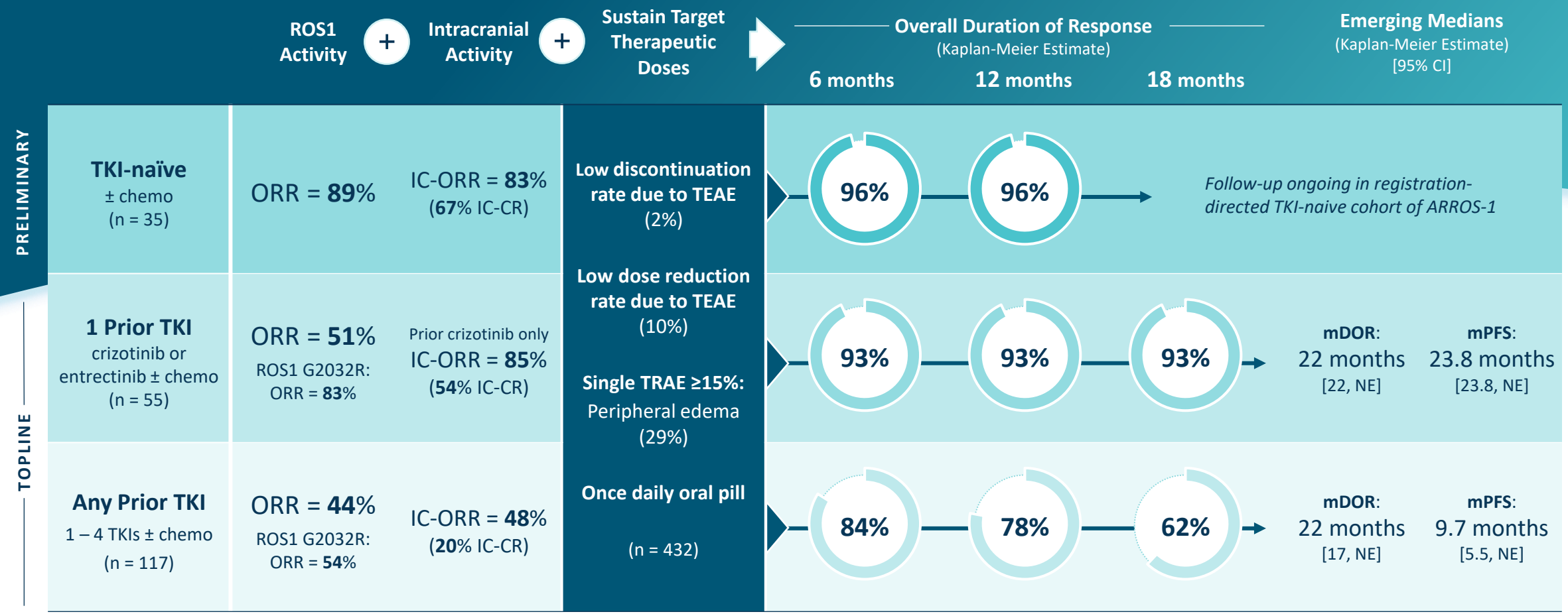
Zidesamtinib: Designed for *all* patients with ROS1+ NSCLC



Source: Data at recommended Phase 2 dose of 100 mg QD reported in Drilon et al., WCLC 2025 (Data cut-off: March 21, 2025).

Nuvalent

ZIDESAMTINIB (NVL-520)

ARROS-1 Subset Analysis: Prior Repotrectinib and/or Taletrectinib

- Significant patient enrollment in ARROS-1 generated a robust data set that enables characterization of zidesamtinib's activity in ROS1-positive NSCLC beyond initial pivotal data
- Post-hoc analysis conducted of patients receiving prior repotrectinib (n = 46) or prior taletrectinib (n = 19)
- Clinically meaningful activity observed, including in those with CNS disease or ROS1 resistance mutations
- Safety profile remains consistent with previously reported results, including low rates of dose reductions and treatment discontinuations, and the avoidance of TRK-related neurologic adverse events

Treatment history	Prior repotrectinib (n = 46) [a]	Prior taletrectinib (n = 19) [a]
Prior anticancer therapy, median (range)	3 (1 – 7)	3 (1 – 6)
Prior chemotherapy	29 (63%)	10 (53%)
Prior ROS1 TKI, median (range)	2 (1 – 4)	2 (1 – 4)
Prior ROS1 TKI ± chemotherapy		
1 prior ROS1 TKI	7 (15%)	2 (11%)
≥2 prior ROS1 TKIs	39 (85%)	17 (89%)
with lorlatinib	15 (33%)	4 (21%)
Reason for prior repotrectinib or taletrectinib discontinuation		
Disease progression	36 (78%)	17 (89%)
Intolerability	5 (11%)	1 (5%)
Other	5 (11%)	1 (5%)

Patients received at least 1 dose of zidesamtinib at RP2D as of a data cut-off date of September 22, 2025. All data shown as n (%) unless otherwise specified.

BICR, blinded independent central review; **CNS**, central nervous system; **NSCLC**, non-small cell lung cancer; **RP2D**, recommended phase 2 dose (100 mg QD); **TKI**, tyrosine kinase inhibitor.

[a] 3 patients received both prior repotrectinib and prior taletrectinib.

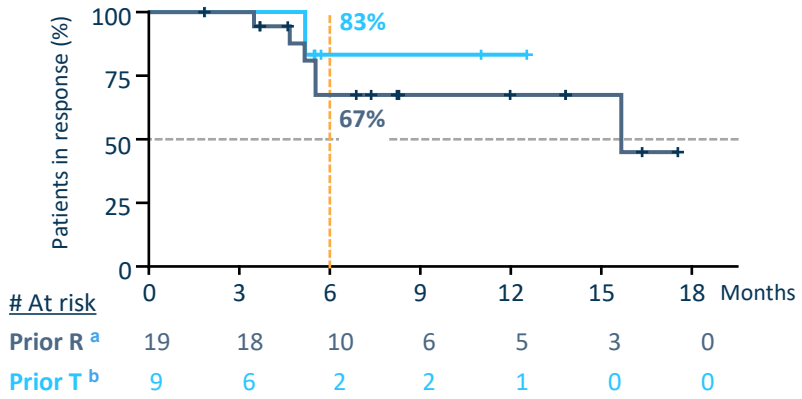
Source: Liu, G. et al., AACR 2026.

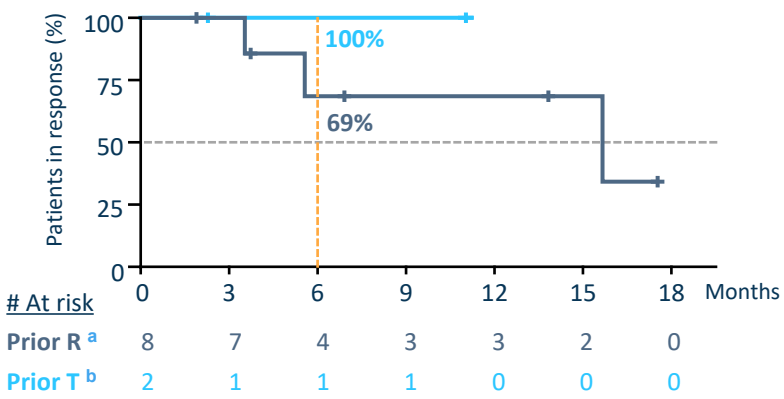
Nuvalent

ZIDESAMTINIB (NVL-520)

Efficacy in Patients with Prior Repotrectinib and/or Taletrectinib

Advanced *ROS1*+ NSCLC Analysis by BICR	Overall		ROS1 G2032R resistance mutation	
	Prior repotrectinib [a]	Prior taletrectinib [b]	Prior repotrectinib [a]	Prior taletrectinib [b]
ORR, % (n/N) [95% CI]	**41%** (19/46) [27, 57]	**47%** (9/19) [24, 71]	**67%** (8/12) [35, 90]	**50%** (2/4) [c] [7, 93]
CR, % (n/N)	**7%** (3/46) [d]	**5%** (1/19)	**8%** (1/12)	**0%**
Median DOR, months [e] [95% CI]	**15.7** [5.6, NE]	**Not reached** [5.2, NE]	**15.7** [3.5, NE]	**Not reached** [NE, NE]
DOR ≥6 months, % [e] [95% CI]	**67%** [38, 85]	**83%** [27, 97]	**69%** [21, 91]	**100%** [100, 100]





Data cut-off: September 22, 2025

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

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

[c] Responses also observed in patients with *ROS1* D2033N (n = 1) and L2086F (n = 1).

[d] Includes one single-timepoint CR pending confirmation in an ongoing patient who previously experienced confirmed PR.

[e] Kaplan-Meier estimate.

Source: Liu G. et al., AACR 2026.

Activity indicates tumors may remain ROS1-dependent beyond treatment with repotrectinib or taletrectinib

Nuvalent

ZIDESAMTINIB (NVL-520)

Intracranial Activity in Patients with Prior Repotrectinib and/or Taletrectinib

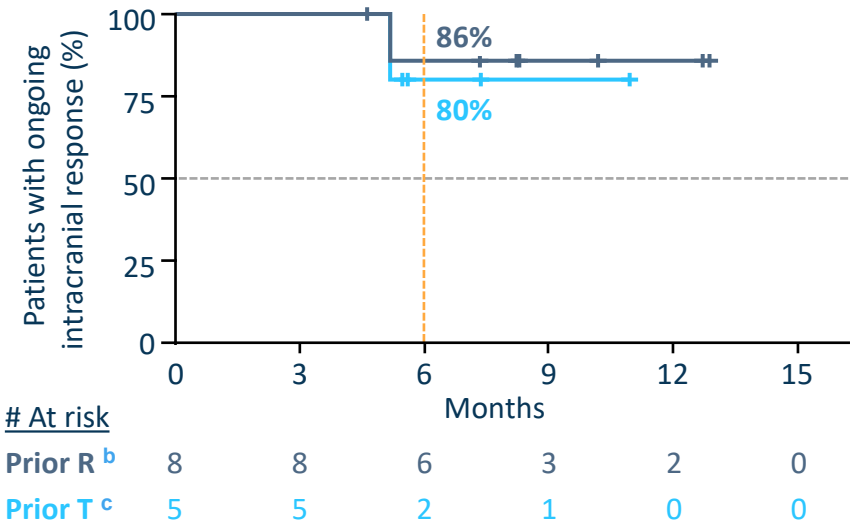
Zidesamtinib demonstrated CNS activity beyond CNS-active repotrectinib and taletrectinib

Advanced *ROS1*+ NSCLC Analysis by BICR	**Prior repotrectinib** [b]	**Prior taletrectinib** [c]
IC-ORR, % (n/N) (95% CI)	**44%** (8/18) [22, 69]	**71%** (5/7) [29, 96]
CR, % (n/N)	**11%** (2/18)	**43%** (3/7)
Median IC-DOR, months [d] (95% CI)	**Not reached** [5.2, NE]	**Not reached** [5.2, NE]
% IC-DOR ≥ 6 months [d] (95% CI)	**86%** [33, 98]	**80%** [20, 97]

- Among patients without brain metastases at baseline, no CNS progression was observed before RECIST PD in any patient that received prior repotrectinib and/or taletrectinib

Kaplan-Meier Plot of IC-DOR

Measurable CNS Lesions at Baseline



Data cut-off date: September 22, 2025. Responses were confirmed per RECIST 1.1 as assessed by blinded independent central review (BICR).

CI, confidence interval; **CNS**, central nervous system; **CR**, complete response; **DOR**, duration of response; **IC**, intracranial; **ORR**, objective response rate; **RP2D**, recommended phase 2 dose (100 mg QD); **TKI**, tyrosine kinase inhibitor.

[a] Includes patients with measurable (≥5 mm) CNS lesions by BICR at baseline. [b] Prior repotrectinib (R) ± other ROS1 TKIs and/or chemotherapy. [c] Prior taletrectinib (T) ± other ROS1 TKIs and/or chemotherapy. [d] Kaplan-Meier estimate.

Source: Liu G. et al., AACR 2026.

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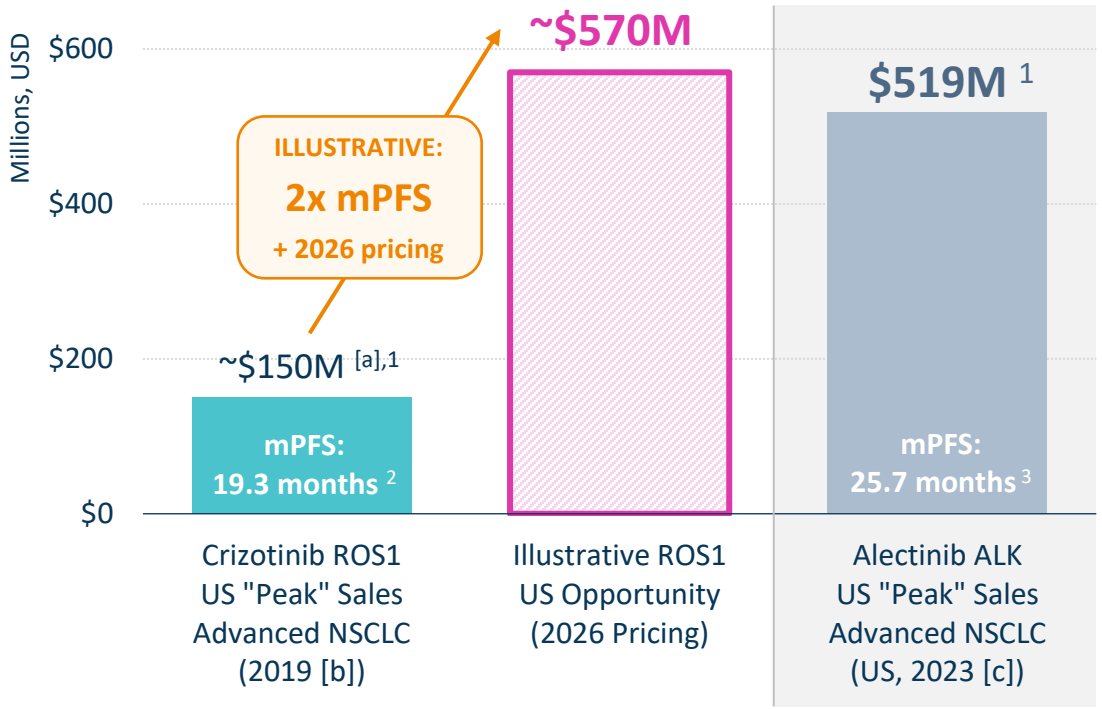
Reimagine what is possible with a ROS1 TKI

The ROS1+ NSCLC market has the potential to match or exceed today's opportunity in advanced/metastatic ALK+ NSCLC

Illustrative ROS1+ NSCLC "Peak" Sales Opportunity (US)



US "Peak" Sales Benchmark for ROS1+ NSCLC	~$150M (Crizotinib, 2019) [a,b]
	x
Potential Durability Increase (i.e., "Time on therapy")	**~2 - 3x mPFS** [c] Crizotinib 1L mPFS: 19.3 months [2] Zidesamtinib 1L mPFS: *Not reached* Zidesamtinib 2L mPFS: 23.8 months [4]
	x
Illustrative 2026 Price/Month	**~1.9x** ~$17,000 (Crizotinib, 2019) [5] → ~$32,000 (Repotrectinib, 2026) [5]
Illustrative Potential US "Peak" Sales Opportunity	**~$570M - 855M**
Illustrative Potential WW "Peak" Sales Opportunity	**~$1.4B - 2.1B** Illustrative if US = 40% of global [e]

Illustrative projections are based on management assumptions as of January 2026 and are subject to change. **m**, median; **NSCLC**, non-small cell lung cancer; **PFS**, progression-free survival.

[a] Sales not reported by ALK vs. ROS1 indication; Assumes the large majority of crizotinib sales are for ROS1 following alectinib 1L ALK approval in 2017. [b] "Peak" estimated in 2019 due to share erosion following FDA approval of 2nd ROS1 TKI (entrectinib) in August 2019. [c] "Peak" for adv/met indication estimated in 2023 due to FDA approval for adjuvant ALK+ NSCLC indication in April 2024. [d] Single-arm studies, which lack a comparator arm, may be inadequate to sufficiently evaluate time-to-event endpoints, such as mPFS. The clinical significance of these mPFS data is not known and the observed effect may be attributable to the drug or to other factors. [e] 2023 - 2024 reference: alectinib US = 30 - 34% of global net revenue, lorlatinib US = 42% of global net revenue.

Sources: [1] Year-end earnings reports for Pfizer (2019) and Roche (2023); [2] Shaw A. et al., Ann Oncol. 2019. [3] ALECENSA FDA prescribing information, revised 04/2024. [4] Drilon et al., WCLC 2025. [5] NAVLIN, accessed January 2026.

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NUVALENT VISION

ALK+ NSCLC

Realize the full potential

Nuvalent

Kirk S, patient living with advanced ALK+ NSCLC
President of the Board, ALKPositive

ALK+ NSCLC Treatment Paradigm

~3 – 5% of NSCLC [1] | Majority are advanced/metastatic at diagnosis [2]

	STANDARD OF CARE	KEY LIMITATIONS
1L	**Alectinib** ($1.9B WW sales, 2025) [3]	**Single ALK resistance mutations** *Observed in ~50% of patients progressing on 2G TKIs (i.e., alectinib, brigatinib, ceritinib)* [7, 8] **Brain penetrance** • *30 – 40% present with brain metastases at diagnosis* [9, 10, 11] • *~50% will develop brain metastases overall* [11]
2L	**Lorlatinib** ($1.0B WW sales, 2025) [4] 3G TKI, designed to address single ALK mutations and improve brain penetrance [5]	**Single & Compound ALK resistance mutations** *ALK mutations observed in ~75% of patients progressing on sequential 2G to 3G TKIs, including ~25 – 50% with compound mutations* [7, 12] **Treatment-limiting off-target adverse events** *CNS adverse events associated with TRK inhibition observed in >50% of patients receiving lorlatinib* [13, 14, 15]
3L+	**No clear standard of care** Patients may consider clinical trials or chemotherapy/I-O [6]	**Activity** *No approved therapies have demonstrated activity after sequential 2G to 3G TKIs* [16]

POTENTIAL OPPORTUNITY *for* PATIENT IMPACT

- **Demonstrate superiority to alectinib in 1L head-to-head study, while also avoiding CNS adverse events**
  - Alectinib ORR: **79%** [17]
  - Alectinib mPFS: **25.7** months [17]
- **Improve durability of response after ≥ 1 2G ALK TKI:**
  - Lorlatinib ORR: **31 – 40%** [13, 18, 19]
  - Lorlatinib mDOR: **7.1 – 9.6 months** [18, 19]
- **Demonstrate activity after 2+ prior ALK TKIs, including in patients who are lorlatinib experienced**

1G, 1st generation; **1L**, 1st line; **2G**, 2nd generation; **3G**, 3rd generation; **CNS**, central nervous system; **DOR**, duration of response; **m**, median; **ORR**, objective response rate; **PFS**, progression-free survival; **TKI**, tyrosine kinase inhibitor.

Sources: [1] Gainor J.F. and Shaw A.T., Oncologist. 2013. [2] Chia P.L. et al., Clin Epidemiol. 2014. [3] Roche 2025 Year-end Earnings Report. [4] Pfizer 2025 Year-end Earnings Report. [5] Johnson T.W. et al., J. Med. Chem. 2014. [6] NCCN Guidelines for NSCLC (version 8.2025). [7] Dagogo-Jack I. et al., Clin Cancer Res 2019.* [8] Gainor J. et al. Cancer Discov. 2016.* [9] Gainor J et al. JCO Precis Oncol. 2017. [10] Solomon BJ et al., NEJM 2014. [11] Uprety D et al., Lung Cancer 2025. [12] Shiba-Ishii et al., Nature Cancer 2022. [13] Lorlatinib FDA USPI. [14] Cocco E et al., Nat Rev Clin Oncol. 2018. [15] Shaw A. et al., Lancet Onc 2017. [16] Ensartinib FDA USPI. [17] Alectinib FDA USPI. [18] Shaw et al., JCO 2019; [19] Felip et al., Ann of Oncol. 2021. [*] Most patients also received prior crizotinib.

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NUVALENT VISION

Realize the full potential of an ALK TKI

Patient Outcomes

BACKGROUND: Next generation ALK TKIs that address key drivers of disease progression, including **brain penetrance** and **resistance mutations,** are transforming expectations for durability

Alectinib *for* ALK+ NSCLC	Lorlatinib *for* ALK+ NSCLC
1L mPFS = **25.7** months [1]	1L mPFS = **Not reached** at 60 months [3]
2nd Generation TKI & Global Market Leader [2]	3rd Generation TKI & 1L Alternative

INSIGHT: While long-term benefit is possible with lorlatinib, improvements are needed:

Of patients receiving lorlatinib for 1L ALK+ NSCLC, **38% are no longer on therapy by 24 months** [3]

Market Opportunity

BACKGROUND: Reported sales reflect the continued global market leadership of alectinib

Alectinib WW sales (2025): **$1.9B** [5]

Lorlatinib WW sales (2025): **$1.0B** [6]

WW sales of other ALK+ TKIs (2025): est. < $300M [7]

INSIGHT: For this patient population that is often diagnosed at a younger age, new options are needed to avoid the **risk of CNS adverse events** observed with the dual TRK/ALK inhibitor lorlatinib, and offer both durability **and** tolerability [4,8]

NUVALENT VISION

Address the liabilities of lorlatinib

Deliver transformative durability **and** tolerability, across lines of therapy, with an ALK-selective TKI

&

Realize the full potential within ALK+ NSCLC

Grow a prevalent population of patients living with ALK+ NSCLC as a “chronic”, long-term condition

Sources: [1] ALECENSA FDA prescribing information, revised 04/2024. [2] Cortellis, product sales accessed 01/2026. [3] Solomon B.J. et al., J Clin Oncol. 2024. [4] LORBRENA FDA prescribing information, revised 02/2024. [5] Roche 2025 Year-end Earnings Report. [6] Pfizer 2025 Year-end Earnings Report. [7] Estimated from Takeda 2025 Year-end Earnings Reports for brigatinib; 2025 sales not reported for crizotinib, ceritinib, ensartinib. [8] Jimenez Munarriz B.E. et al., Cancer 2025.

Nuvalent

NVL-655

Neladalkib

A Rationally Designed **ALK**-selective, TRK-sparing Inhibitor

Potential Best-in-Class Target Product Profile designed in collaboration with physician-scientists to address the limitations of existing agents for ALK+ NSCLC

DESIGN GOAL *for* NELADALKIB

ALK Activity

- Primary oncogenic driver in ~3 – 5% of NSCLC [1]

+

ALK Single Mutant Activity

- ~50% single resistance mutations, such as G1202R, after treatment with a 2G ALK TKI, and ~75% after sequential 2G and 3G ALK TKIs [2, 3]

+

ALK Compound Mutant Activity

- ~25 – 50% compound mutations after sequential treatment with 2G and 3G ALK TKIs [2, 4]

+

CNS Activity

- ~30 – 40% CNS disease at diagnosis [5, 6, 7]
- ~50% develop CNS disease overall [7]

+

Avoiding TRK

- Treatment-limiting neurological adverse events observed with brain-penetrant, dual TRK/ALK inhibitors [8, 9]

Neladalkib is an investigational candidate and has not been approved by FDA or any other regulatory authority.

1L, 1st line; **2G**, 2nd generation (alectinib, brigatinib, ceritinib); **3G**, 3rd generation (lorlatinib); **CNS**, central nervous system; **NSCLC**, non-small cell lung cancer; **TKI**, tyrosine kinase inhibitor.

Source: [1] Gainor J.F. and Shaw A.T., Oncologist. 2013. [2] Dagogo-Jack I. et al., Clin Cancer Res 2019.* [3] Gainor J. et al. Cancer Discov. 2016.* [4] Shiba-Ishii et al., Nature Cancer 2022. [5] Solomon BJ et al., NEJM 2014. [6] Shaw A. et al., Lancet Onc 2017. [7] Uprety D et al., Lung Cancer 2025. [8] Shaw A. et al., Lancet Onc 2017. [9] LORBRENA FDA prescribing information, revised 4/2023. [*] Most patients also received prior crizotinib.

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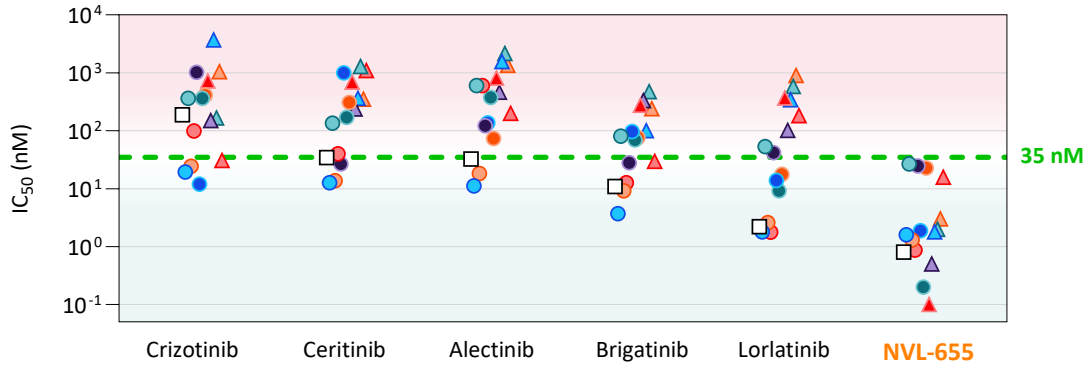
Preclinical Characterization Demonstrates Desired Target Product Profile

Inhibited Diverse ALK Fusions and Resistance Mutations

In Vitro Activity

Potent activity (IC_{50} = 0.1 – 30 nM) against ALK-driven cell lines, including ALK single and compound mutants [1-6]



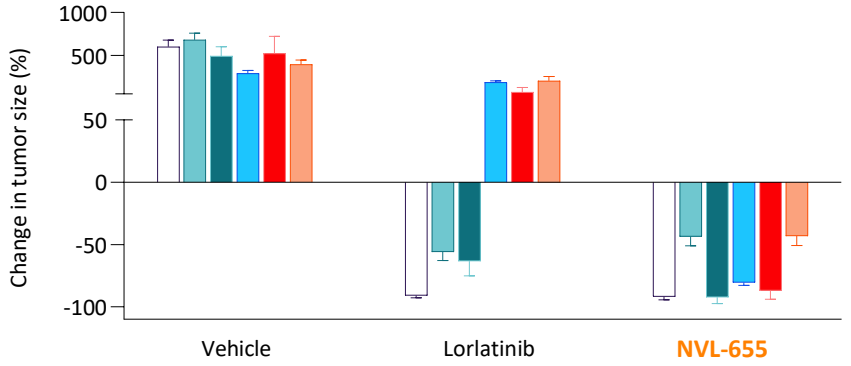
Cell lines harboring EML4-ALK fusion
3-day cell viability assay

Compound mutant
- G1202R/T1151M | MR448re (v3)
- G1202R/F1174L | Ba/F3 (v3)
- G1202R/L1196M | MGH953-7 (v3)
- G1202R/L1198F | Ba/F3 (v1)
- G1202R/G1269A | Ba/F3 (v1)
- I1171N/L1198F | Ba/F3 (v1)

Single mutant
- No resistance mutations | MGH048-1 (v1)
- T1151M | Ba/F3 (v3)
- I1171N | Ba/F3 (v1)
- F1174L | Ba/F3 (v3)
- V1180L | Ba/F3 (v1)
- L1196M | MGH045-1 (v1)
- L1198F | Ba/F3 (v1)
- G1202R | YU-1077 (v3)
- D1203N | Ba/F3 (v1)

In Vivo Activity

Tumor regression at well-tolerated doses in ALK models, including ALK single and compound mutants [1-6]



Xenograft models harboring ALK fusion

Single mutant
- No resistance mutations | Lu-01-0015 (HIP1-ALK)
- I1171N | Ba/F3 (EML4-ALK v1)
- G1202R | MR619 (STRN-ALK)

Compound mutant
- G1202R/L1196M | MGH953-7 (EML4-ALK v3)
- G1202R/T1151M | MR448re (EML4-ALK v3)
- G1202R/G1269A | Ba/F3 (EML4-ALK v1)

NVL-655: 0.5 - 7.5 mg/kg, PO, BID; Lorlatinib: 5 mg/kg, PO, BID or 10 mg/kg, PO, QD
In some cases, dosing was not performed on weekends

BID, twice daily; **IC_{50}**, half-maximal inhibitory concentration; **PO**, orally; **QD**, once daily; **v**, EML4 breakpoint variant.
Sources: Lin J.J. et al., AACR-NCI-EORTC 2023. [1]Lee, J. *et al.* AACR 2023; [2]Fujino, T. *et al.* EORTC-NCI-AACR 2022; [3]Mizuta, H. *et al.* WCLC-IASLC 2022; [4]Tangpeerachaikul, A. *et al.* AACR 2022; [5]Tangpeerachaikul, A. *et al.* AACR-NCI-EORTC 2021; [6]Pelish, H. *et al.* AACR 2021. Data also reflect additional repeat testing and models.

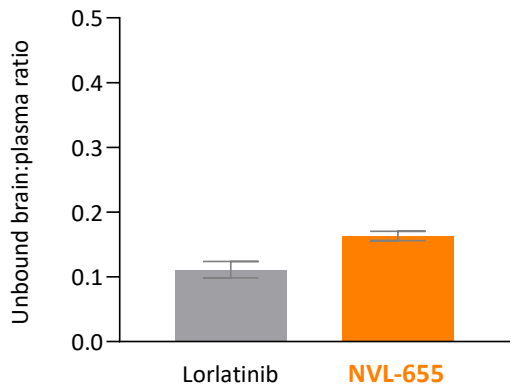
Nuvalent

Preclinical Characterization Demonstrates Desired Target Product Profile

Brain-Penetrant with the Potential to Avoid TRK-Related CNS Adverse Events

Brain Penetrance

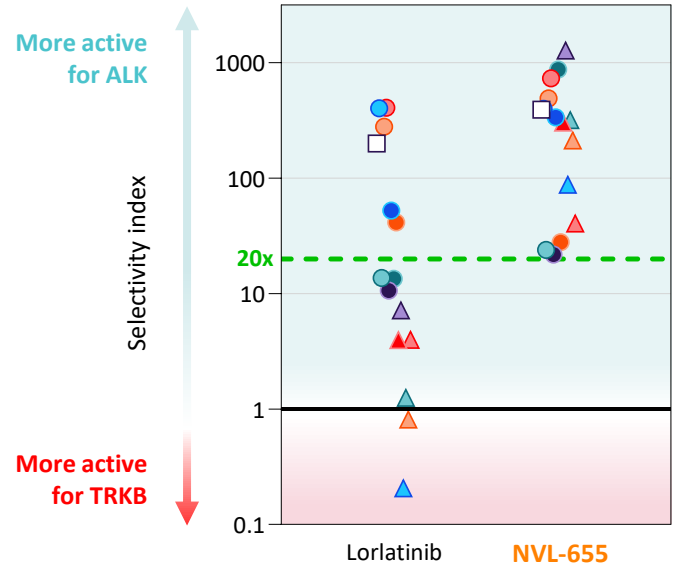
Pharmacokinetic data similar to preclinical observations for lorlatinib



Wistar Han rats
10 mg/kg, single dose PO
1 hour timepoint

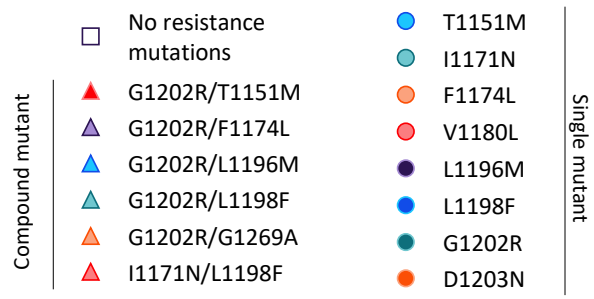
Avoiding TRK Inhibition

Selective inhibition of ALK and ALK mutants over TRK



$$\text{Selectivity index} = \frac{IC_{50}\ (\text{pTRKB})}{IC_{50}\ (\text{Ba/F3 EML4-ALK})}$$

Selectivity for ALK over TRKB



Head-to-head clinical studies comparing neladalkib (NVL-655) with currently approved or investigational therapies have not been conducted. Above data from preclinical studies and no clinical conclusions can be drawn.
CNS, central nervous system; **IC50**, half-maximal inhibitory concentration; **PO**, orally; pTRKB, BDNF-stimulated TRKB phosphorylation.
Source: Lin J.J. et al., AACR-NCI-EORTC 2023. Mizuta, H. et al. WCLC-IASLC 2022; Tangpeerachaikul, A. et al. AACR-NCI-EORTC 2021; Pelish, H. et al. AACR 2021. Data presented here reflect updated values following additional repeat testing.

Nuvalent

ALK+ NSCLC | Global Development Strategy

Parallel development paths ongoing to establish neladalkib as a best-in-class drug for all patients with ALK+ NSCLC

ALKOVE-1

Phase 2: TKI Pre-treated Cohorts
*Global enrollment complete**

Topline data supports opportunity for broad TKI pre-treated label:

- 2L+ TKI pre-treated ALK+ NSCLC receiving neladalkib at RP2D (N = 235)

NDA accepted for filing by FDA with Priority Review with PDUFA target action date of November 27, 2026

ALKAZAR

Randomized Phase 3: TKI-naïve
Global enrollment ongoing

Randomized, controlled study designed to assess superiority to current 1L standard of care:

- 1L No prior ALK TKI (N ~450), with 1:1 randomization of neladalkib (NVL-655) vs. alectinib
  - Plan for ~160 sites across North America, Europe, Asia, and Latin America

Designed for line-agnostic label expansion

ALKOVE-1

Enrollment ongoing for adult and pediatric patients with other ALK+ solid tumors

** Continued enrollment available for adolescent patients with ALK+ NSCLC.*

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ALKove-1

A Global First-in-Human Phase 1/2 Clinical Trial of Neladalkib in Advanced **ALK-Positive** NSCLC and Other Solid Tumors (NCT05384626)

PHASE 1 INITIATED JUNE 2022

First-in-human dose-escalation in heavily pre-treated ALK+ NSCLC & other solid tumors

Preliminary data demonstrated clinical proof-of-concept for neladalkib's target product profile:

OCTOBER 2023

Preliminary Phase 1 Data: Clinical proof-of concept in heavily pre-treated population

Lin et al., AACR-NCI-EORTC 2023

OCTOBER 2024

Updated Phase 1 Data: Durable responses in heavily pre-treated population

Drilon et al., ESMO 2024

PHASE 2 INITIATED FEBRUARY 2024 (RP2D: 150 mg QD)

Global open-label, multi-cohort design with registrational intent for TKI pre-treated ALK+ NSCLC, and exploratory cohort for TKI-naïve ALK+ NSCLC

ALKOVE-1 PHASE 2	PRIOR ALK TKI	PRIOR CHEMO/I-O	ALKOVE-1 PHASE 2 OBJECTIVES
ALK+ NSCLC	**2-3 prior, any generation** *(crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib [a])*	0-2 lines	• **Primary:** ORR by blinded, independent central review (BICR) • **Secondary:** Additional efficacy measures (DOR, TTR, CBR, PFS, OS), intracranial activity, overall safety and tolerability, confirmation of PK profile
	1 prior 2G *(ceritinib, alectinib, or brigatinib)*	0-2 lines	
	1 prior 3G *(lorlatinib)*	≤ 1	
	None (TKI-naïve)	≤ 1	
	Any *(not eligible for other cohorts)*	Any	
Other ALK+ Solid Tumors	**≥ 1 prior ALK TKI or systemic therapy** (or for whom no satisfactory standard therapy exists)	Any	

JUNE 2026

Pivotal TKI pre-treated (pooled Phase 1/2) & preliminary TKI-naïve data for ALK+ NSCLC

Lin et al., ASCO 2026

CBR, clinical benefit rate; **DOR**, duration of response; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression free survival; **PK**, pharmacokinetics; **PRO**, patient reported outcomes; **QD**, once daily; **RP2D**, recommended phase 2 dose; **TKI**, tyrosine kinase inhibitor; **TTR**, time to response.

[a] Excludes patients who received lorlatinib as the 1st prior ALK TKI.

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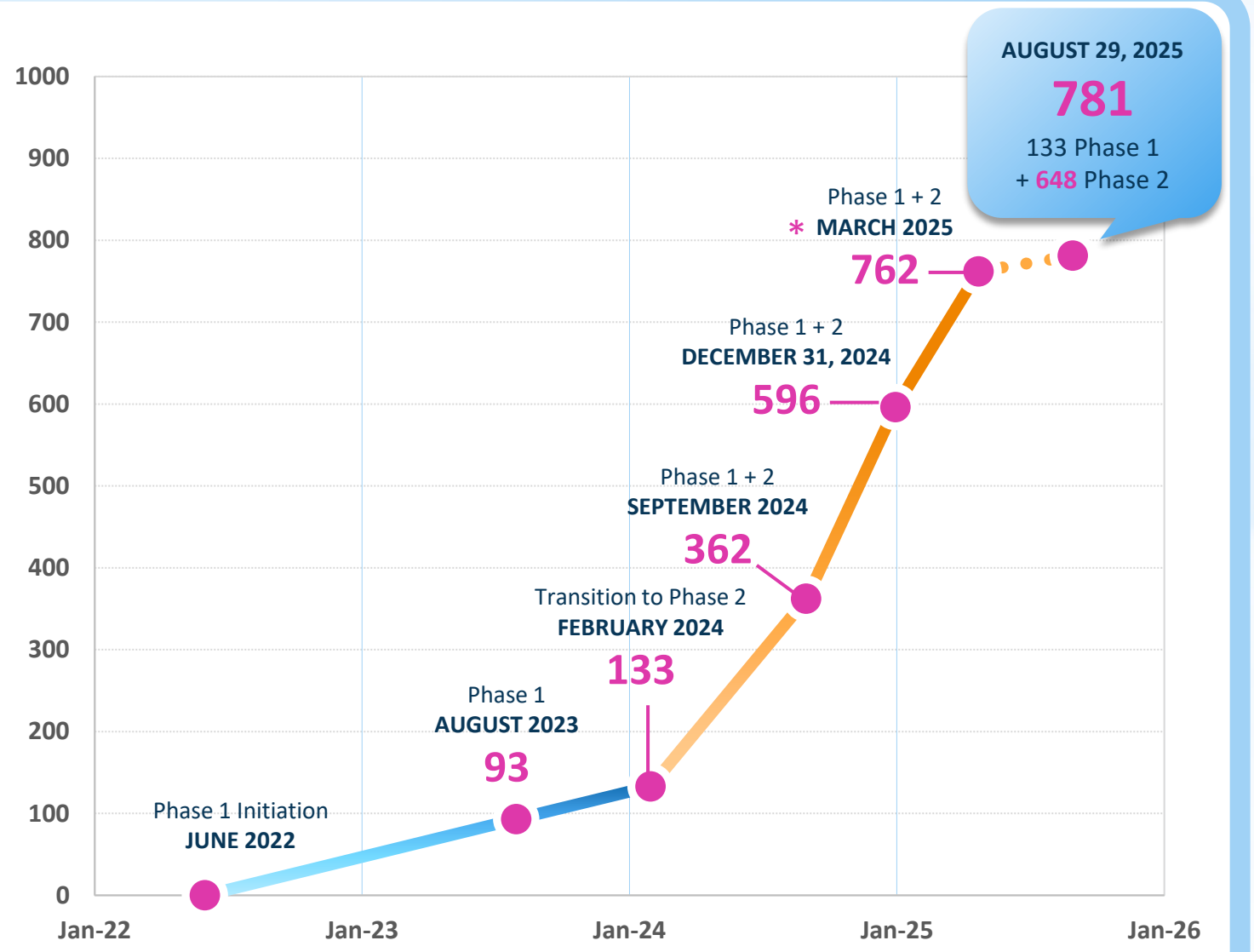
ALKove-1

PHASE 1 + PHASE 2 PATIENT ENROLLMENT

Strong enrollment momentum demonstrates enthusiasm for neladalkib & clear medical need for TKI pre-treated patients



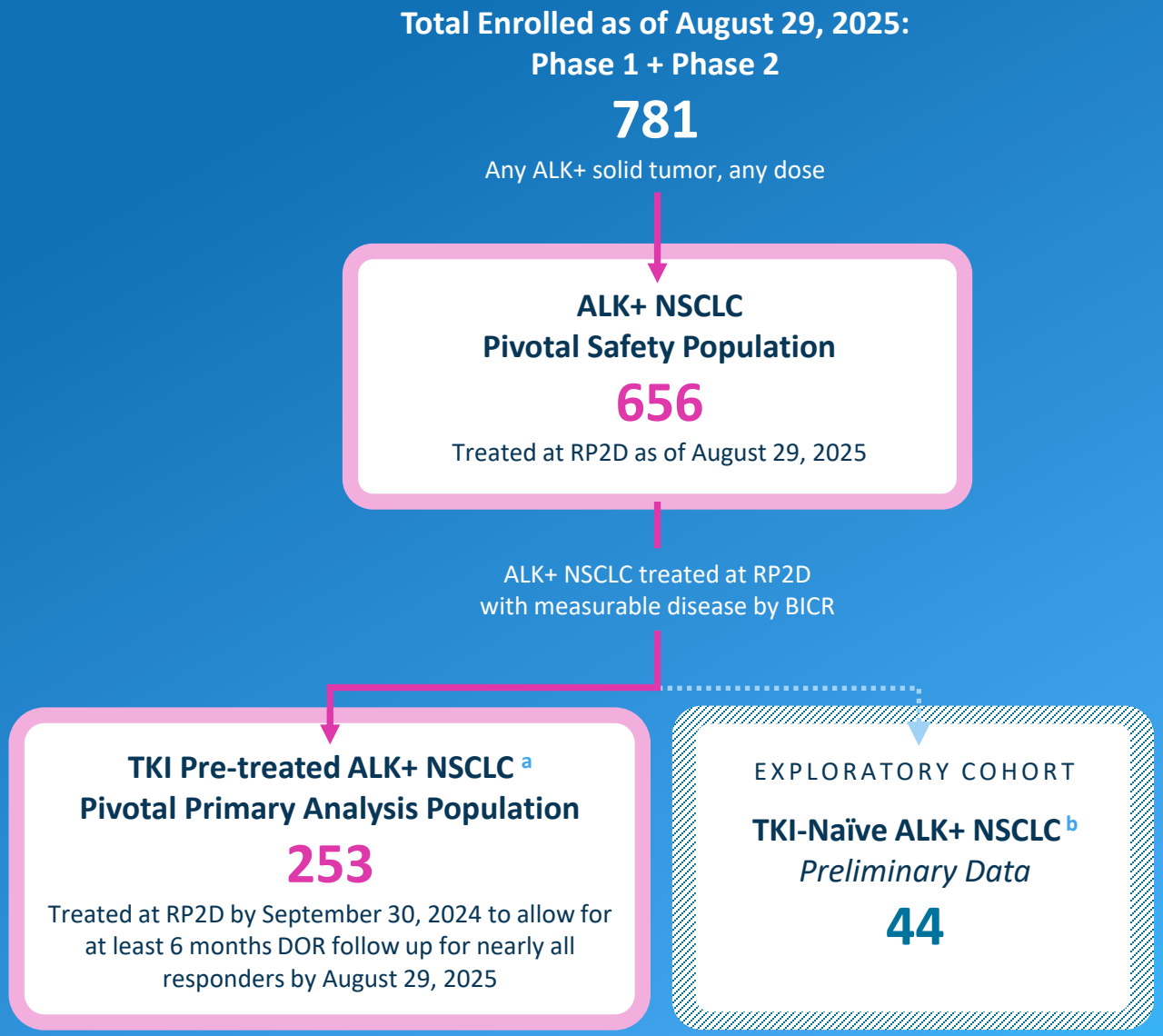
* Transition to Expanded Access Protocol for adult patients with advanced ALK+ TKI pre-treated NSCLC. Enrollment continues for adult and adolescent patients with ALK+ solid tumors other than NSCLC, and adolescent patients with ALK+ NSCLC.

Nuvalent | ALKove-1

ALKOVE-1

Pivotal Data Populations

- Pivotal ALK+ NSCLC safety population (n = **656**) and TKI pre-treated efficacy population (n = **253**)
- Preliminary data available from exploratory cohort of **44** TKI-naïve patients with ALK+ NSCLC in ALKOVE-1
  - Enrollment of TKI-naïve patients is ongoing in the ALKAZAR Phase 3 randomized controlled trial



BICR, blinded independent central review; **DOR**, duration of response; **NSCLC**, non-small cell lung cancer; **RP2D**, recommended phase 2 dose (150 mg QD); **TKI**, tyrosine kinase inhibitor.

[a] Includes 25 patients with other oncogenic driver(s) in addition to ALK: MET amplification (n = 9), KRAS G12C (n = 4*), MET mutation (n = 4), BRAF mutation (n = 4*), RET fusion (n = 2), ERBB2 mutation (n = 1), NTRK fusion (n = 1), FGFR3 fusion (n = 1). [*One patient had both KRAS G12C and BRAF mutations.]

[b] No patients with other oncogenic driver(s) in addition to ALK.

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Pre-treated ALK+ NSCLC Population at RP2D

Distinct overall TKI pre-treated population (n = 253):

- **3** median lines of prior anticancer treatment (Range: 1 – 11)
- **51%** received prior chemotherapy
- **78%** received ≥ 2 prior ALK TKIs, of whom **91**% received prior lorlatinib
- **19%** with secondary ALK G1202R mutation [a,b,c]
- **40%** with active CNS disease (BICR)

Lorlatinib-naïve subpopulation (n = 63):

- **25%** of overall TKI pre-treated population
- **25%** received prior chemotherapy
- **100%** received ≥ 1 prior 2G ALK TKI, of whom **70**% received prior alectinib only [d]
- **19%** with secondary ALK G1202R mutation [a,c]
- **35%** with active CNS disease (BICR)

2G, 2nd generation (i.e., alectinib, brigatinib, ceritinib, ensartinib); **BICR,** blinded independent central review; **CNS**, central nervous system; **NSCLC**, non-small cell lung cancer; **RP2D**, recommended phase 2 dose (150 mg QD); **TKI**, tyrosine kinase inhibitor.

[a] ALK mutations as per local or central testing of blood (ctDNA) or tissue.

[b] Patients may have had other mutations in addition to ALK G1202R.

[c] 36% (91/253) of patients overall had any ALK mutation, including 22 lorlatinib-naïve patients. 17% (43/253) of patients overall had compound resistance mutations, including 3 lorlatinib-naïve patient(cis-allelic configuration not confirmed in all cases).

[d] 73% (46/63) had 1 prior ALK TKI only (alectinib, n = 44; brigatinib, n = 2). No patients received crizotinib as their only prior ALK TKI. 14% (9/63) received crizotinib in addition to ≥ 1 prior 2G ALK TKI. 13% (8/63) received ≥ 2 prior 2G ALK TKIs only. Patients may have also received prior chemotherapy.

Topline Efficacy Results: TKI Pre-treated ALK+ NSCLC

ALK ACTIVITY + ALK MT ACTIVITY + CNS ACTIVITY + AVOIDING TRK

Neladalkib demonstrated durable activity against ALK and ALK G1202R in a uniquely heavily pre-treated patient population:

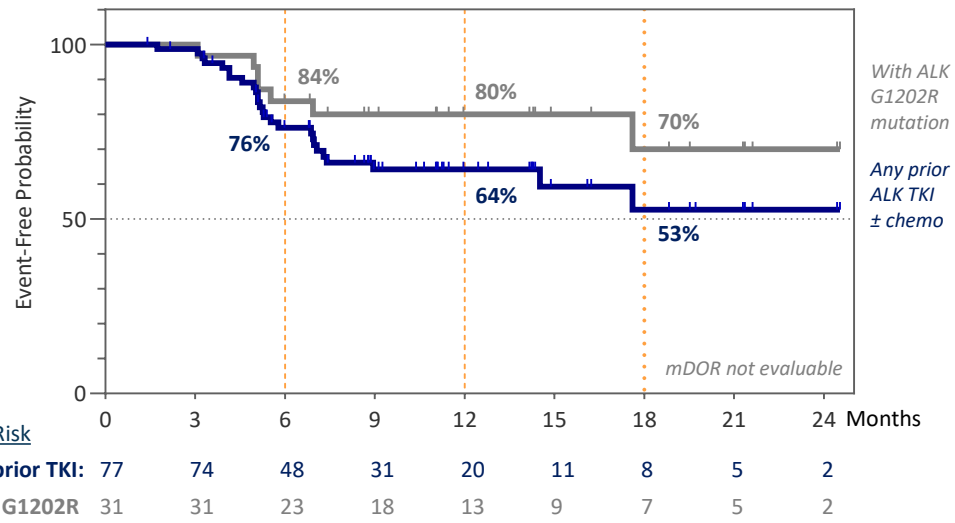
RECIST 1.1, BICR	Any prior ALK TKI ± chemotherapy [a] (n = 253)	With G1202R Mutation [b] (n = 47)
ORR, % (n/N) (95% CI)	**31%** (79/253) [c, d] (26, 37)	**68%** (32/47) [e] (53, 81)
% DOR ≥ 6 months [f] (95% CI)	**76%** (64, 84)	**84%** (65, 93)
% DOR ≥ 12 months [f] (95% CI)	**64%** (51, 75)	**80%** (61, 91)
% DOR ≥ 18 months [f] (95% CI)	**53%** (34, 68)	**70%** (42, 86)

Responses were also observed in:

- Lorlatinib-experienced patients, where no approved therapies have demonstrated activity:
  ORR = **26%** (50/190) [g], mDOR = **17.6 months** (95% CI: 6.9, NE)
- Patients with compound ALK mutations after ≥ 2 prior ALK TKIs:
  ORR = **58%** (25/43) [h], DOR ≥ 12 months = **69%** (95% CI: 45, 84) [i]

Kaplan-Meier Plot of DOR

All TKI Pre-treated



# At Risk									
Any prior TKI:	77	74	48	31	20	11	8	5	2
With G1202R	31	31	23	18	13	9	7	5	2

*Data pooled for patients treated by September 30, 2024 at RP2D in the Phase 1 or Phase 2 portion of ALKOVE-1 with a data cut-off of August 29, 2025 allowing for 6 months of follow-up for nearly all responders. Responses were confirmed per RECIST 1.1 as assessed by blinded independent central review (**BICR**).*

CI, confidence interval; **DOR**, duration of response; **ORR**, objective response rate; **PR**, partial response; **RP2D**, recommended phase 2 dose (150 mg QD); **TKI**, tyrosine kinase inhibitor; **u**, unconfirmed.

[a] Median duration of follow-up of 11.3 months; [b] Patients may have had other mutations in addition to ALK G1202R; [c] Includes 2 uPRs; [d] Responses also observed in patients with ALK mutations other than G1202R, including C1156Y, I1171N, I1171T, F1174C, F1174L, V1180L, L1196M, L1198F, D1203N, E1210K, and G1269A; [e] Includes 1 uPR; [f] Analyses of DOR based on Kaplan-Meier estimates; [g] Includes 2 uPRs; [h] Includes 1 uPR; [i] mDOR not evaluable.

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Topline Efficacy Results: TKI Pre-treated, Lorlatinib-naïve

ALK ACTIVITY + ALK MT ACTIVITY + CNS ACTIVITY + AVOIDING TRK

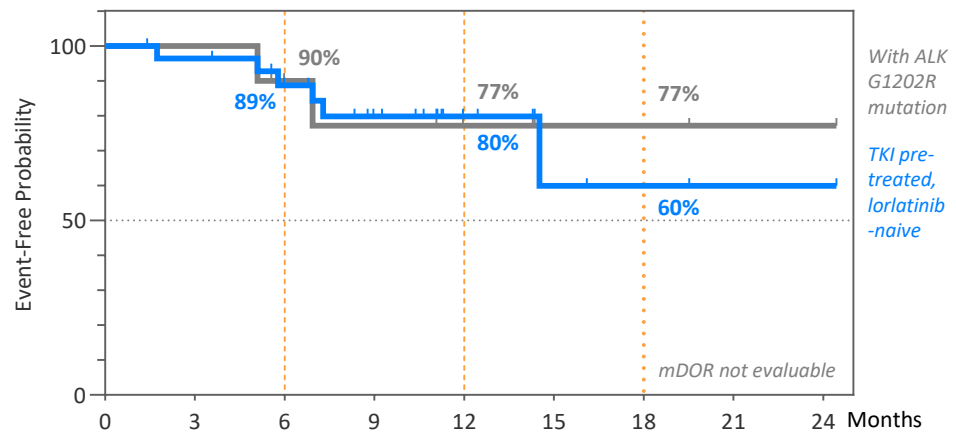
Neladalkib demonstrated potential for differentiated durability in TKI pre-treated patients who are lorlatinib-naïve:

RECIST 1.1, BICR	TKI pre-treated, Lorlatinib-naïve (n = 63)	With G1202R Mutation (n = 12)
ORR, % (n/N) (95% CI)	**46%** (29/63) (33, 59)	**83%** (10/12) (52, 98)
% DOR ≥ 6 months [a] (95% CI)	**89%** (69, 96)	**90%** (47, 99)
% DOR ≥ 12 months [a] (95% CI)	**80%** (58, 91)	**77%** (34, 94)
% DOR ≥ 18 months [a] (95% CI)	**60%** (19, 85)	**77%** (34, 94)

- No patients received crizotinib as their only ALK TKI
- Similar activity was observed in patients receiving 1 prior 2nd generation ALK TKI (alectinib [n = 44] or brigatinib [n = 2]) ± chemo: ORR = **48%** (22/46), DOR ≥ 12 and 18 months = **74%** (95% CI: 48, 88) [b]

Kaplan-Meier Plot of DOR

TKI Pre-treated, Lorlatinib-naïve



At Risk

Lorlatinib-naïve	29	27	21	15	7	3	2	1	1
With G1202R	10	10	7	6	4	2	2	1	1

*Data pooled for patients treated by September 30, 2024 at RP2D in the Phase 1 or Phase 2 portion of ALKOVE-1 with a data cut-off of August 29, 2025 allowing for 6 months of follow-up for nearly all responders. Responses were confirmed per RECIST 1.1 as assessed by blinded independent central review (**BICR**).*

CI, confidence interval; **DOR**, duration of response; **MT**, mutation; **ORR**, objective response rate; **PR**, partial response; **RP2D**, recommended phase 2 dose (150 mg QD); **TKI**, tyrosine kinase inhibitor; **u**, unconfirmed.

[a] Analyses of DOR based on Kaplan-Meier estimates; [b] mDOR not evaluable.

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Intracranial Activity

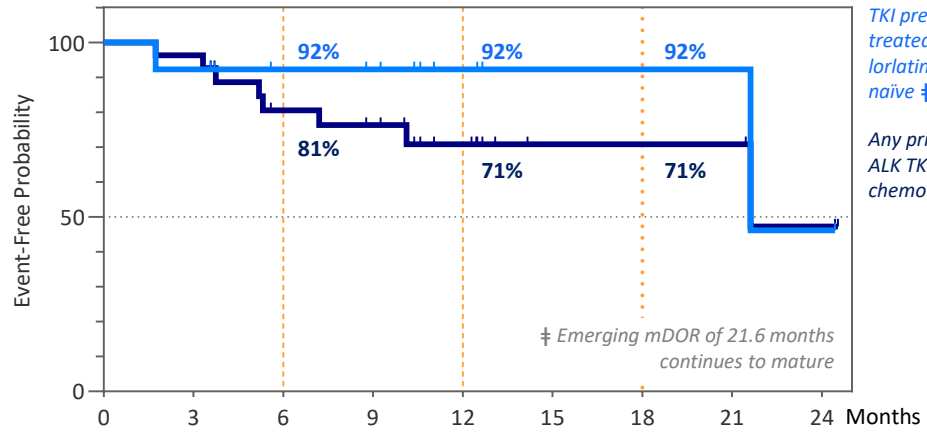
Durable intracranial responses observed in patients with measurable CNS lesions:

Measurable CNS lesions RECIST 1.1, BICR	Any prior ALK TKI ± chemotherapy (n = 92)	TKI pre-treated, Lorlatinib-naïve (n = 24)
IC-ORR, % (n/N) (95% CI)	**32%** (29/92) [a] (22, 42)	**63%** (15/24) [a] (41, 81)
IC-CR, % (n/N)	**13%** (12/92) [b]	**21%** (5/24) [b]
% IC-DOR ≥ 6 months [c] (95% CI)	**81%** (59, 91)	**92%** (57, 99)
% IC-DOR ≥ 12 months [c] (95% CI)	**71%** (48, 85)	**92%** (57, 99)
% IC-DOR ≥ 18 months [c] (95% CI)	**71%** (48, 85)	**92%** (57, 99)

- Intracranial responses were also observed in lorlatinib-experienced patients with measurable CNS lesions:
  IC-ORR = **21**% (14/68), IC-DOR ≥ 6 months = **71**% (95% CI: 41, 88), IC-DOR ≥ 12 and 18 months = **55**% (95% CI: 26, 77) [d]

Kaplan-Meier Plot of IC-DOR

Intracranial Responders



At Risk

Any prior TKI	27	26	19	16	10	4	4	4	2
Lorlatinib-naïve	13	12	9	8	4	2	2	2	1

*Data pooled for patients treated by September 30, 2024 at RP2D in the Phase 1 or Phase 2 portion of ALKOVE-1 with a data cut-off of August 29, 2025 allowing for 6 months of follow-up for nearly all responders. Responses were confirmed per RECIST 1.1 as assessed by blinded independent central review (**BICR**).*

CI, confidence interval; **CR**, complete response; **DOR**, duration of response; **IC**, intracranial; **ORR**, objective response rate; **PR**, partial response; **RP2D**, recommended phase 2 dose (150 mg QD); **TKI**, tyrosine kinase inhibitor; **u**, unconfirmed.

[a] Includes 2 IC-uPRs; [b] Includes 1 IC-uCR with prior confirmed IC-PR; [c] Analyses of DOR based on Kaplan-Meier estimates; [d] Median IC-DOR not evaluable.

Nuvalent

Topline Safety Profile

ALK ACTIVITY + ALK MT ACTIVITY + CNS ACTIVITY + AVOIDING TRK

Safety profile of neladalkib was generally well tolerated and consistent with its ALK-selective, TRK-sparing design

- Dose reduction due to TEAE: **17%**
  - Events in ≥1% of patients:
    ALT increased (10%), AST increased (8%) [a]
- Discontinuation due to TEAE: **5%**
  - Events in ≥1% of patients:
    ALT increased (1.8%), AST increased (1.2%)
- Most common TEAE were transaminase elevations
  - Most were asymptomatic lab abnormalities, and observed to be low-grade, transient, and reversible with dose interruptions or reductions
  - Preliminary data suggest increased incidence in less heavily pre-treated patients
  - Enhanced monitoring and prompt dose interventions implemented in the protocol for the Phase 3 ALKAZAR trial
- Overall safety profile consistent with avoiding TRK-related neurotoxicities

Treatment-Emergent Adverse Events (TEAEs) in ≥ 15% of TKI-naïve or TKI Pre-treated Patients with ALK-positive NSCLC Receiving Neladalkib at RP2D (N = 656)

Preferred Term	Any Grade	Grade ≥3
ALT increased	47%	20%
AST increased	44%	16%
Constipation	28%	0.2%
Dysgeusia	23%	0
Peripheral edema	18%	0.3%
Cough	16%	0.5%
Nausea	16%	0.8%

Data pooled for patients in the Phase 1 or Phase 2 portion of ALKOVE-1 with a data cut-off of August 29, 2025. Patients received at least 1 dose of neladalkib at RP2D with median duration of exposure of 6.0 months (range: 0.1, 28.4); **NSCLC**, non-small cell lung cancer; **RP2D**, recommended phase 2 dose (150 mg QD); **TEAE**, treatment emergent adverse event; **TRK**, proteins encoded for by the neurotrophic receptor tyrosine kinase (NTRK) family of genes.

[a] Not mutually exclusive: Dose reduction due to any transaminase elevation observed in 11% of patients.

Nuvalent

NELADALKIB (NVL-655)

Encouraging Preliminary Data for Exploratory TKI-naïve Population

TKI-naïve patients with ALK+ NSCLC enrolled in exploratory cohort of ALKOVE-1:

ORR	% DOR ≥ 6 and 12 months [b]
86% (38/44, 4 CRs) [a]	**91%** (95% CI: 70, 98)

- 2 progression events among responders
- DOR range: 1.7+ to 14.8+ months

Subset of patients with measurable intracranial lesions:

IC-ORR	No CNS progression events observed among IC-responders
78% (7/9, 4 IC-CRs) [c]	

- IC-DOR range: 3.1+ to 7.0+ months

Global enrollment of TKI-naïve patients is ongoing in ALKAZAR, a Phase 3 randomized controlled trial of neladalkib versus alectinib

*Data for patients treated in the TKI-naïve Phase 2 cohort of ALKOVE-1 with a data cut-off of August 29, 2025. Responses were confirmed per RECIST 1.1 as assessed by blinded independent central review (**BICR**).*
CI, confidence interval; **CR**, complete response; **DOR**, duration of response; **IC**, intracranial; **NSCLC**, non-small cell lung cancer; **ORR**, objective response rate; **PR**, partial response; **TKI**, tyrosine kinase inhibitor; **u**, unconfirmed.
[a] Includes 2 uPRs and 1 uCR with prior confirmed PR; [b] Analyses of DOR based on Kaplan-Meier estimates; [c] Includes 1 IC-uCR with prior confirmed IC-PR.

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Neladalkib: Designed for *all* patients with ALK+ NSCLC

PRELIMINARY

TOPLINE

	ALK Activity	+	Intracranial Activity	+	Sustain Target Efficacious Doses	Overall Duration of Response (Kaplan-Meier Estimate) 6 months / 12 months / 18 months	Emerging Median (Kaplan-Meier Estimate)
TKI-naïve ± chemo (n = 44)	ORR = **86%** (ALKOVE-1)		IC-ORR = **78%** (**44%** IC-CR)		**Low discontinuation rate due to TEAE** (5%) **Low dose reduction rate due to TEAE** (17%) **Once daily oral pill** (n = 656)	91% → 91%	• *Follow-up ongoing for patients enrolled in exploratory cohort of ALKOVE-1* • *Enrollment ongoing in ALKAZAR Phase 3 randomized, controlled trial versus alectinib*
TKI Pre-treated, Lorlatinib-naïve 1 – 3 TKIs ± chemo (n = 63)	ORR = **46%** ALK G1202R: ORR = **83%**		IC-ORR = **63%** (**21%** IC-CR)			89% → 80% → 60%	**mDOR**: NE
Any Prior TKI* 1 – 5 TKIs ± chemo (n = 253)	ORR = **31%** ALK G1202R: ORR = **68%**		IC-ORR = **32%** (**13%** IC-CR)			76% → 64% → 53%	**mDOR**: NE
Lorlatinib-experienced (n = 190)	ORR = **26%**						**mDOR**: 17.6 months

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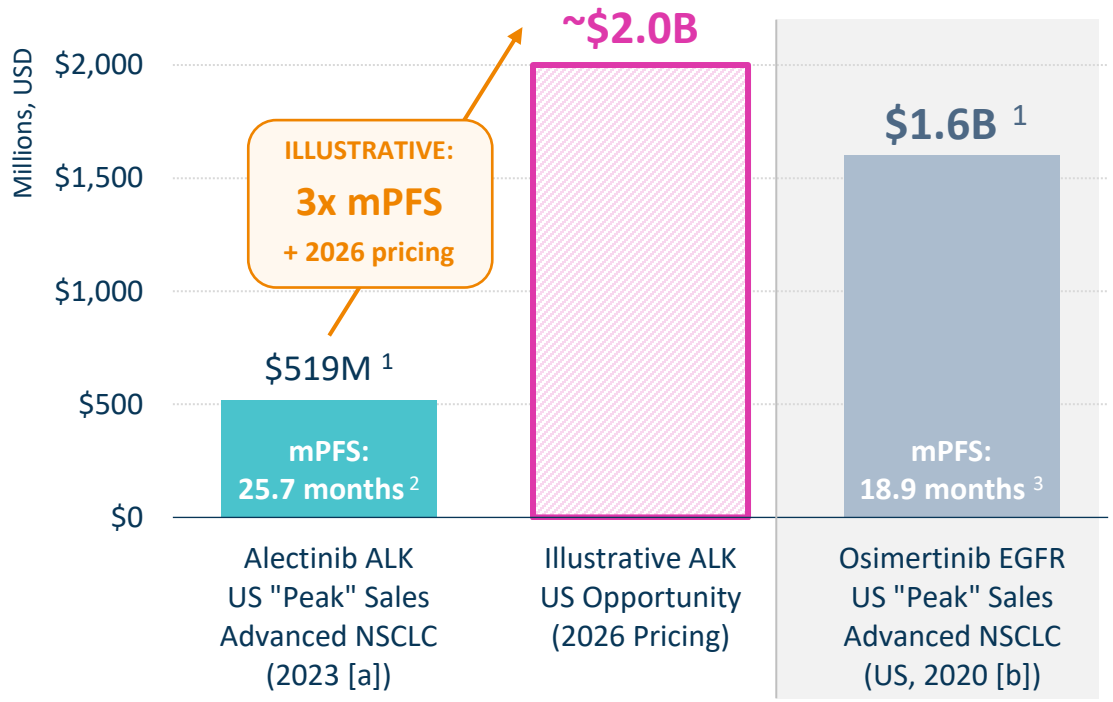
Realize the full potential of an ALK TKI

The ALK+ NSCLC market has the potential to match or exceed today's opportunity in advanced/metastatic EGFR+ NSCLC

Illustrative ALK+ NSCLC "Peak" Sales Opportunity (US)



US "Peak" Sales Benchmark for ALK+ NSCLC	$519M (Alectinib, 2023) [a]
	x
Potential Durability Increase (i.e., "Time on therapy")	**~2 - 3x mPFS** Alectinib 1L mPFS: 25.7 months [2] Lorlatinib 1L mPFS: *NR at 60 months* [4]
	x
Illustrative 2026 Price/Month	**~1.3x** ~$17,500 (Alectinib, 2023) [5] → ~$22,500 (Lorlatinib, 2026) [5]
Illustrative Potential US "Peak" Sales Opportunity	**~$1.35B - 2B**
Illustrative Potential WW "Peak" Sales Opportunity	**~$3.4B - 5B** Illustrative if US = 40% of global [c]

Illustrative projections are based on management assumptions as of January 2026 and are subject to change. **m**, median; **NSCLC**, non-small cell lung cancer; **PFS**, progression-free survival.

[a] "Peak" for adv/met indication estimated in 2023 due to FDA approval for adjuvant ALK+ NSCLC indication in April 2024. [b] "Peak" for adv/met indication estimated in 2020 due to FDA approval for adjuvant EGFR+ NSCLC indication in December 2020.

[c] 2023 - 2024 reference: alectinib US = 30 - 34% of global net revenue, lorlatinib US = 42% of global net revenue.

Sources: [1] Year-end earnings reports for Roche (2023) and AstraZeneca (2020); [2] ALECENSA FDA prescribing information, revised 04/2024. [3] TAGRISSO FDA prescribing information, revised 09/2024. [4] Solomon B.J. et al., J Clin Oncol. 2024. [5] NAVLIN, accessed January 2026.

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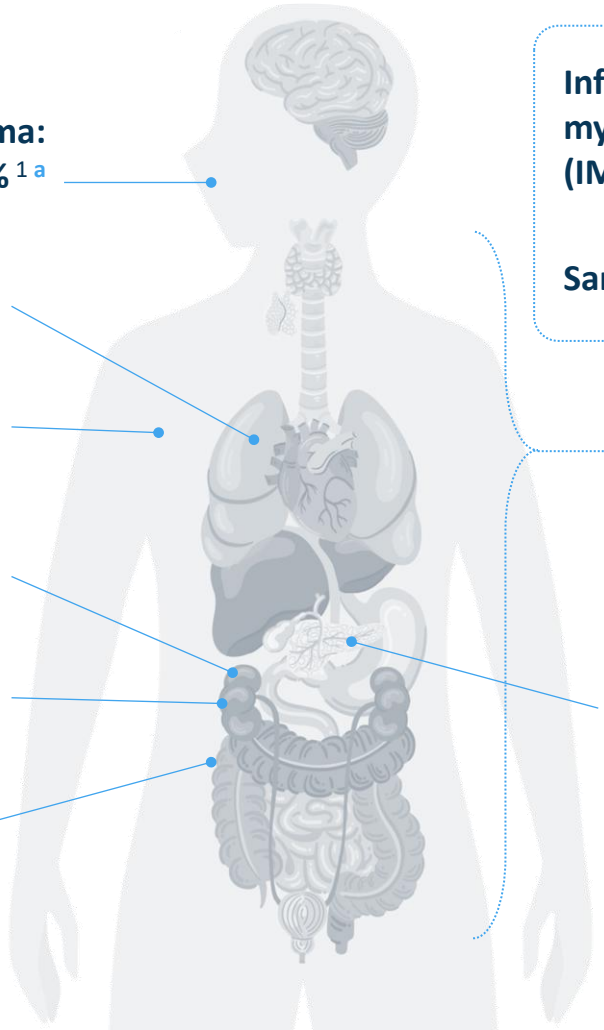
Opportunity for an ALK-selective Inhibitor Beyond NSCLC

- **ALK alterations have been identified as oncogenic drivers in a wide range of solid tumors beyond NSCLC, and in hematologic malignancies such as ALCL**
  - ALK alteration types may include overexpression, amplification, copy number variation, mutation, and fusion
- **Today, ALK TKIs are only approved for NSCLC, IMT, and ALCL**
- **Patients with advanced or metastatic ALK+ solid tumors other than NSCLC were enrolled in the ALKOVE-1 study of neladalkib as part of the completed Phase 1 dose escalation and in one cohort within the ongoing Phase 2 study**

Reported incidence of *ALK* alterations across diverse solid tumors



Salivary gland carcinoma: <1% [1] [a]

NSCLC: ~3 – 5% [2]

Breast: ~2 – 13% [7]

Neuroblastoma: ~6 – 16% [8-11]

Renal cell: <1 – ~2% [3,12]

Peritoneal mesothelioma: ~3 – 13% [13]

Inflammatory myofibroblastic tumor (IMT): ~50% [4]

Sarcomas: ~1 – ~2.4% [5,6]

Digestive tract cancers (including esophageal, gastric, and colorectal) <1 – ~5% [3,14]

Pancreatic: <1% [3,15]

[a] Incidence reported for ALK fusions.

[1] Majewska et al., Virchows Archiv 2021. [2] Kwak E. et al., NEJM 2010. [3] TCGA PanCancer Atlas, internally accessed September 2025. [4] Antonescu et al., Am J Surg Pathol. 2015. [5] Davis et al., Mol Cancer Res. 2019. [6] Groisberg et al., Connective Tissue Oncology Society 2020. [7] Shreenivas et al., NPJ Precis. Oncol. 2023. [8] De Brouwer et al., Clin Cancer Res 2010. [9] Bresler et al. Cancer Cell 2014. [10] Bellini et al. JCO 2021. [11] O'Donohue et al., JCO Precis Oncol 2021. [12] Sukov et al., Modern Pathology 2012. [13] Hung et al., JAMA Oncology 2018. [14] Ying et al., PLOS One 2015. [15] Singhi et al., JNCCN 2017.

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Preliminary Activity in ALK+ Solid Tumors Beyond NSCLC

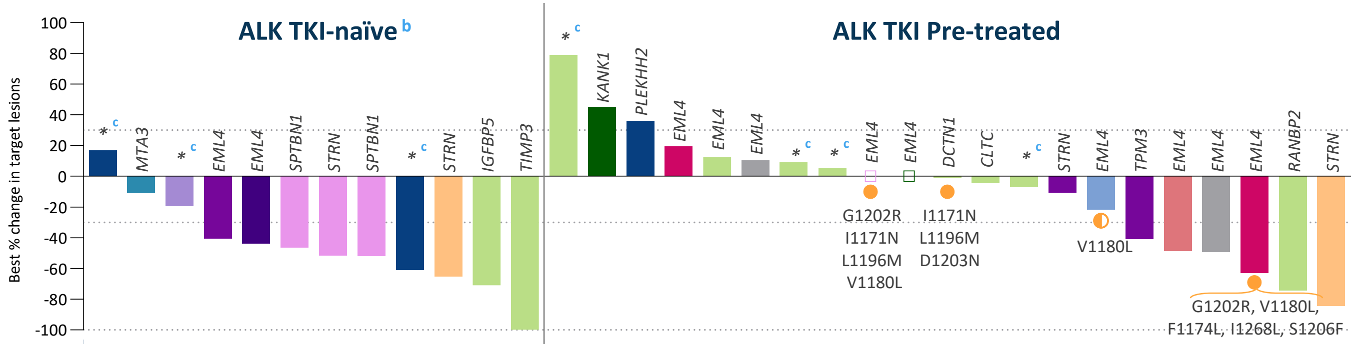
Enrollment for ALK+ solid tumors beyond NSCLC continues in the Phase 2 portion of ALKOVE-1 clinical trial

Encouraging activity seen in both ALK TKI-naïve and previously treated patients, including those refractory to prior therapies

RECIST 1.1, investigator assessed:

- Overall ORR: **44% (15/34)**
  - ALK TKI-naïve: 9/13
  - ALK TKI Pre-treated: 6/21
- Durable responses observed in patients with ALK+ solid tumors, including an intracranial complete response in a patient who previously received the brain-penetrant TKI, alectinib
- 80% (12/15) of responders remained on treatment without disease progression as of the data cutoff date

Radiographic tumor responses in patients with *ALK*+ solid tumors other than NSCLC



ALK TKI-naïve:

Best overall response	SD	SD	SD	PR	PR	PR	PR	PR	PR	PR	PR	uPR
Prior ALK TKIs	-	-	-	-	-	-	-	-	-	-	-	-
crizotinib												
alectinib												
brigatinib												
ceritinib												
lorlatinib												
Prior lines, chemo	-	2	-	1	2	3	2	1	1	-	1	-
Prior anticancer therapies	-	2	-	1	2	4	2	1	1	1	1	-

ALK TKI Pre-treated:

Best overall response	PD	PD [d]	PD	SD	SD	PD	NE	SD	PD	SD	PD	SD	SD	SD	SD	PR	PR	PR	PR [e]	PR	PR
Prior ALK TKIs	1	1	2	1	2	2	2	1	2	1	4	3	1	2	1	1 [f]	1	1	2	1	1
crizotinib		●	●								●	●		●						●	
alectinib				●	●	●	●	●	●	●	●	●		●	●		●	●	●		
brigatinib							●				●										
ceritinib													●								●
lorlatinib	●		●		●	●			●		●	●							●		
Prior lines, chemo	-	2	-	-	2	1	1	-	1	3	1	-	-	2	-	2	-	1	2	-	1
Prior anticancer therapies	1	3	2	1	6	4	3	1	3	4	8	4	1	3	1	3	1	2	5	1	2

KEY:

- Adenocarcinoma of unknown origin (n = 1)
- Clear cell odontogenic carcinoma (n = 1)
- Colorectal cancer (CRC, n = 4)
- Inflammatory myofibroblastic tumor (IMT, n = 10)
- Medullary glioma (n = 1)
- Neuroendocrine carcinoma of lung (n = 2)
- Neuroendocrine carcinoma of pancreas (n = 2)
- Pancreatic adenocarcinoma (n = 3)
- Peritoneal mesothelioma (n = 2)
- Renal cell cancer (RCC, n = 1)
- Salivary duct carcinoma (n = 2)
- Sarcoma (n = 3)
- Small bowel adenocarcinoma (n = 1)
- ◐ Single ALK resistance mutation
- ● Compound (≥ 2) ALK resistance mutation

ALK fusion partner listed above column;
ALK resistance mutations listed below

Data cut-off: August 7, 2025. Patients received RP2D of 150 mg QD unless otherwise noted. [a] Includes 1 ongoing single-timepoint PR pending confirmation. [b] One response-evaluable ALK TKI-naïve patient with cholangiocarcinoma is not shown due to no post-baseline tumor assessment in the setting of symptomatic deterioration. [c] *Enrolled by FISH or IHC; ALK fusion partner not determined. [d] Received Phase 1 starting dose of 25 mg QD. [e] Received Phase 1 starting dose of 100 mg QD. [f] Received prior entrectinib.

Source: Solomon B. et al., ESMO 2025.

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NVL-330 *for* HER2-altered NSCLC

A brain-penetrant, HER2-selective inhibitor with activity against HER2 mutations and the potential to minimize EGFR-related adverse events

AT · A · GLANCE

Mechanism of Action:
HER2-selective tyrosine kinase inhibitor

Stage of Development:
Phase 1

Initial Development Indication:
HER2-altered NSCLC

CNS involvement and treatment-related adverse events are associated with available and investigational HER2 targeted therapies

HER2-altered NSCLC

Mutant: ~2 – 4% of NSCLC [1,2] | Amplified: ~1 – 5% of NSCLC [1,2]

~19% CNS disease at diagnosis [3]

1L *Standard of care:* **Pemetrexed + Platinum + Pembrolizumab**

Opportunity for deeper, more durable responses: 48% ORR, 11.2 month mDOR, 8.8 month mPFS with chemo/I-O [4]

~50% CNS disease at 1L progression [3]

2L *Standard of care:* **Trastuzumab deruxtecan (T-DXd)**

Opportunity for more durable responses: 58% ORR, 8.7 month mDOR with T-DXd [5]

T-DXd safety signals are indicative of chemotherapy: Serious Adverse Reactions occurred in 30% of patients [5]

3L+ **No standard of care**

Investigational HER2 TKIs may also inhibit the related EGFR kinase, which is associated with skin rash and diarrhea [6,7,8]

Targeted therapies *for* HER2-altered NSCLC	Oral Small Molecule	HER2 Activity	HER2ex20 Activity	Avoiding EGFR	CNS Activity
T-Dxd (Enhertu) [5] *FDA Approved ADC (Accelerated Approval)*	✓	✓	✓	✓	*May be suboptimal*
Zongertinib [9, 10] *FDA Approved TKI (Accelerated Approval)*	✓	✓	✓	✓	*May be suboptimal*
HER2ex20 TKIs (Other) [6, 7, 8] *Investigational*	✓	✓	✓	*Varies, TBD*	*TBD*

KEY: ✓ Observed in clinical investigation. ✗ **LIMITATION: Not observed in clinical investigation.**

Head-to-head clinical studies comparing the currently approved or investigational therapies have not been conducted and no comparative clinical conclusions can be drawn.

ADC, antibody-drug conjugate; **CNS,** central nervous system; **HER2ex20**, HER2 exon 20 insertion mutations; **NSCLC,** non-small cell lung cancer; **TKI**, tyrosine kinase inhibitor.

Sources: [1] Liu et al., Clin Cancer Res 2018. [2] Li et al., JTO 2016. [3] Offin et al., Cancer 2020. [4] KEYTRUDA (pembrolizumb) FDA package insert. [5] ENHERTU (T-DXd) FDA package insert. [6] (pyrotinib) Zhou C. et al., JCO 2020. [7] (ORIC-114) Hong et al., ESMO 2023. [8] (sevabertinib) Le X. et al., NEJM 2025. [9] HERNEXEOS (zongertinib) FDA package insert. [10] Heymach J.V. et al., NEJM 2025.

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NVL-330

A Rationally Designed **HER2** and **HER2ex20**-selective, EGFR-sparing Inhibitor

Potential Best-in-Class Target Product Profile designed in collaboration with physician-scientists to address the limitations of existing agents for HER2-altered NSCLC

NVL-330 is an investigational candidate and has not been approved by FDA or any other regulatory authority.

CNS, central nervous system; **HER2ex20**, HER2 exon 20 insertion mutations; **NSCLC**, non-small cell lung cancer; **TKI**, tyrosine kinase inhibitor.

Sources: [1] Liu et al., Clin Cancer Res 2018. [2] Li et al., JTO 2016. [3] Pillai et al., Cancer 2017. [4] Nagasaka et al., Clin Lung Cancer 2022. [5] (pyrotinib) Zhou C. et al., JCO 2020. [6] (ORIC-114) Hong et al., ESMO 2023. [7] (sevabertinib) Le X. et al., NEJM 2025. [8] Offin et al., Cancer 2020.

DESIGN GOAL *for* NVL-330

Oral Small Molecule

+

HER2 Activity

- Oncogenic HER2 amplification is detected in ~1 – 5% of NSCLC [1,2]

+

HER2ex20 Activity

- Oncogenic mutations in HER2, of which exon 20 insertions are most common, are detected in ~2 – 4% of NSCLC [1,2]

+

Avoiding EGFR

- Treatment limiting adverse events, such as skin rash and diarrhea, are associated with dual EGFR/HER2 inhibitors [5,6,7]

+

CNS Activity

- ~19% CNS disease at diagnosis [8]
- ~50% CNS disease at 1L progression [8]

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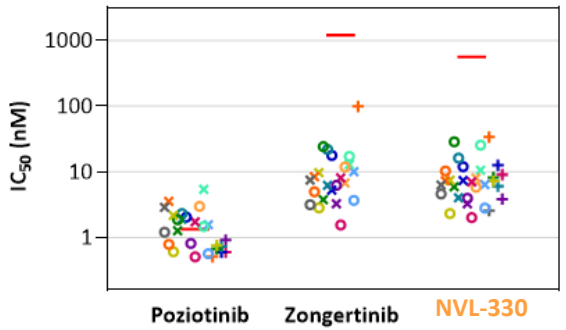
Preclinical Characterization Demonstrates Desired Target Product Profile

In Vitro Activity, HER2 AND HER2ex20

Broad activity on HER2 oncogenic alterations, including HER2 exon20ins, activating point mutations, and amplified wild-type HER2

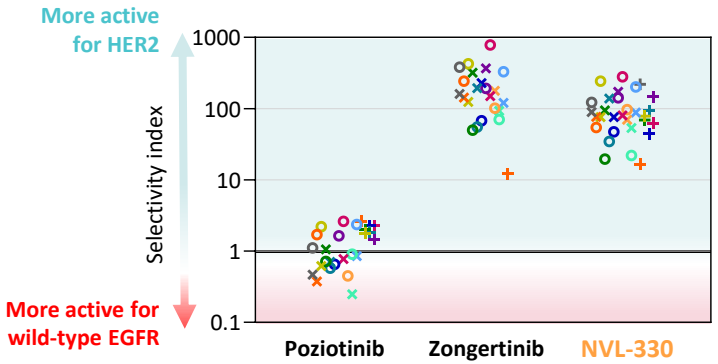


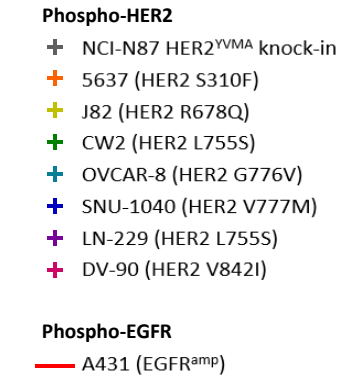
Avoiding EGFR Inhibition

Greater selectivity for HER2ex20 mutations over EGFR than pan-ERBB inhibitors (e.g. poziotinib)

Selectivity index =

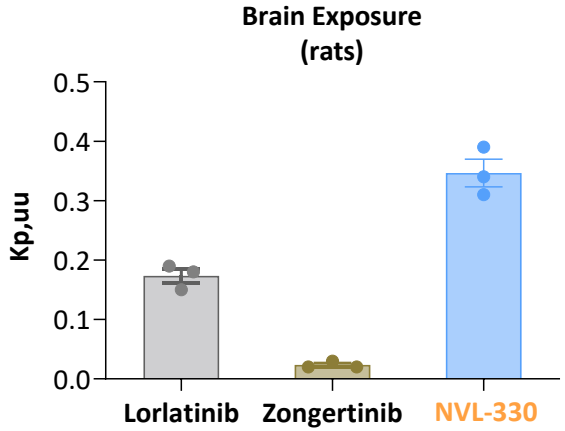
$$\frac{IC_{50}\text{ (phospho-EGFR}^{WT}\text{ in A431)}}{IC_{50}\text{(phospho-HER2 or viability)}}$$





Brain Penetrance

Pharmacokinetic data similar to preclinical observations for lorlatinib



Wistar Han rats
10 mg/kg, single dose PO
1 hour timepoint

Head-to-head clinical studies comparing NVL-330 with currently approved or investigational therapies have not been conducted. Above data from preclinical studies and no clinical conclusions can be drawn.
HER2ex20, HER2 exon 20 insertion; **IC50**, half-maximal inhibitory concentration; **PO**, orally.
Source: Updated data on file.; Sun, Y. et al., AACR 2024.

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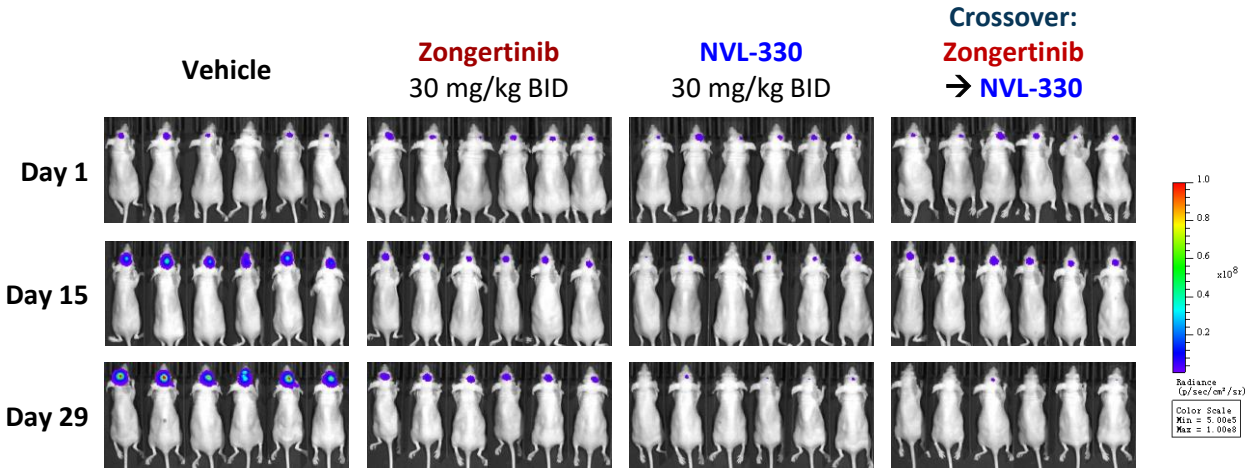
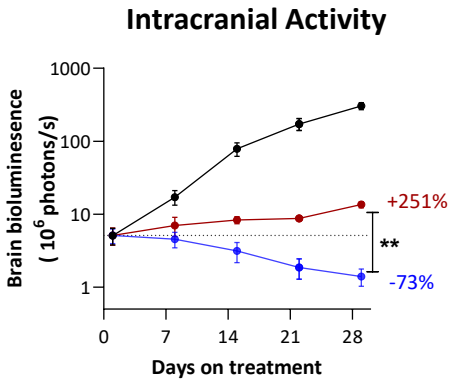
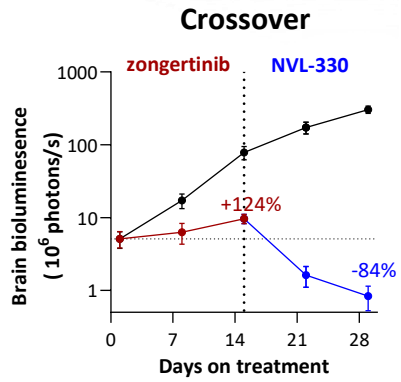
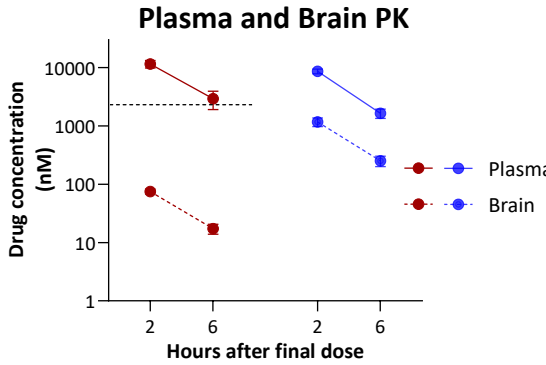
Potential for Differentiated Brain-penetrant Profile

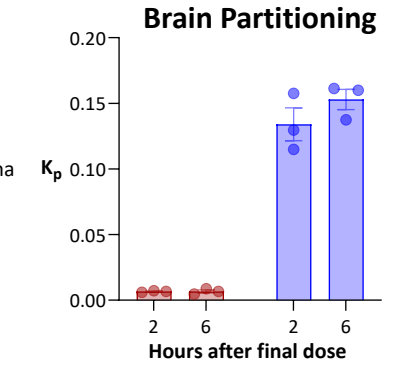
- In the intracranial NCI-N87 tumor model, NVL-330 (30 mg/kg BID) induced intracranial tumor regression in mice progressing in the CNS on zongertinib (30 mg/kg BID)
- Zongertinib 30 mg/kg BID provided exposures estimated to be above its approved human doses of 120 and 180 mg QD, and did not induce regression in this model

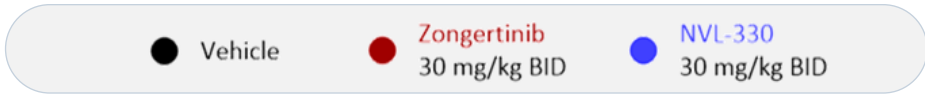












Head-to-head clinical studies comparing NVL-330 with currently approved or investigational therapies have not been conducted. Above data from preclinical studies and no clinical conclusions can be drawn.
BID, twice daily; **QD**, once daily.
Source: Sun Y. et al., AACR-NCI-EORTC 2025

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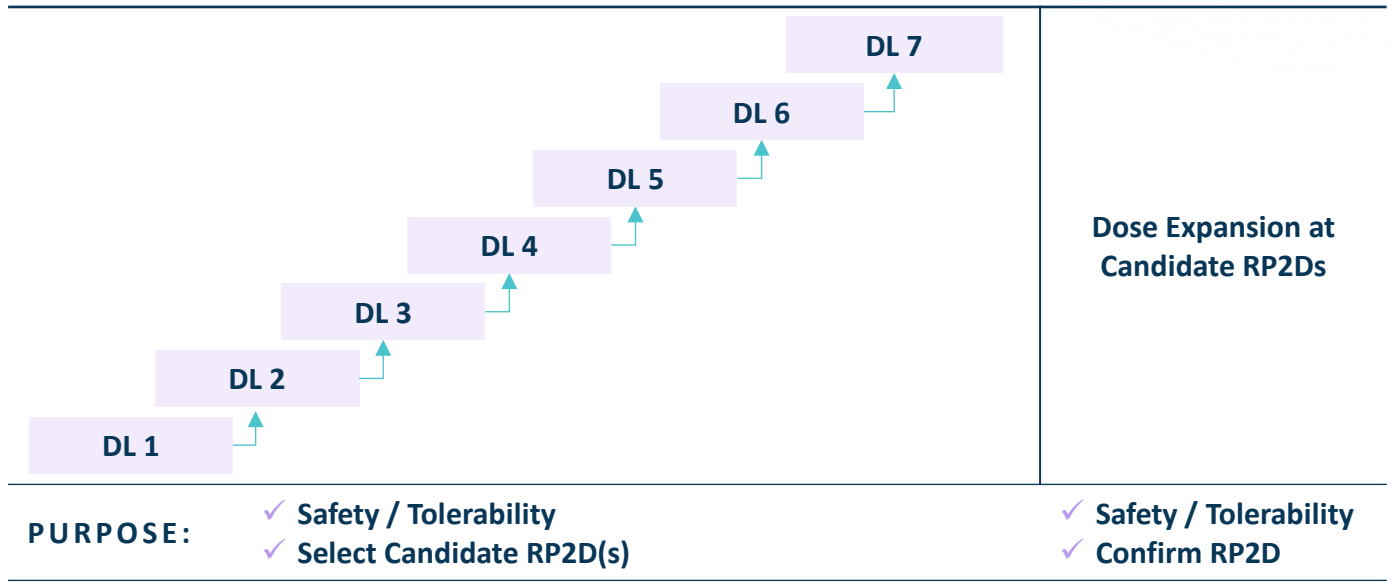
HERoex-1

A First-in-Human Phase 1a/1b Clinical Trial of NVL-330 in Advanced **HER2-Altered** NSCLC (NCT06521554)

Enrollment ongoing (up to N ~120)

- **Phase 1a**: HER2 mutation or HER2 amplification allowed
- **Phase 1b:** HER2 mutation only



PATIENT POPULATION

- ≥ 1 prior systemic therapy, including platinum-based chemotherapy +/- immunotherapy
  - Excluded: Prior selective HER2 TKI [a]
  - Prior HER2-directed antibodies and HER2-directed ADCs are allowed.
- Excluded: concurrent oncogenic drivers (e.g., EGFR, BRAF, MET, ROS1, ALK, or RET)
- Evaluable but non-measurable disease allowed in Phase 1a

ADC, antibody-drug conjugate; **BOIN**, Bayesian optimal interval; **NSCLC**, non-small cell lung cancer; **RP2D**, recommended phase 2 dose; **TKI**, tyrosine kinase inhibitor.

[a] For at least 6 patients in each Phase 1a dose level cohort expansion, and for all patients in Phase 1b.

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Goal by Year-End 2026

Fully integrated, commercial-stage biotech capable of not only discovering and developing, but *delivering* new medicines for patients living with cancer, building an initial franchise in NSCLC with an expanding portfolio of wholly-owned programs

Discover

Proven in-house discovery:

- Goal by year-end 2026 for **internally discovered, parallel lead programs**:
  2 FDA approved for initial indications, with label expansion strategies underway
- Goal by year-end 2026 for **active internal R&D pipeline**:
  1 in Phase 1 + 1 new development candidate **+** Ongoing discovery

Develop

Proven leaders in global development:

- 4 concurrent, active clinical trials, including 1 global randomized, controlled trial
- > 700 patients treated with zidesamtinib through ARROS-1 or expanded access
- > 1,000 patients treated with neladalkib through ALKOVE-1 or expanded access

Deliver

First US commercial launch:

- Foundation laid for a potential lung franchise, beginning with ROS1+ NSCLC

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The Path to Patient Impact

Looking Forward: 2027 – 2030

MISSION: Bringing new, potential best-in-class medicines to patients with cancer

OPPORTUNITIES FOR GROWTH BEYOND 2026

Launch neladalkib for TKI pre-treated ALK+ NSCLC & fully unlock the potential in advanced ROS1+ and ALK+ NSCLC with potential TKI-naïve indication expansions

Achieve a sustainable US business as a commercial leader in NSCLC

$1.4 billion in cash, cash equivalents and marketable securities as of December 31, 2025 expected to support operations into 2029 excluding potential revenues

Expand commercial capabilities to deliver new medicines outside the US

Advance discovery and development opportunities within & beyond NSCLC

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