



Nuvation Bio[®]

DRIVEN BY SCIENCE, FOCUSED ON LIFE

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Founder, President, & CEO**

TD Cowen Health Care Conference
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Forward looking statements

Certain statements included in this presentation (this “Presentation”) that are not historical facts are forward-looking statements for purposes of the safe harbor provisions under the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements are sometimes accompanied by words such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” “should,” “would,” “plan,” “predict,” “potential,” “seem,” “seek,” “future,” “outlook” and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These forward-looking statements include, but are not limited to, our expectations and timing of FDA approval and commercial launch, expectations and timing of establishing a commercial organization, a full NDA approval for taletrectinib for the treatment of advanced ROS1+ NSCLC (line agnostic), the potential for taletrectinib to become a new therapeutic option for ROS1+ NSCLC, taletrectinib’s and safusidenib’s best-in-class therapeutic potential, potential therapeutic benefit of Nuvation Bio’s product candidates and planning and advancement of clinical studies for such product candidates, success of clinical study design, the potential of the DDC platform, and strength of pro forma cash position providing a path to profitability without need to raise additional capital. These statements are based on various assumptions, whether or not identified in this Presentation, and on the current expectations of the management team of Nuvation Bio and are not predictions of actual performance. These forward-looking statements are subject to a number of risks and uncertainties that may cause actual results to differ from those anticipated by the forward-looking statements, including but not limited to the challenges associated with conducting drug discovery and initiating or conducting clinical studies due to, among other things, difficulties or delays in the regulatory process, enrolling subjects or manufacturing or acquiring necessary products; the emergence or worsening of adverse events or other undesirable side effects; risks associated with preliminary and interim data, which may not be representative of more mature data; and competitive developments. Risks and uncertainties facing Nuvation Bio are described more fully in its Form 10-Q filed with the SEC on November 6, 2024 under the heading “Risk Factors,” and other documents that Nuvation Bio has filed or will file with the SEC. You are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this Presentation. Nuvation Bio disclaims any obligation or undertaking to update, supplement or revise any forward-looking statements contained in this Presentation.



Nuvation Bio is tackling some of the greatest unmet needs in oncology



Global oncology company aimed at **making best-in-class drugs** by improving validated mechanisms that have encountered safety liabilities or limitations in efficacy



Taletrectinib is a 3rd generation, potentially **best-in-class ROS1 inhibitor** approved for advanced ROS1+ NSCLC in China; NDA accepted by U.S. FDA for priority review (line agnostic) with PDUFA date of 6/23/25



Safusidenib is a **potentially best-in-class, brain penetrant, mIDH1 inhibitor** entering **pivotal studies** for diffuse IDH1-mutant glioma



NUV-1511, the Company's **first clinical-stage drug-drug conjugate (DDC)**, is being evaluated in a **Phase 1/2 study**; **NUV-868** is a **BD2-selective BET inhibitor** that has completed **Phase 1 and Phase 1b studies**



Robust cash balance of \$549 million as of 9/30/24¹ and **taletrectinib PDUFA date of 6/23/25** position Nuvation Bio to potentially become a **U.S. commercial stage organization** as early as **June 2025**



1. Does not include \$200 million in non-dilutive financing from Sagard Healthcare Partners to be funded subject to U.S. FDA approval of taletrectinib.

Nuvation Bio has four differentiated oncology programs ranging from China approval / U.S. NDA under review, to Phase 1 ongoing

Program	Potential Indication(s)	Current Stage of Development					Anticipated Milestones & Recent Updates
		Preclinical	Phase 1	Phase 2	Pivotal	NDA Review	
Taletrectinib ¹ (ROS1)	Advanced ROS1+ NSCLC (treatment line agnostic)	Approved for advanced ROS1+ NSCLC in China; NDA accepted for priority review in U.S. with PDUFA date of 6/23/25					<ul style="list-style-type: none"> NDA accepted by U.S. FDA for priority review (line agnostic) Approved by China's NMPA for advanced ROS1+ NSCLC⁵ Pooled data from pivotal TRUST-I & TRUST-II studies presented at ESMO in September 2024
Safusidenib ² (mIDH1)	Diffuse IDH1-mutant glioma	Phase 1 ongoing					<ul style="list-style-type: none"> Entering pivotal studies in 2025 Phase 2 study ongoing
NUV-1511 (DDC)	Advanced solid tumors ³	Phase 1 ongoing					<ul style="list-style-type: none"> Phase 1/2 dose escalation study ongoing
NUV-868 (BET)	Currently under internal evaluation ⁴	Phase 1 ongoing					<ul style="list-style-type: none"> Completed Phase 1 monotherapy and Phase 1b combination studies in advanced solid tumors

BET: Bromodomain and Extra-Terminal motif; ESMO: European Society of Medical Oncology Congress; mIDH1: mutant isocitrate dehydrogenase 1; NSCLC: Non-small cell lung cancer; PDUFA: Prescription Drug User Fee Act; ROS1+: c-ros oncogene 1-positive; 1. Taletrectinib has been granted Orphan Drug Designation from the U.S. FDA for the treatment of patients with ROS1+ NSCLC and other NSCLC indications, and Breakthrough Therapy Designations by both the U.S. FDA and China's NMPA for the treatment of patients with locally advanced or metastatic ROS1+ NSCLC; worldwide development and commercial rights in-licensed from Daiichi Sankyo; rights to taletrectinib have been out-licensed in China and Japan. 2. Worldwide development and commercial rights in-licensed from Daiichi Sankyo, excluding Japan where Daiichi Sankyo retains development and commercial rights. 3. Includes patients with advanced solid tumors who previously received and progressed on or after treatment with Enhertu® and/or Trodelvy® per approved U.S. FDA labeling, human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer, metastatic castration-resistant prostate cancer (mCRPC), advanced pancreatic cancer, and platinum-resistant ovarian cancer. 4. Nuvation Bio has decided not to initiate a Phase 2 study of NUV-868 as a monotherapy or in combination with olaparib or enzalutamide in the advanced solid tumor indications that were part of the Phase 1 and Phase 1b study designs. The Company is evaluating next steps for the NUV-868 program, including further development in combination with approved products for indications in which BD2-selective BET inhibitors may improve outcomes for patients. 5. Based on results of the TRUST-I clinical study, China's NMPA approved taletrectinib for the treatment of adult patients with locally advanced or metastatic ROS1+ NSCLC who have or have not previously been treated with ROS1 TKIs.



\$250 million non-dilutive financing with Sagard validates taletrectinib's commercial potential and provides Nuvation Bio with path to profitability

\$150 million royalty financing

- Tiered, declining mid-single-digit royalty on annual U.S. net sales of taletrectinib:
 - **\$0 – \$600M:** 5.5%;
 - **\$600M – \$1B:** 3.0%
- Nuvation retains all annual U.S. net sales above \$1B (0% royalty) and after 1.6x – 2.0x return cap is met

\$100 million senior term loan

- \$50M funded upon U.S. FDA approval of taletrectinib
- \$50M available at Company's option for 12 months
- Interest-only to 5-year maturity at SOFR + 6.00%
- Single financial covenant: \$25M of minimum liquidity

Opportunistic transaction solidifies financial position without need to raise additional capital



Royalty financing fully funds U.S. launch of taletrectinib



Pro forma cash balance fully funds clinical-stage pipeline



Improves flexibility for strategic deployment of capital



Taletrectinib | ROS1i

Advanced ROS1+
NSCLC

NDA accepted by U.S.
FDA for priority review
in December 2024



Taletrectinib is a 3rd generation, potentially best-in-class ROS1 TKI obtained from the acquisition of AnHeart Therapeutics, which closed in April 2024



Commercial opportunity

- **NDA accepted by U.S. FDA (line agnostic, full approval) with PDUFA goal date of June 23, 2025**
- Recently approved in China for advanced ROS1+ NSCLC¹
- Breakthrough Therapy Designations in 1L & 2L (U.S. and China)²



Differentiated profile

- Potentially best-in-class efficacy and safety profile
- Durable responses and prolonged progression-free survival³
- Highly brain penetrant and active against common mutations



Strong partnerships

- AnHeart in-licensed taletrectinib from Daiichi Sankyo in 2018
- Maintain global rights except in China and Japan where rights have been out-licensed⁴



Taletrectinib has the highest overall response rate and median progression-free survival of any ROS1 inhibitor in the first line (TKI-naïve) setting

Study	Taletrectinib ² <i>Pooled TRUST-I & TRUST-II</i>	Repotrectinib ³ <i>TRIDENT-1</i>	Entrectinib ⁴ <i>ALKA-372-001, STARTRK-1, STARTRK-2</i>	Crizotinib ⁵ <i>PROFILE 1001</i>
n	160	71	168	53
cORR	89%	79%	68%	72%
Median DOR	44 months	34 months	21 months	25 months
Median PFS	46 months	36 months	16 months	19 months
IC-cORR ¹	77% (13/17)	89% (8/9)	80% (20/25)	N/A



Note: These data are derived from different clinical studies, with differences in study design and patient populations. No head-to-head studies have been conducted. Comparisons in a head-to-head study may yield different results. cORR: confirmed Overall response rate; DOR: Duration of response; IC-cORR: Intracranial confirmed overall response rate; PFS: Progression free survival. 1. Reflects IC-cORR in patients with measurable CNS tumors. 2. Perol et al., ESMO Presentation, 2024. 3. AUGTYRO prescribing information and Drilon et al., *New England Journal of Medicine*, 2024. 4. Drilon et al., *JTO Clinical Research Reports*, 2022. 5. XALKORI prescribing information and Shaw et al., *Annals of Oncology*, 2019.

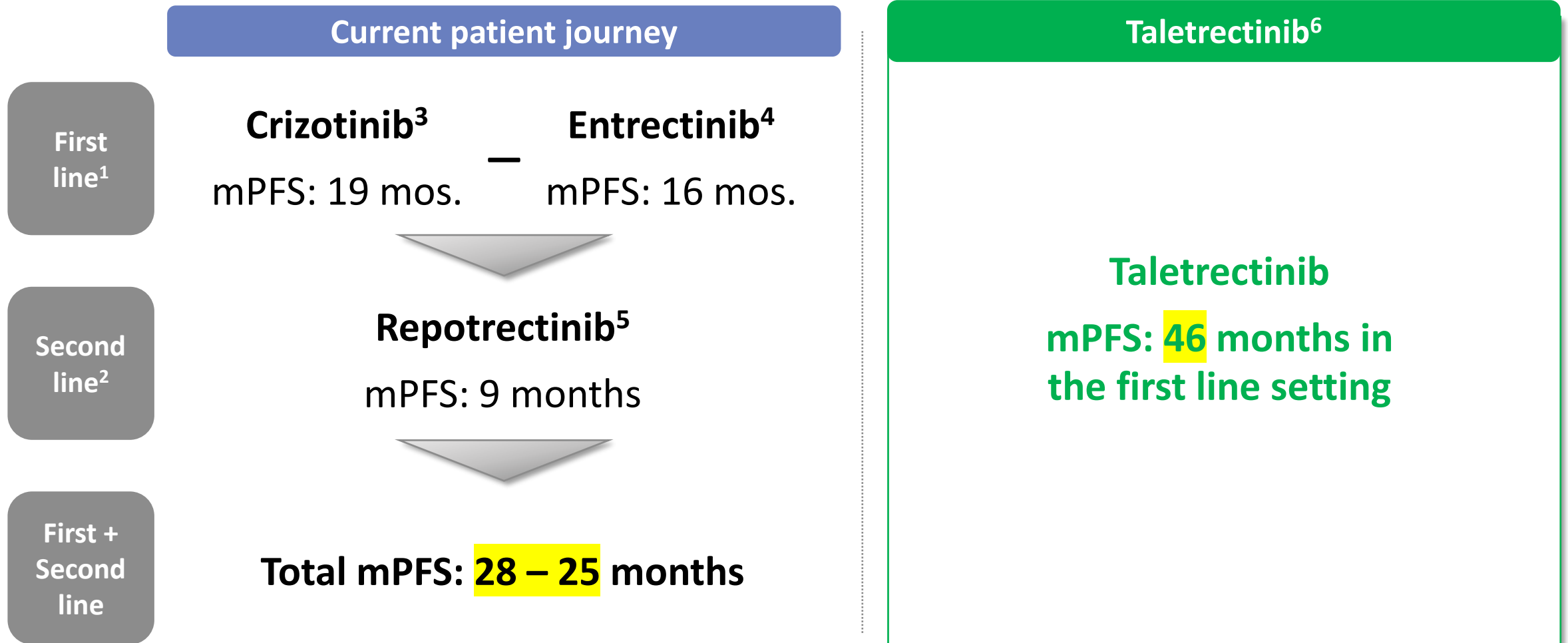
Few drugs in oncology have matched the 89% ORR and 46-month mPFS seen with taletrectinib in the first line (TKI-naïve) setting

Program	ORR	mPFS	mDOR
Taletrectinib¹	89%	46 months	44 months
RETEVMO (selpercatinib) ²	84%	22 months	20 months
AUGTYRO (repotrectinib) ³	79%	36 months	34 months
ALECENSA (alectinib) ⁴	79%	26 months	< 18 months
TAGRISSO (osimertinib) ⁵	77%	19 months	17 months
VITRAKVI (larotrectinib) ⁶	75%	--	33 months
XTANDI (enzalutamide) ⁷	59%	20 months	--



Note: Each product is approved for use in their respective indications and the data shown are derived from different clinical studies with differences in cancer types, study design and patient populations. mDOR: median Duration of response; ORR: Overall response rate; mPFS: median Progression-free survival. Source: 1. Perol et al., ESMO Presentation, 2024. 2. RETEVMO prescribing information; Dilon et al., Journal of Clinical Oncology, 2022. 3. AUGTYRO prescribing information; Dilon et al., New England Journal of Medicine, 2024. 4. ALECENSA prescribing information. 5. TAGRISSO prescribing information; Soria et al., New England Journal of Medicine, 2018. 6. VITRAKVI prescribing information. 7. Beer et al., New England Journal of Medicine, 2014; Beer et al., European Urology (Final Analysis of PREVAIL study), 2016.

The mPFS of patients given 1st and then 2nd gen. ROS1 inhibitors is still 18-21 months shorter than the mPFS of taletrectinib in the 1st line setting



Note: These data are derived from different clinical studies, with differences in study design and patient populations. No head-to-head studies have been conducted. Comparisons in a head-to-head study may yield different results. mPFS: Median progression-free survival; TKI: tyrosine kinase inhibitor. 1. Represents TKI-naïve patients. 2. Represents TKI-pretreated patients. 3. Shaw et al., *Annals of Oncology*, 2019. 4. Drilon et al., *JTO Clinical Research Reports*, 2022. 5. Drilon et al., *New England Journal of Medicine*, 2024. 6. Perol et al., ESMO Presentation, 2024 - median follow-up: 21 months (range: 4-47 months in the TKI-naïve population, data cutoff June 7, 2024).

PFS is considered the most important factor in making treatment decisions, followed by other efficacy parameters and then safety-related attributes

Nuvation Bio's market research suggests the highest patient risk is disease progression

Relative Importance of Product Attributes When Making Tx Decisions for ROS1+ NSCLC

100-point allocation

Favorable efficacy and safety profile

Relevant Product Statistics

	Product Attribute	Overall (n=146)	Taletrectinib	AUGTYRO™ (repotrectinib) 40 mg capsules	ROZLYTREK™ entrectinib 100mg 200mg capsules	XALKORI CRIZOTINIB
1	Progression-Free Survival (PFS)	21	46 months	36 months	16 months	19 months
2	Overall Response Rate (ORR)	15	89%	79%	68%	72%
3	Efficacy treating acquired mutation	12	62% ORR (2L G2032R)	59% ORR (2L G2032R)	–	–
4	Durability of Response	11	44 months	34 months	21 months	25 months
5	Overall Tolerability	9	–	–	–	–
6	Efficacy Treating Brain Metastases (IC-ORR)	9	77%	89%	80%	–
7	Incidence of Overall Grade 3/4 AEs	9	52%	51%	60%	--
8	Product Discontinuation Rate	5	7%	7%	9%	12%
9	Incidence of CNS AEs	4	(20% Dysgeusia) (21% Dizziness)	(54% Dysgeusia) (65% Dizziness)	(44% Dysgeusia) (38% Dizziness)	(26% Dysgeusia) (20% Dizziness)
10	Treatment Reduction Rate	4	29%	38%	29%	11%
11	Frequency of Dosing	3	600mg QD	160mg BID ¹	600mg QD	250mg BID

■ Efficacy-Related ■ Safety-Related ■ Dosing and RoA Related

Note: These data are derived from different clinical studies, with differences in study design and patient populations. No head-to-head studies have been conducted. Comparisons in a head-to-head study may yield different results. No significant differences between practice setting, practice location or treater volume at 95% CI; Source: Internal market research. Perol et al., ESMO Presentation, 2024. Drilon et al., *New England Journal of Medicine*, 2023; Drilon et al., *JTO Clinical Research Reports*, 2022; Shaw et al., *Annals of Oncology*, 2019. Prescribing information for AUGTYRO, ROZLYTREK, and XALKORI. 1. Recommended dosing of 160mg QD for 14 days, then increased to 160mg BID.



Taletrectinib has the highest overall response rate and median progression-free survival of any ROS1 inhibitor in the second line (TKI-pretreated) setting

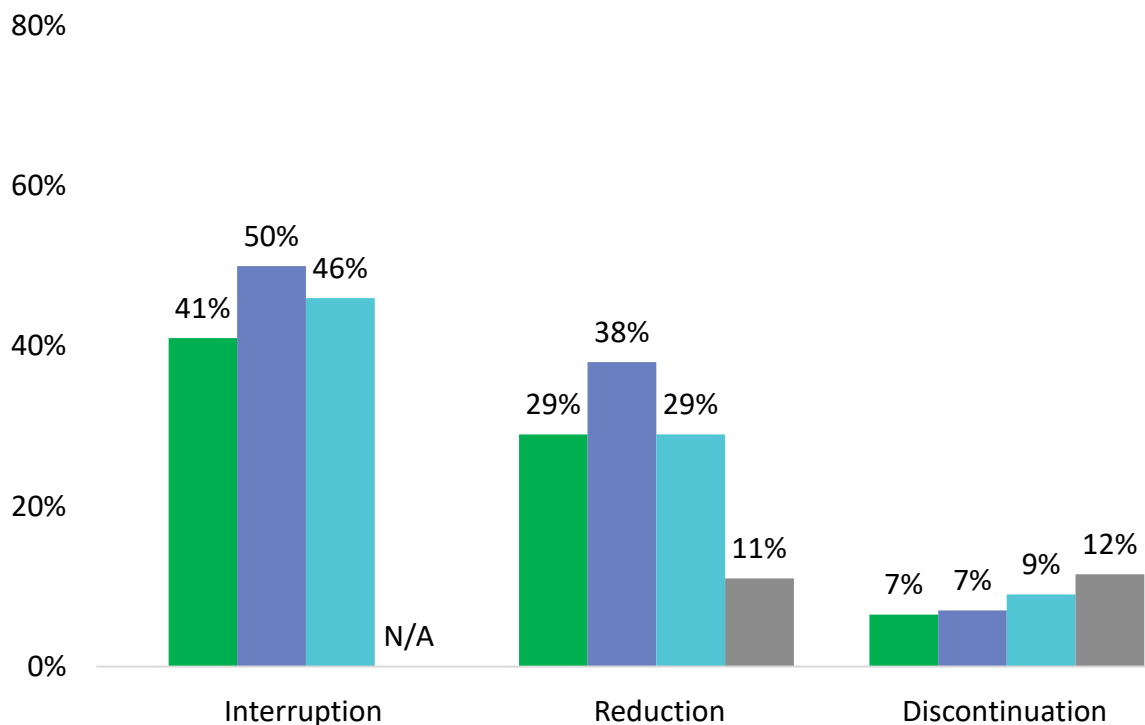
Study	Taletrectinib ² <i>Pooled TRUST-I & TRUST-II</i>	Repotrectinib ³ <i>TRIDENT-1</i>	Zidesamtinib ⁴ <i>ARROS-1</i>	
n	113	56	Crizotinib & entrectinib 17	Repotrectinib 3
cORR	56%	38%	53%	0%
Median DOR	17 months	15 months	N/A	
Median PFS	10 months	9 months	N/A	
G2032R cORR	62% (8/13)	59% (10/17)	62% (16/26)	
IC-cORR ¹	66% (21/32)	38% (5/13)	50% (4/8)	



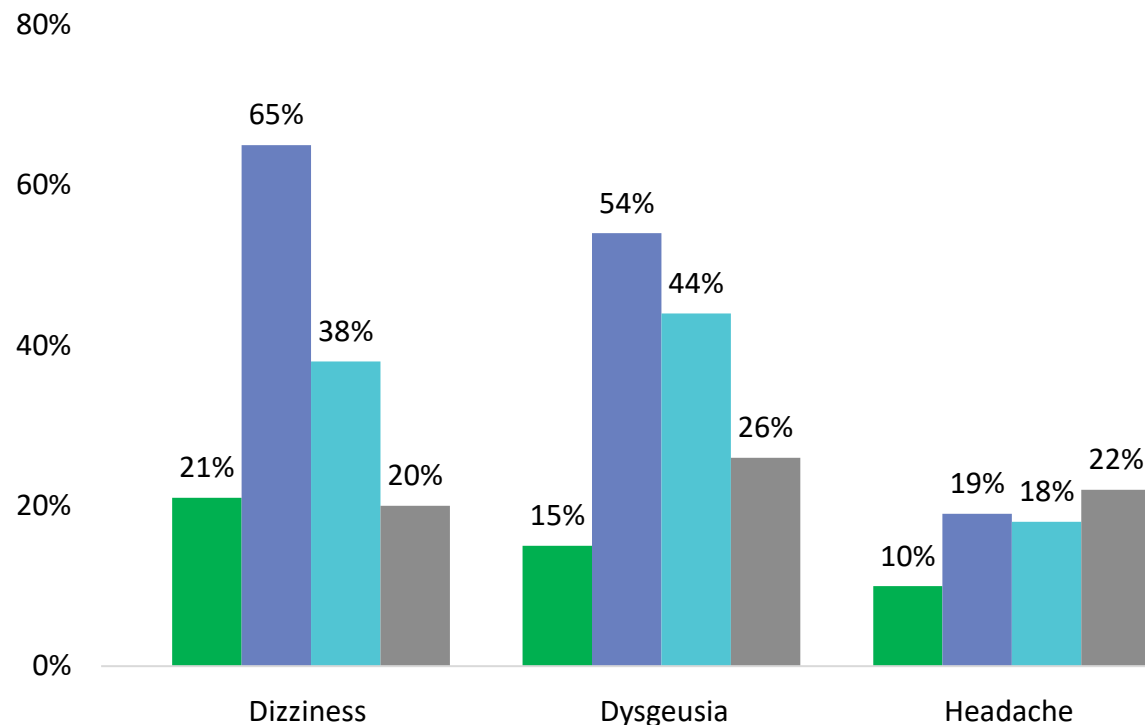
Note: These data are derived from different clinical studies, with differences in study design and patient populations. No head-to-head studies have been conducted. Comparisons in a head-to-head study may yield different results. cORR: confirmed Overall response rate; DOR: Duration of response; IC-ORR: Intracranial confirmed overall response rate; PFS: Progression free survival. 1. Reflects IC-cORR in patients with measurable CNS tumors. 2. Perol et al., ESMO Presentation, 2024; includes patients previously treated with crizotinib or entrectinib. 3. Drilon et al., *New England Journal of Medicine*, 2024; includes 98% of patients previously treated with crizotinib or entrectinib. 4. Besse et al., ESMO Presentation, 2024; includes 20 response evaluable patients who received 1 prior ROS1 TKI; includes nine confirmed partial responses in patients previously treated with: crizotinib (n=11), entrectinib (n=6, implied based on standard medical practices and available data), and repotrectinib (n=3); median DOR and median PFS "N/A" for subgroup of all patients who received 1 prior ROS1 TKI; G2032R cORR and IC-cORR include patients that received ≥ 2 prior ROS1 TKIs.

Taletrectinib data show an encouraging safety profile relative to approved ROS1 TKIs, including fewer dose modifications and low rates of neuro AEs

Dose Modification



Neurological AEs



■ Taletrectinib¹
■ Repotrectinib²
■ Entrectinib²
■ Crizotinib²



Note: These data are derived from different clinical studies, with differences in study design and patient populations. No head-to-head studies have been conducted. Comparisons in a head-to-head study may yield different results. AE: Adverse Event. 1. Perol et al., ESMO Presentation, 2024. 2. AUGTYRO prescribing information (includes patients with NTRK+ solid tumor), ROZLYTREK prescribing information (includes patients with NTRK+ solid tumor), and XALKORI prescribing information (combined analysis of Study 1 & 2 of patients with ALK+ NSCLC patients; Headache adverse event rate from Study 1 only).

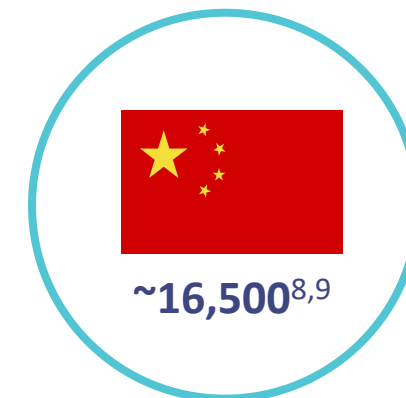
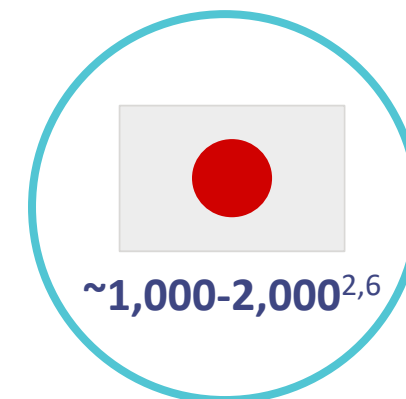
ROS1+ NSCLC market represents a sizeable commercial opportunity; 1st generation ROS1 TKIs with ~1.5-year mPFS still sold ~\$500 million in 2023

Key takeaways

- NSCLC accounts for ~80-85%¹ of all lung cancers
- ROS1+ lung cancer represents ~2%² of new NSCLC cases
- There are currently three therapies approved in the U.S. to treat patients with ROS1+ NSCLC:

- 1st gen.
 - Crizotinib (Pfizer, approved 2016³)
 - Entrectinib (Roche, approved 2019⁴)
- 2nd gen.
 - Repotrectinib (Bristol-Myers Squibb, approved 2023⁵)

Estimated newly diagnosed patient population

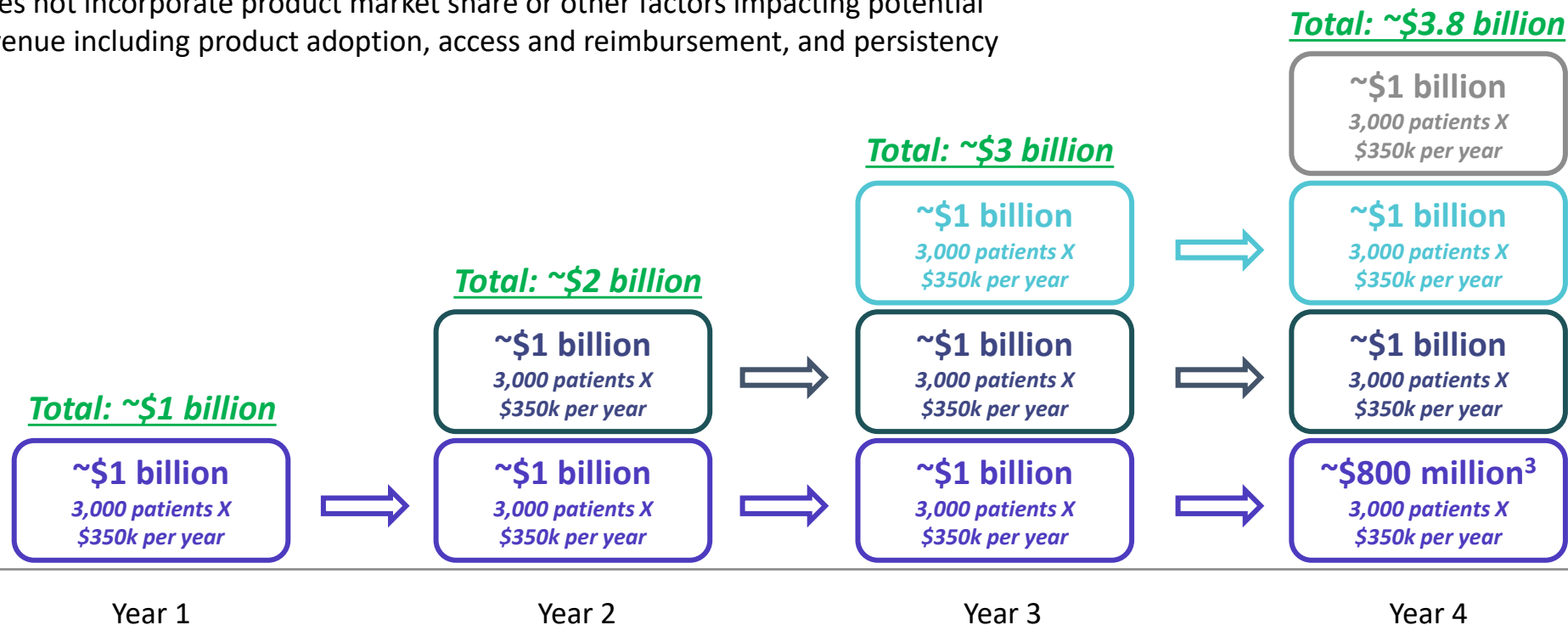


Taletrectinib's median progression-free survival of almost four years generates a potentially substantial market opportunity

Theoretical maximum U.S. ROS1+ NSCLC market opportunity

Key assumptions and commentary

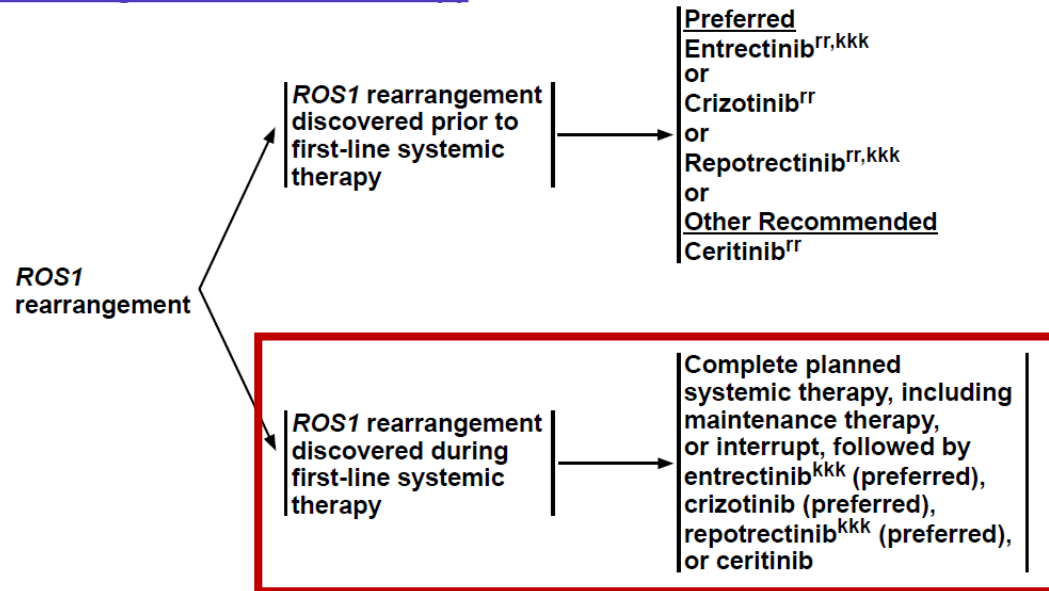
- Incidence: ~3,000¹ newly diagnosed ROS1+ NSCLC patients in the U.S. each year
- Pricing: ~\$350,000² per year, based on gross repotrectinib annual price
- Does not incorporate product market share or other factors impacting potential revenue including product adoption, access and reimbursement, and persistency



New NCCN Guidelines (as of January 7, 2025) now specifically contraindicate IO/chemo and recommend ROS1 TKIs for ROS1+ NSCLC

NCCN Guidelines 2024

ROS1 Rearrangement: First Line Therapy

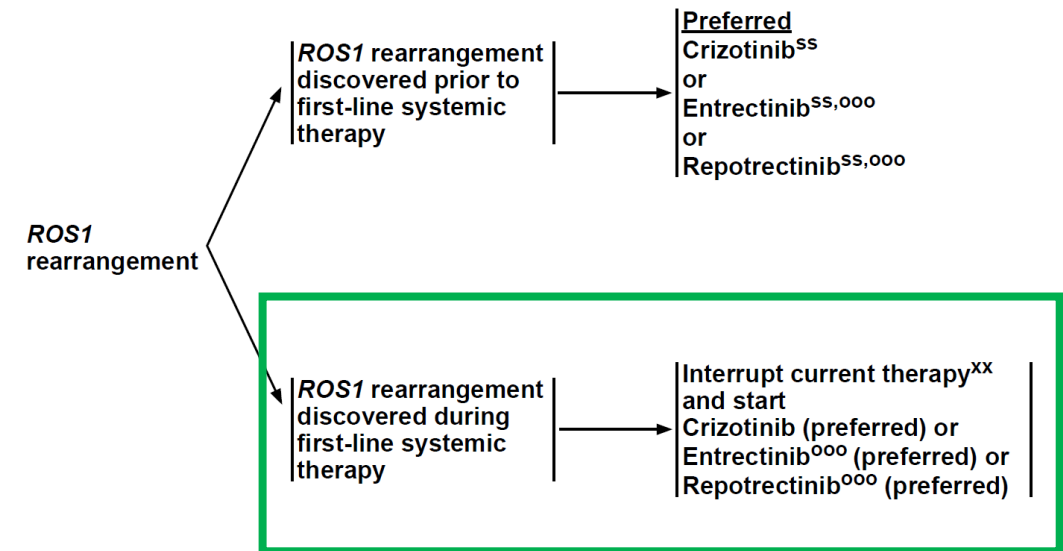


PD-L1 Positive (>1%): First Line Therapy

CONTRAINDICATIONS for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents; some oncogenic drivers (ie, EGFR exon 19 deletion or L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

NCCN Guidelines 2025

ROS1 Rearrangement: First Line Therapy



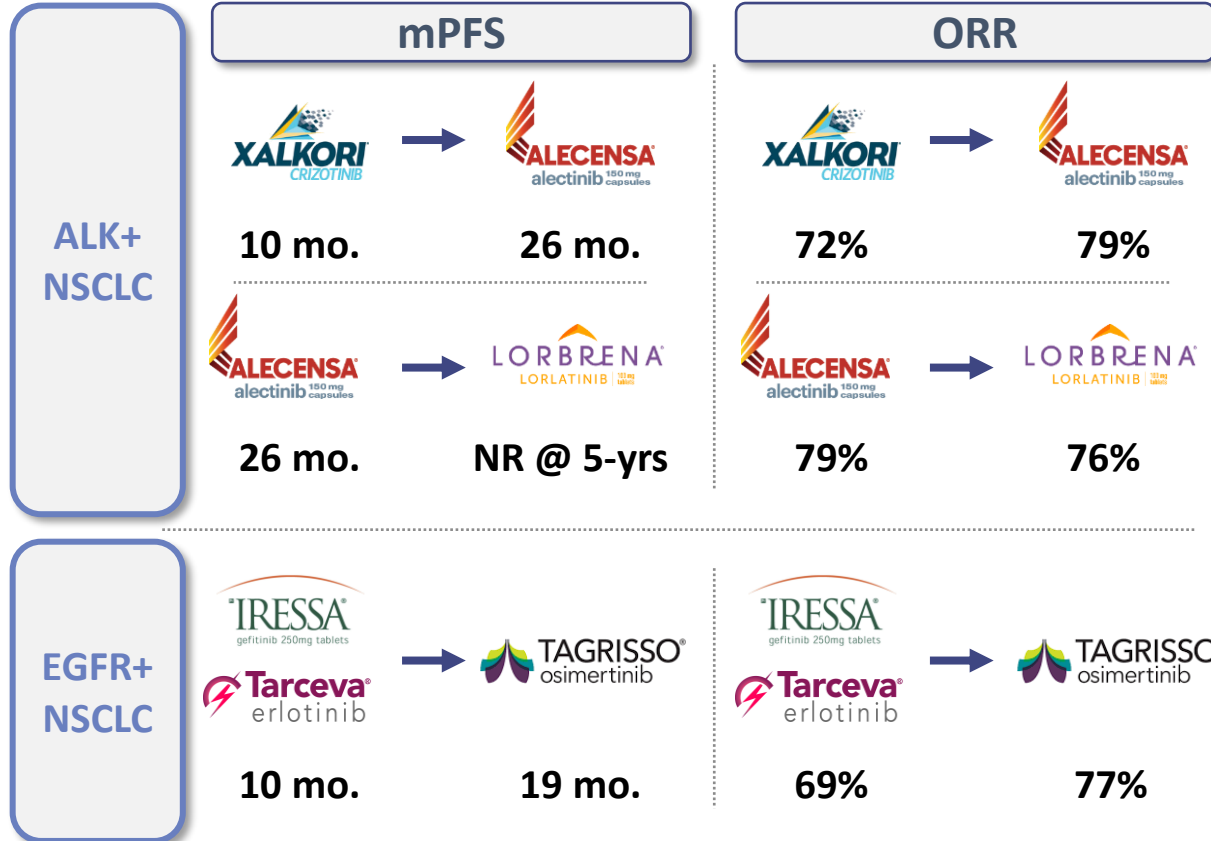
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CONTRAINDICATIONS for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents; some oncogenic drivers (ie, EGFR exon 19 deletion or L858R; ALK, RET, or ROS1 rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

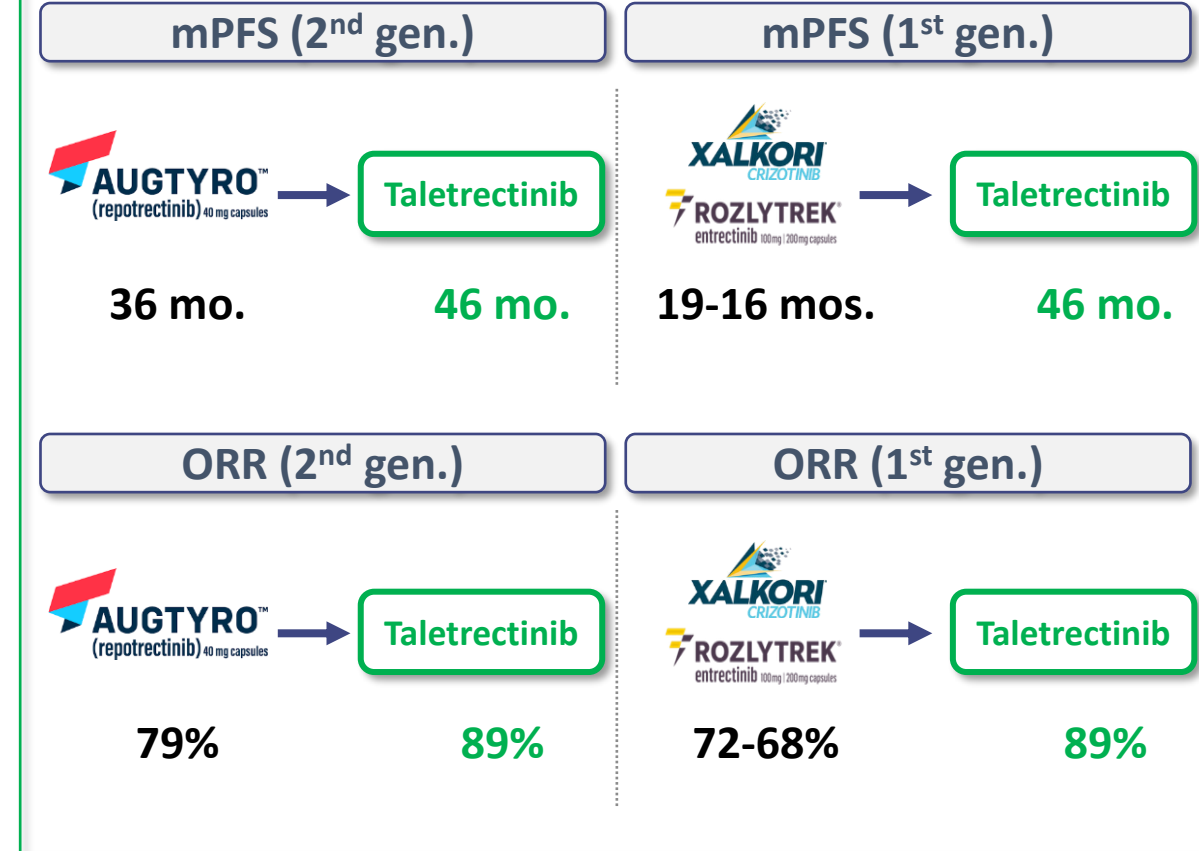


Taletrectinib has greater numerical benefits over its competitors than the leaders of the EGFR and ALK markets over their nearest competitors

Precedent NSCLC markets (1L)¹



ROS1+ NSCLC (1L)²



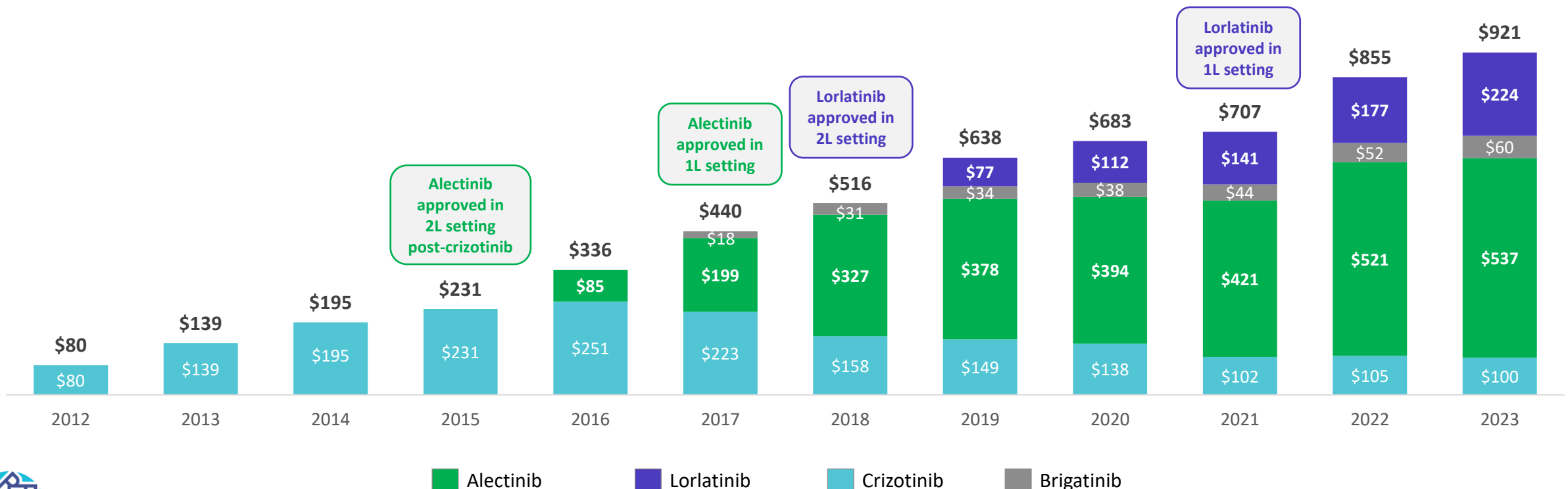
Note: These data are derived from different clinical studies, with differences in study design and patient populations. No head-to-head studies have been conducted. Comparisons in a head-to-head study may yield different results. ORR: Overall response rate; mPFS: median Progression-free survival. 1. ALECENSA prescribing information (ALEX study results comparing alectinib to crizotinib); LORBRENA prescribing information; TAGRISSEO prescribing information. 2. Perol et al., ESMO Presentation, 2024; AUGTYRO prescribing information and Drilon et al., *New England Journal of Medicine*, 2024; Drilon et al., *JTO Clinical Research Reports*, 2022; XALKORI prescribing information and Shaw et al., *Annals of Oncology*, 2019.

Good, but not great drugs (neither alectinib or lorlatinib have best-in-class efficacy and safety), have still increased the ALK market ~4x

Total Net U.S. Revenue (ALK+ NSCLC TKIs)

\$ in millions

Alectinib TKI Market Share:	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8
	0%	19%	37%	54%	55%	56%	55%	57%



Source: Evaluate Pharma, Earning Reports from Pfizer (crizotinib, lorlatinib), Roche (alectinib), Takeda (brigatinib) from 2012 to 2023.

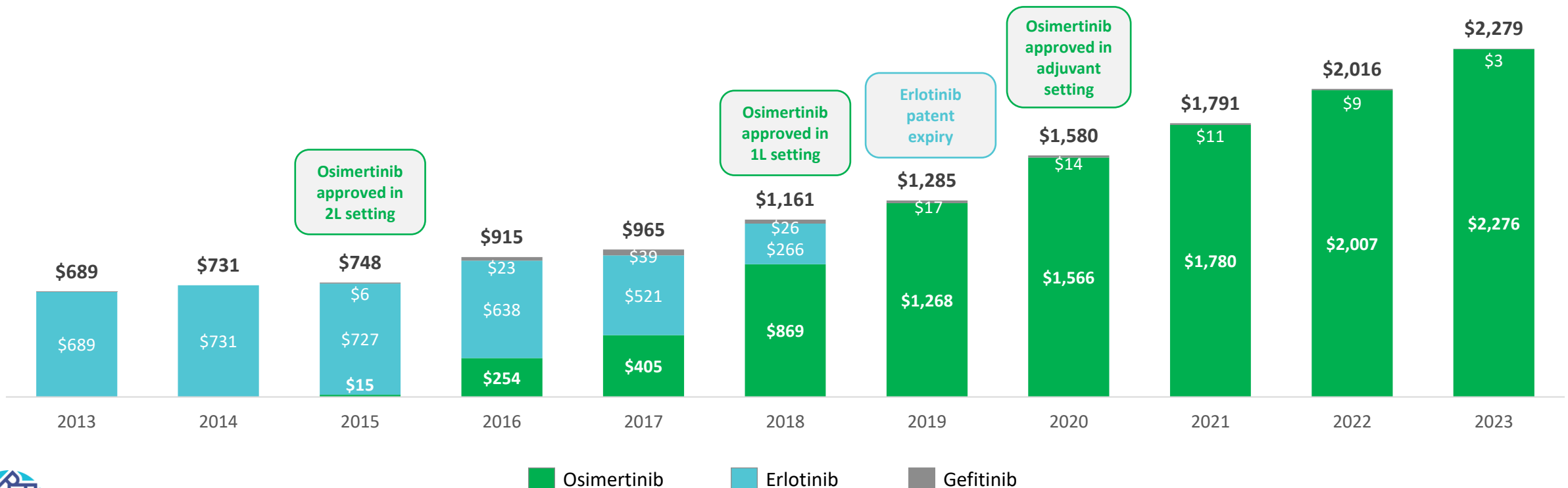
Notes: Total U.S. crizotinib net revenue shown for illustrative purposes (approved for ALK-positive NSCLC in 2011 and ROS1-positive NSCLC in 2016). Net revenue of ceritinib in ALK+ NSCLC is minimal and not broken out by U.S. only – therefore not included in this analysis.

Osimertinib captured >90% market share after only increasing mPFS by ~9 months and ORR by ~8%; US EGFR market has grown ~3x since its launch

Total Net U.S. Revenue (EGFR+ NSCLC TKIs)

\$ in millions

Osimertinib TKI Market Share:	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8
	1%	21%	32%	61%	83%	92%	95%	95%



Source: Evaluate Pharma, Earning Reports from AstraZeneca (Osimertinib, erlotinib) and Roche (gefitinib) from 2013 to 2023.

Notes: Net revenue of afatinib are not available as Boehringer Ingelheim is a private company. Net revenue of dacomitinib in EGFR+ NSCLC is minimal and therefore not included in this analysis.

Nuvation Bio has hired a commercial team with blockbuster experience primed to launch taletrectinib into favorable market dynamics

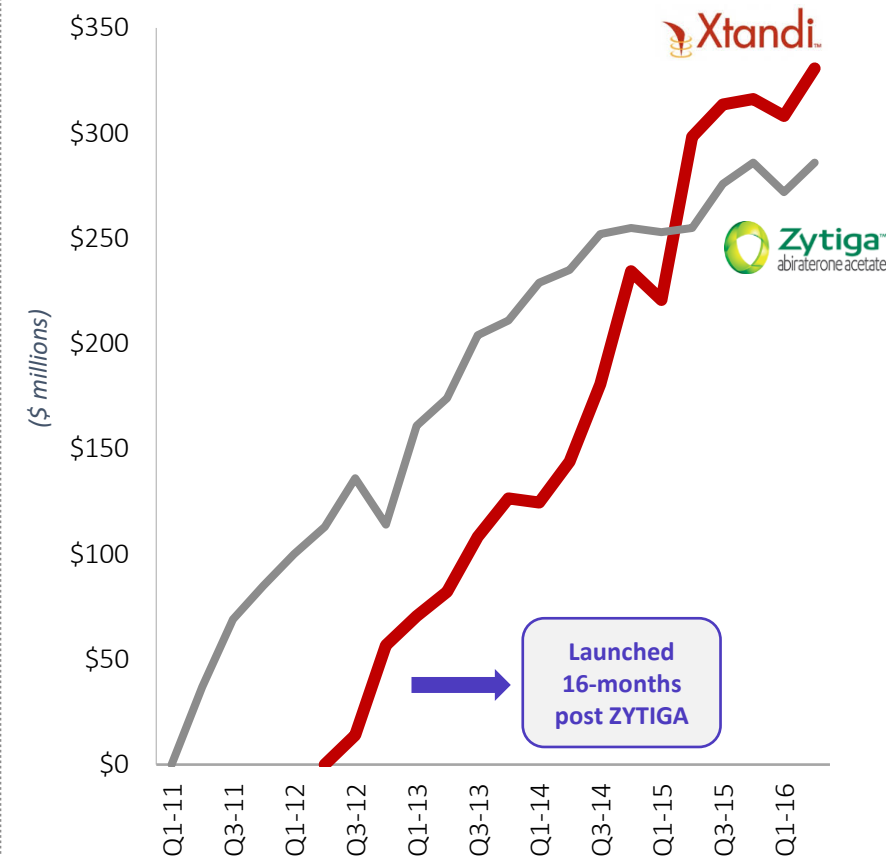
Commercial launch dynamics

- **Chief Commercial Officer and team comprised of Medivation alumni**
 - XTANDI sales surpassed ZYTIGA with a fraction of the sales force
- **Positive momentum for targeted therapies in ROS1+ NSCLC**
 - NCCN now recommends interrupting IO/chemo and starting ROS1 TKIs
 - Improvement in rate of testing and shift toward RNA-based testing
- **Launching taletrectinib into dormant market**
 - Competitive TKIs losing patients too fast to build sales momentum
 - Large pharma has underpromoted and deprioritized ROS1+ NSCLC
- **Internal preparation for commercial launch well underway**
 - Commercial leadership team in place
 - Sales force properly sized and identified; to be hired closer to launch



Source: Evaluate Pharma, SEC filings and press releases for Johnson & Johnson, Bristol Myers Squibb, Pfizer, and Roche; IQVIA.

XTANDI vs. ZYTIGA sales



Safusidenib | mIDH1i

Diffuse
IDH1-mutant glioma

Entering pivotal
studies in 2025



Safusidenib is a potentially best-in-class mIDH1 inhibitor for diffuse IDH1-mutant glioma, which was also obtained from the acquisition of AnHeart Therapeutics



Unmet need

- People diagnosed with glioma are in need of better treatment options



Validated target

- Vorasidenib approved to treat glioma in Aug. '24¹
- 15% royalty on future U.S. sales of vorasidenib acquired for \$905M²



Differentiated profile

- Encouraging early data **including 2 CRs³**
- Potential in broad population
- Limited competition



Global rights

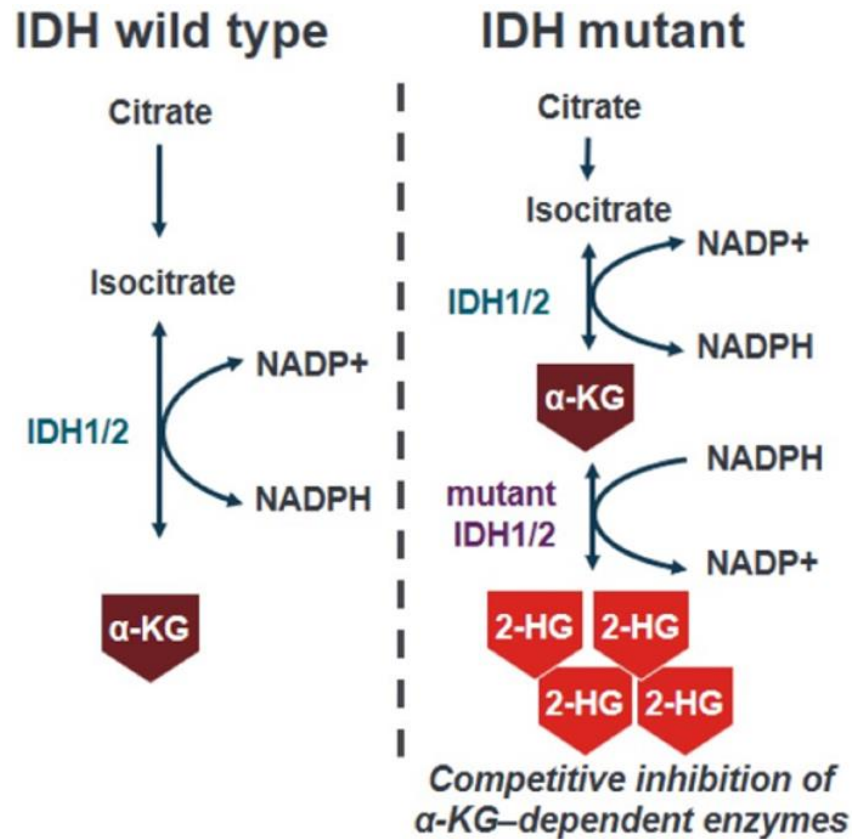
- AnHeart in-licensed safusidenib from Daiichi Sankyo in 2020
- Daiichi Sankyo retains rights in Japan⁴



CR: Complete response. mIDH1: mutant IDH1; 1. In August 2024, the U.S. FDA approved Servier Pharmaceutical's vorasidenib for the treatment of grade 2 astrocytoma or oligodendroglioma following surgery. 2. In May 2024, Royalty Pharma agreed to acquire a 15% royalty on U.S. net sales of vorasidenib in low grade diffuse glioma for \$905 million from Agios Pharmaceuticals; Agios will retain 3% of the 15% royalty on sales above \$1 billion and the right to receive a \$200 million milestone payment from Servier Pharmaceuticals upon U.S. FDA approval. 3. Natsume et al., *Neuro-Oncology*, 2022; two complete responses represent one complete response in a grade 4 astrocytoma and one complete response in the target lesions of a grade 3 oligodendroglioma (with stable disease in non-target lesions). 4. Worldwide development and commercial rights in-licensed from Daiichi Sankyo, excluding Japan where Daiichi Sankyo retains development and commercial rights.

IDH mutations in glioma lead to accumulation of oncometabolite 2-HG, which drives cancer growth and creates an immunosuppressive tumor microenvironment

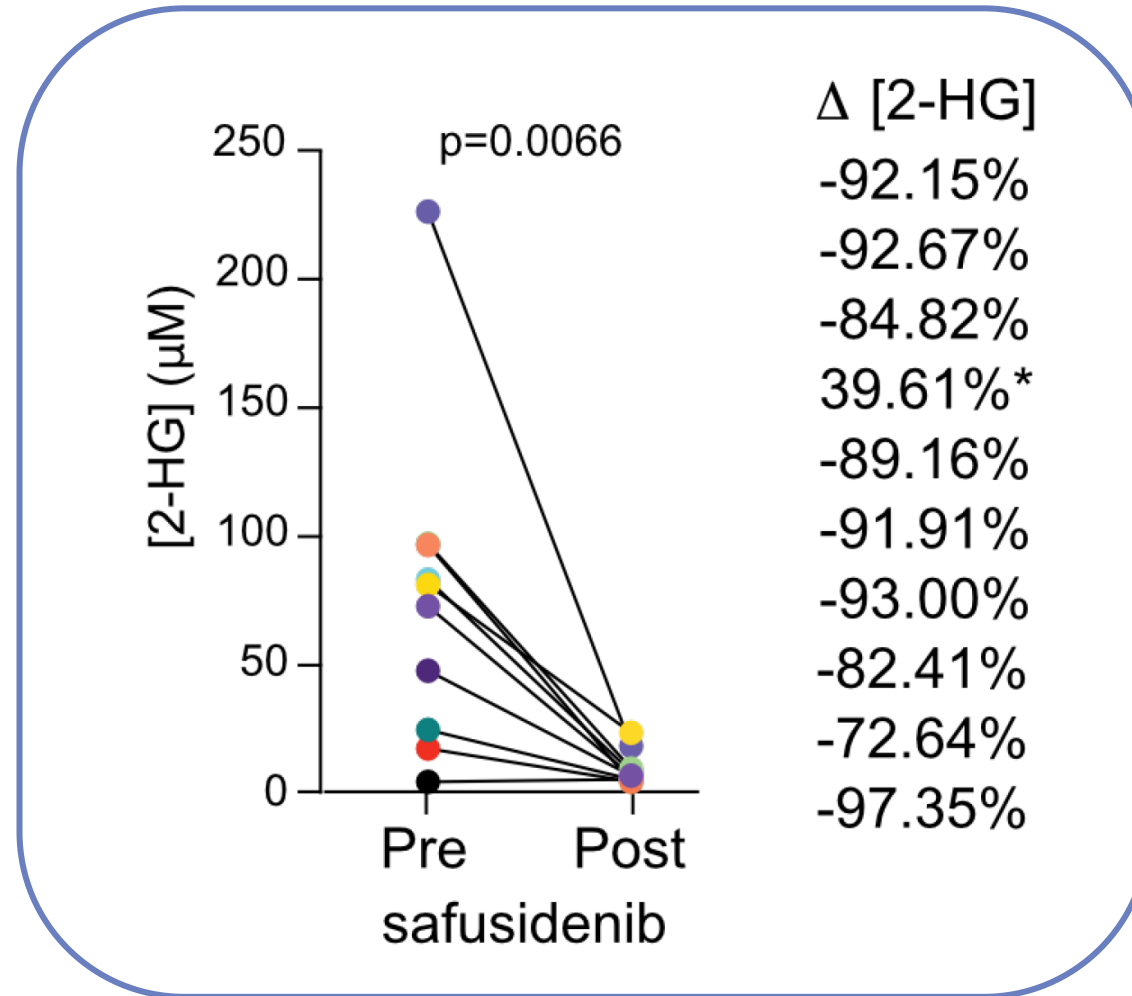
Mechanism of Action: IDH mutations



- Gain-of-function mutation confers novel enzymatic activity, which convert α-KG to 2-HG
 - Epigenetic dysregulation with genome-wide hypermethylation (G-CIMP)
- **2-HG impairs cellular differentiation**
- **2-HG creates an immunosuppressive tumor microenvironment**
- Grade 2 and 3 glioma:
 - 95-97% IDH1 mutations
 - 3 – 5% IDH2 mutations



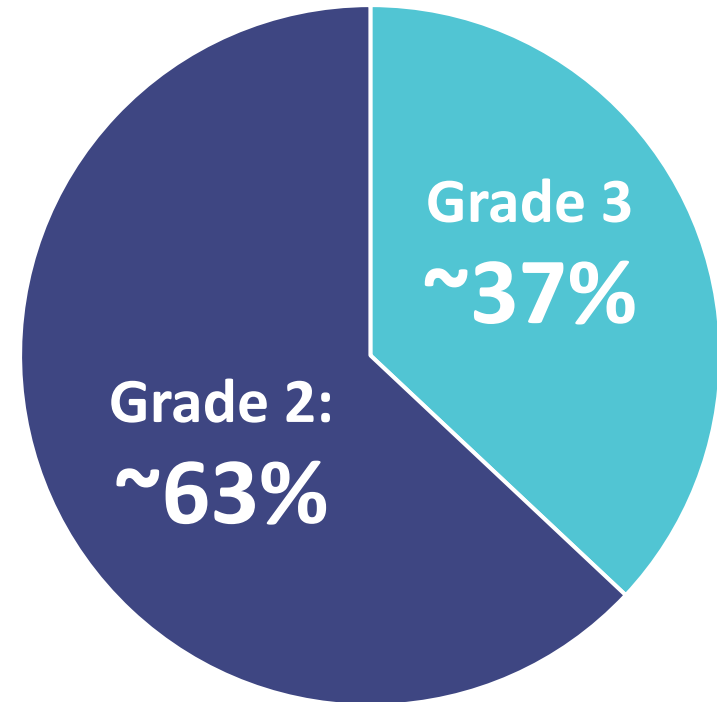
Safusidenib crosses the blood-brain-barrier, inhibits mIDH1, and suppresses 2-HG levels



The diffuse IDH1-mutant glioma market represents a sizeable commercial opportunity, particularly because patients can remain on drug for years

~13.3K – 18.3K

people living with diffuse IDH1-mutant glioma in the U.S.



Royalty Pharma's acquisition of rights to Agios Pharmaceuticals' royalty on U.S. net sales of vorasidenib validates safusidenib's market potential

Transaction Overview

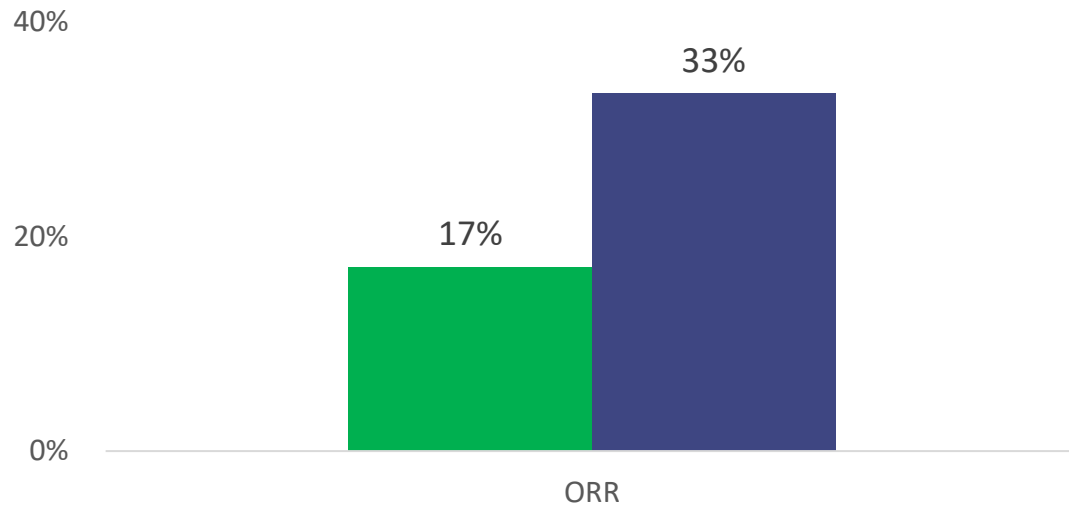
- In May 2024, Royalty Pharma announced it acquired an interest in Agios Pharmaceuticals' royalty on U.S. net sales of Servier's vorasidenib
- Royalty Pharma paid Agios **\$905 million** in cash upon FDA approval of vorasidenib for a **15% royalty on annual U.S. net sales up to \$1 billion**
 - Will receive a 12% royalty and Agios will retain a 3% royalty on potential U.S. net sales >\$1 billion
- **Royalty Pharma forecasts vorasidenib peak U.S. net sales of >\$1 billion**
- **Implies vorasidenib valuation of ~\$6 billion**



Safusidenib early-stage data showed higher response rates than vorasidenib in low-grade (non-enhancing) and high-grade (enhancing) diffuse mIDH1 glioma

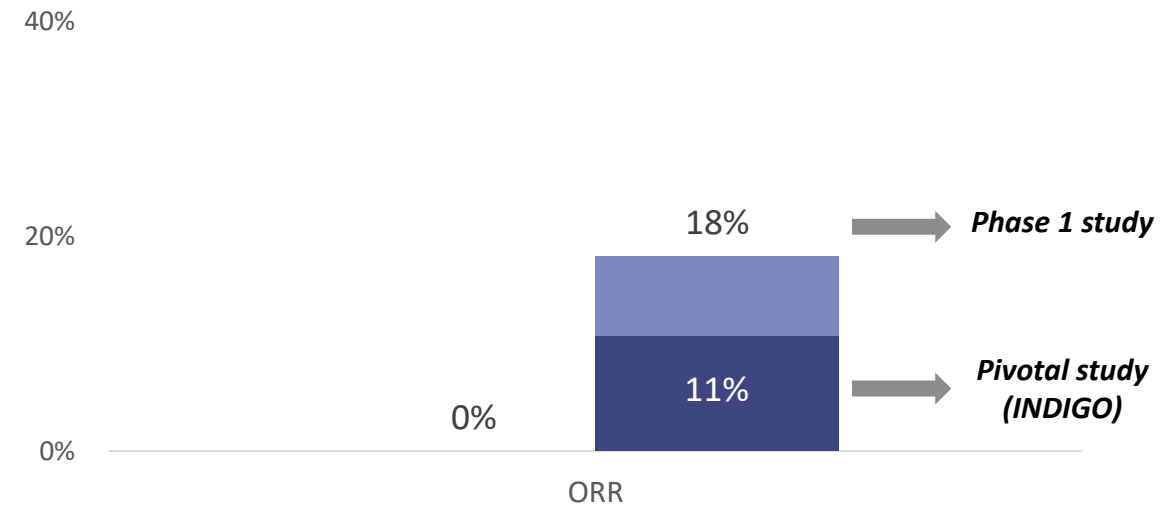
Safusidenib¹

Enhancing glioma n=35
Non-enhancing glioma n=12



Vorasidenib²

Enhancing glioma n=30
Non-enhancing glioma n=22



■ Enhancing ■ Non-enhancing



ORR: Overall response rate. Note: Information depicts response rates with IDH inhibitor in IDH1-mutant gliomas in Phase 1 studies; Enhancing and non-enhancing glioma was assessed by Response Assessment in Neuro-Oncology (RANO) and RANO-LGG, respectively. Contrasting enhancement is generally associated with a higher degree of malignancy. These data are derived from different clinical studies, with differences in study design and patient populations. No head-to-head studies have been conducted. Comparisons in a head-to-head study may yield different results. 1. Natsume et al., *Neuro-Oncology*, 2023. 2. Mellinghoff et al., *Clinical Cancer Research*, 2021 and Mellinghoff et al., *New England Journal of Medicine*, 2023.

Two complete responses observed lasting 174 weeks (grade 4 astrocytoma) and 95 weeks (grade 3 oligodendroglioma), with patients still on treatment at data cutoff

Safusidenib¹

RANO responses	Enhancing n=35	Non-enhancing n=12
Overall response	6 (17%)	4 (33%)
Complete response²	2 (6%)	0 (0%)
Partial response	4 (11%)	1 (8%)
Minor response	N/A	3 (25%)
Stable disease	11 (31%)	8 (67%)
Progressive disease	17 (49%)	0 (0%)
Not evaluable	1 (3%)	0 (0%)

Vorasidenib³

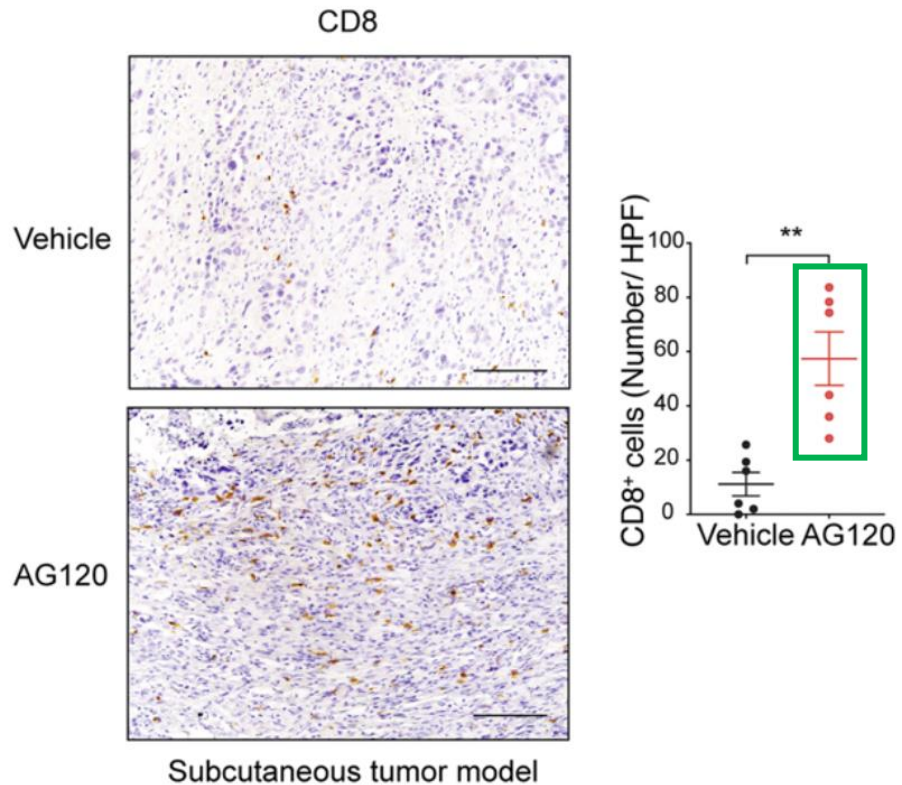
RANO responses	Enhancing n=30	Non-enhancing n=22
Overall response	0 (0%)	4 (18%)
Complete response	0 (0%)	0 (0%)
Partial response	0 (0%)	1 (5%)
Minor response	N/A	3 (14%)
Stable disease	17 (57%)	16 (73%)
Progressive disease	12 (40%)	2 (9%)
Not evaluable	1 (3%)	0 (0%)



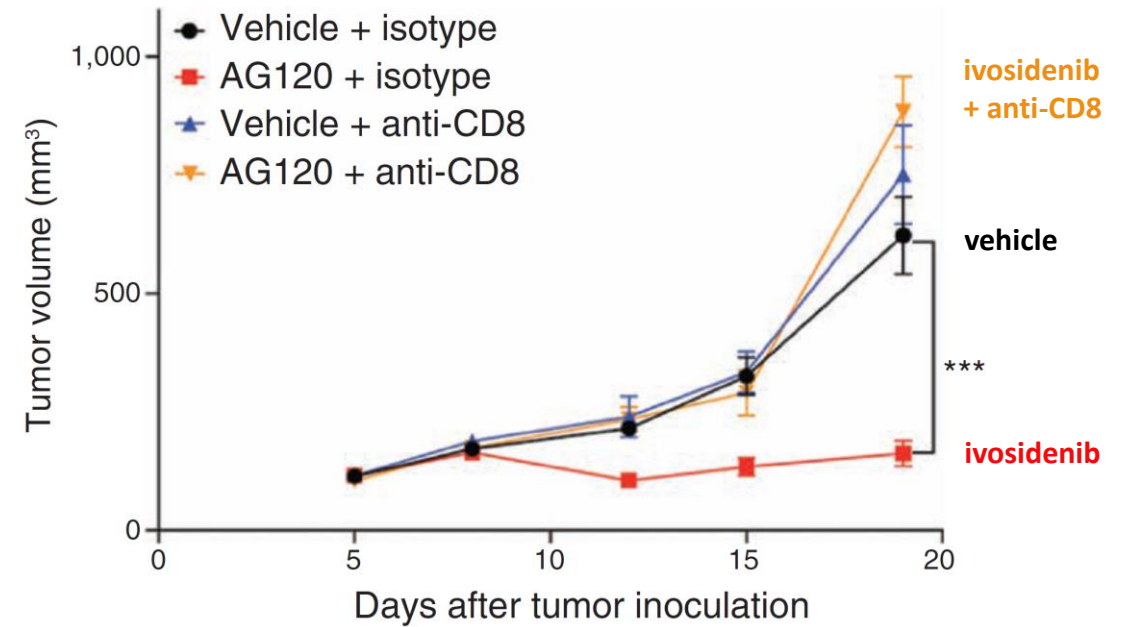
Note: Information depicts response rates with IDH inhibitor in IDH1-mutant gliomas in Phase 1 studies; Enhancing and non-enhancing glioma was assessed by Response Assessment in Neuro-Oncology (RANO) and RANO-LGG, respectively. Minor response not applicable in enhancing glioma patients assessed by RANO. Contrasting enhancement is generally associated with a higher degree of malignancy. These data are derived from different clinical studies, with differences in study design and patient populations. No head-to-head studies have been conducted. Comparisons in a head-to-head study may yield different results. 1. Natsume et al., Neuro-Oncology, 2023. 2. Two complete responses represent one complete response in a grade 4 astrocytoma and one complete response in the target lesions of a grade 3 oligodendroglioma (with stable disease in non-target lesions). 3. Mellinghoff et al., Clinical Cancer Research, 2021.

Another IDH1 inhibitor (ivosidenib) blocks 2-HG synthesis and increases tumor infiltrating CD8+ T cells, demonstrating augmentation of immunity

Ivosidenib promotes tumor CD8+ T-cell infiltration¹



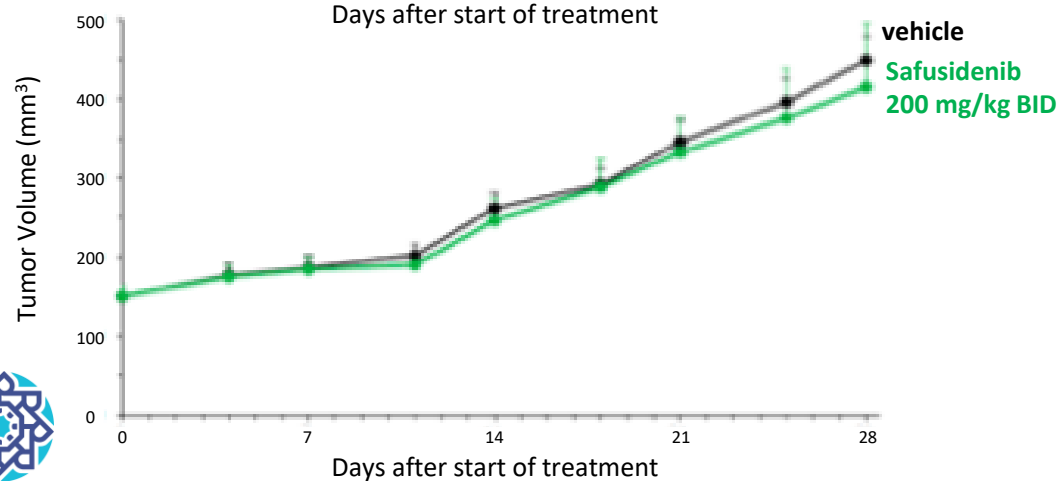
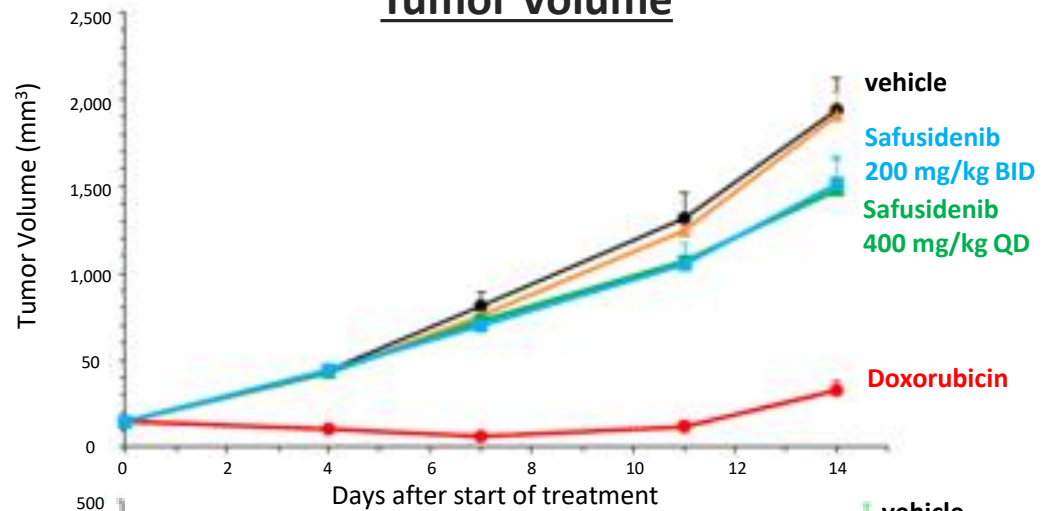
Depletion of CD8+ T-cells blocks anti-tumor activity of ivosidenib²



Safusidenib, unlike vorasidenib, shows far greater activity in mice with an intact immune system rather than immunocompromised mice, suggesting immune MOA

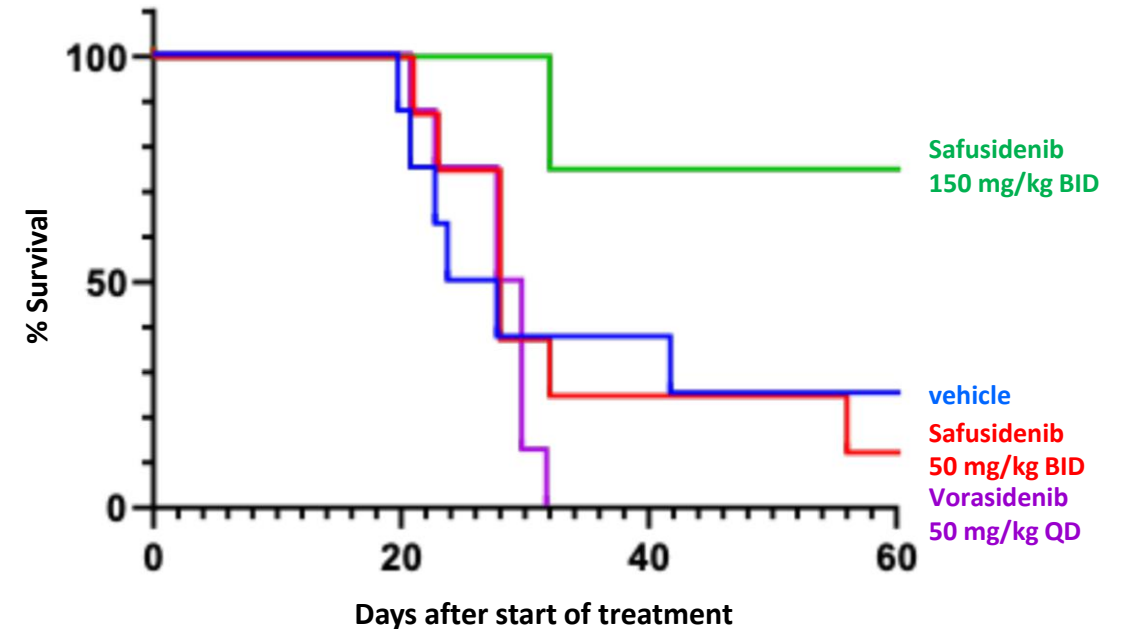
Xenografts in immunodeficient mice

Tumor Volume



Xenografts in immunocompetent mice

Survival



Five of the top eight adverse events seen in a Phase 1 study of safusidenib are consistent with an immune-related MOA

TEAE: n (%); Preferred Term ^{1,2}	All grades	Grade 3
Skin hyperpigmentation	25 (53)	N/A
Diarrhea	22 (47)	2 (4)
Pruritus	14 (30)	0
Alopecia	13 (28)	0
Arthralgia	13 (28)	1 (2)
Nausea	12 (26)	0
Headache	11 (23)	1 (2)
Rash	11 (23)	0



NUV-1511 | DDC

Advanced solid
tumors

Phase 1/2 study ongoing



Nuvation Bio's drug-drug conjugate (DDC) platform is a potentially revolutionary advance beyond ADCs

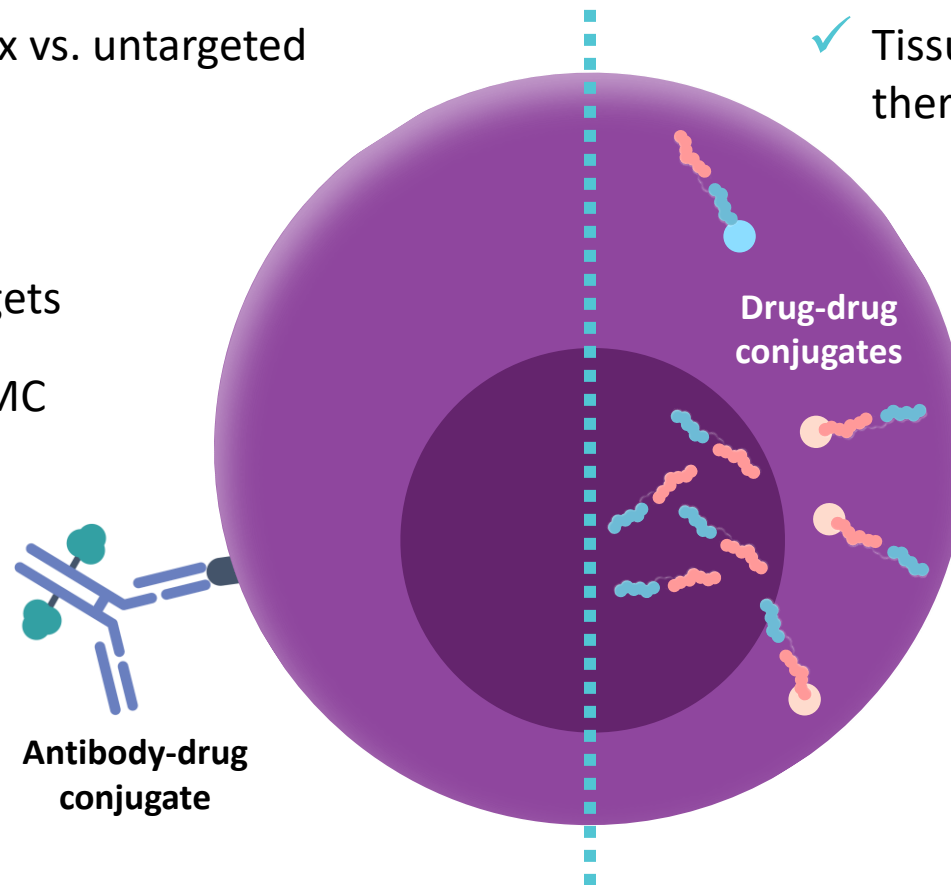
Antibody-drug conjugates

- ✓ Improves therapeutic index vs. untargeted warhead
- ✗ IV delivery
- ✗ Limited to cell-surface targets
- ✗ Complex and expensive CMC



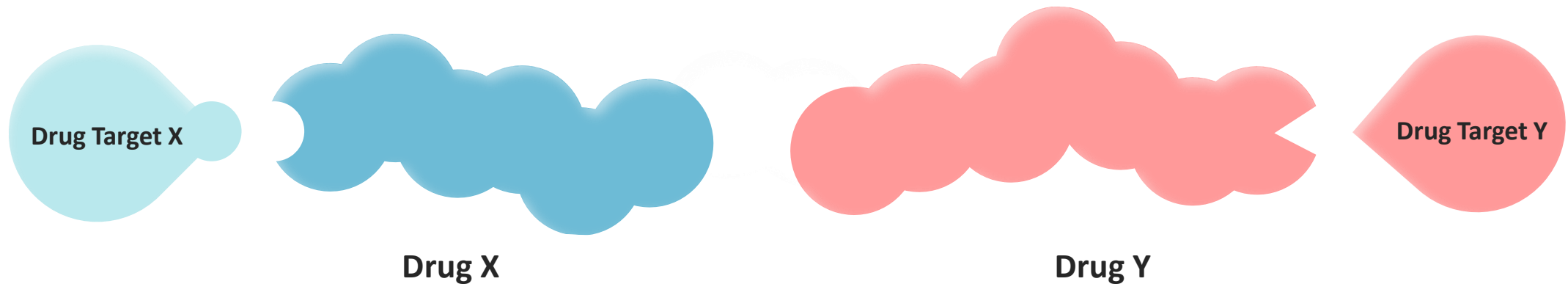
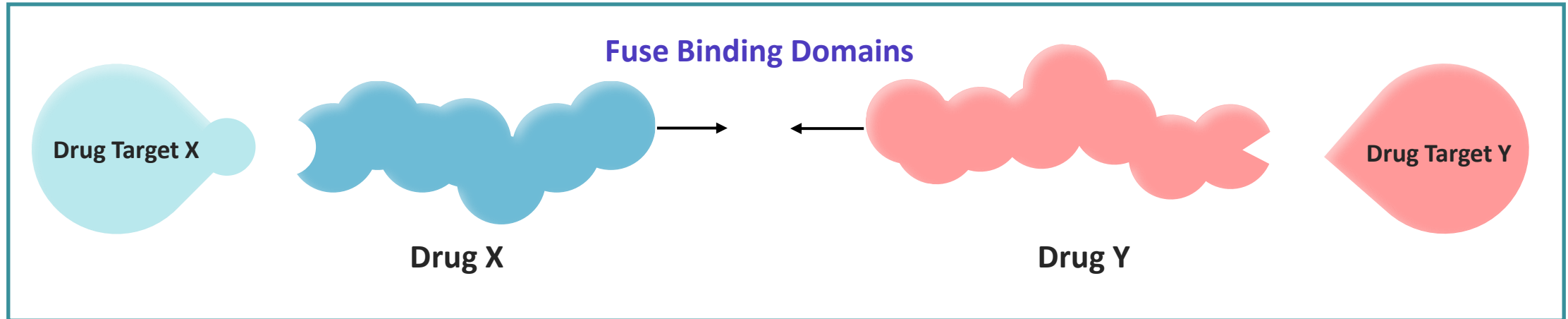
Drug-drug conjugates

- ✓ Tissue-selective targeting improves therapeutic index vs. untargeted warhead
- ✓ Oral or IV delivery
- ✓ Binds intracellular and cell membrane targets
- ✓ Highly cell permeable
- ✓ Simpler and less expensive to manufacture



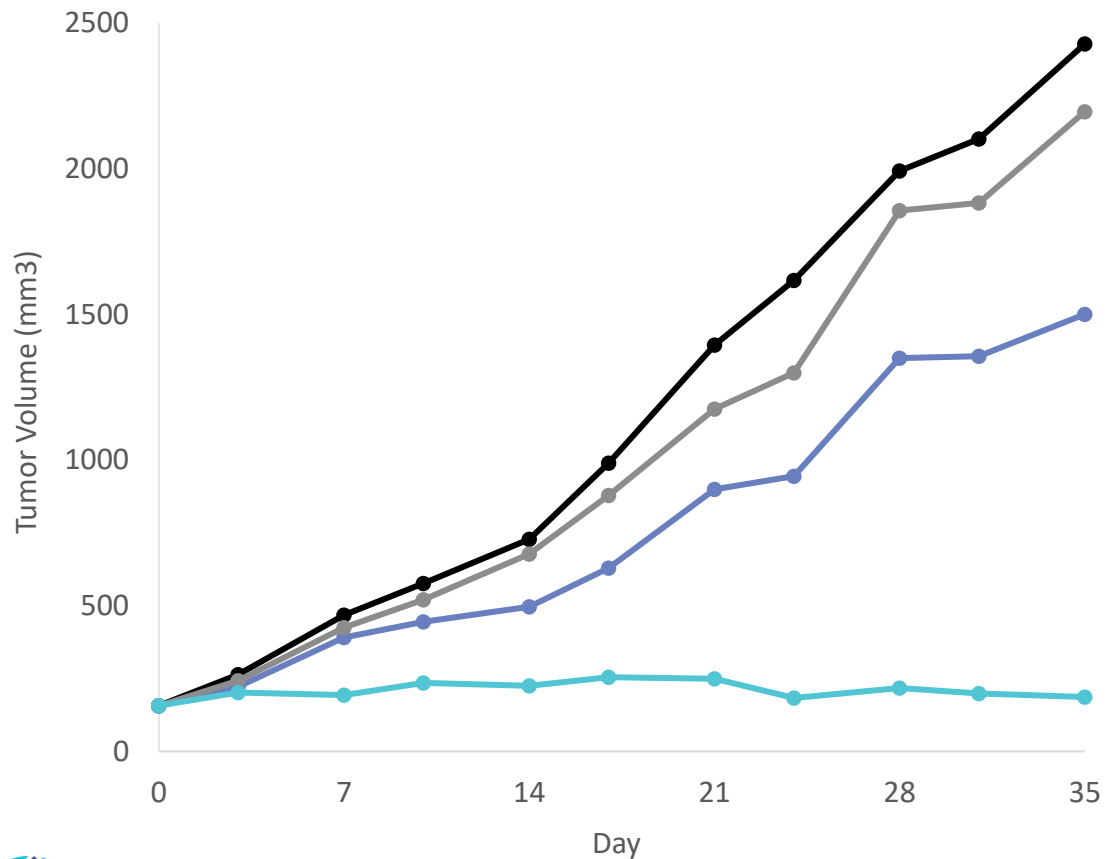
DDCs are designed to bind TWO different targets simultaneously

Two separate drugs with two separate targets

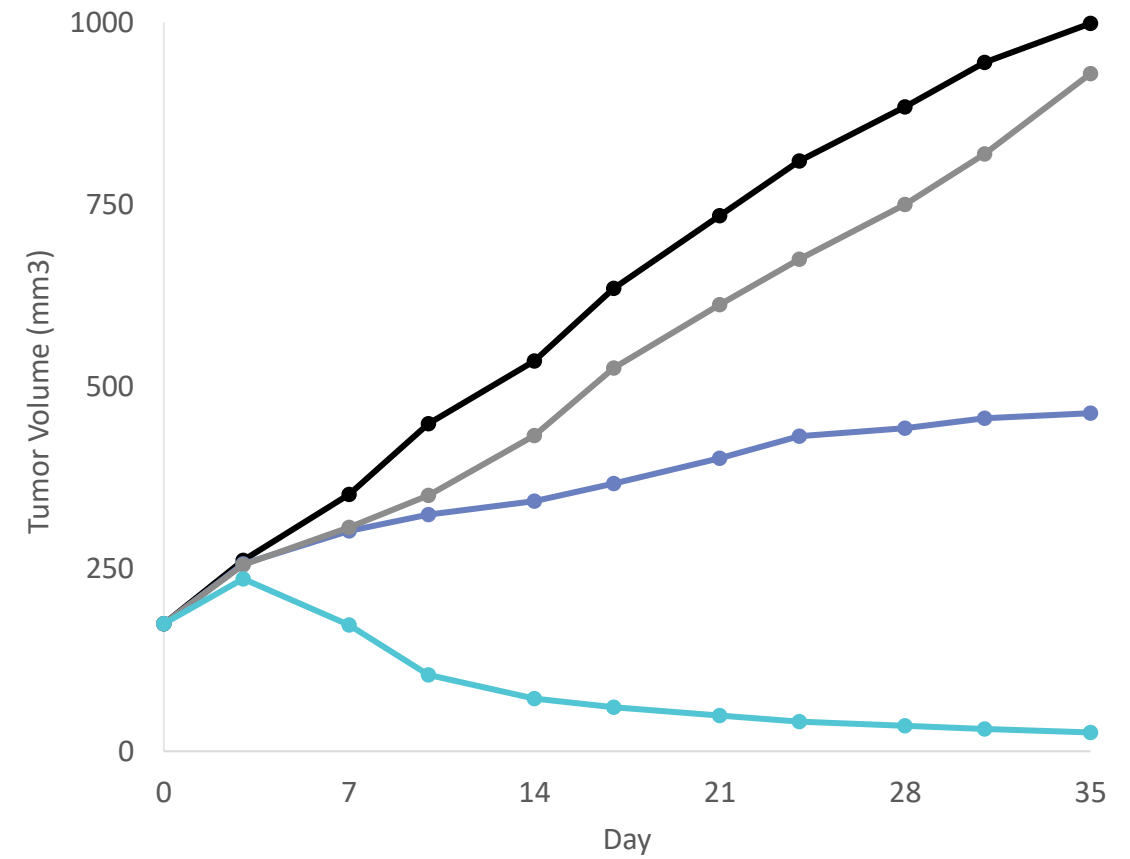


NUV-1511, a DDC derivative of a widely used chemotherapy agent, suppresses prostate and breast cancer growth in xenografts

Prostate cancer CDX (LNCAP)

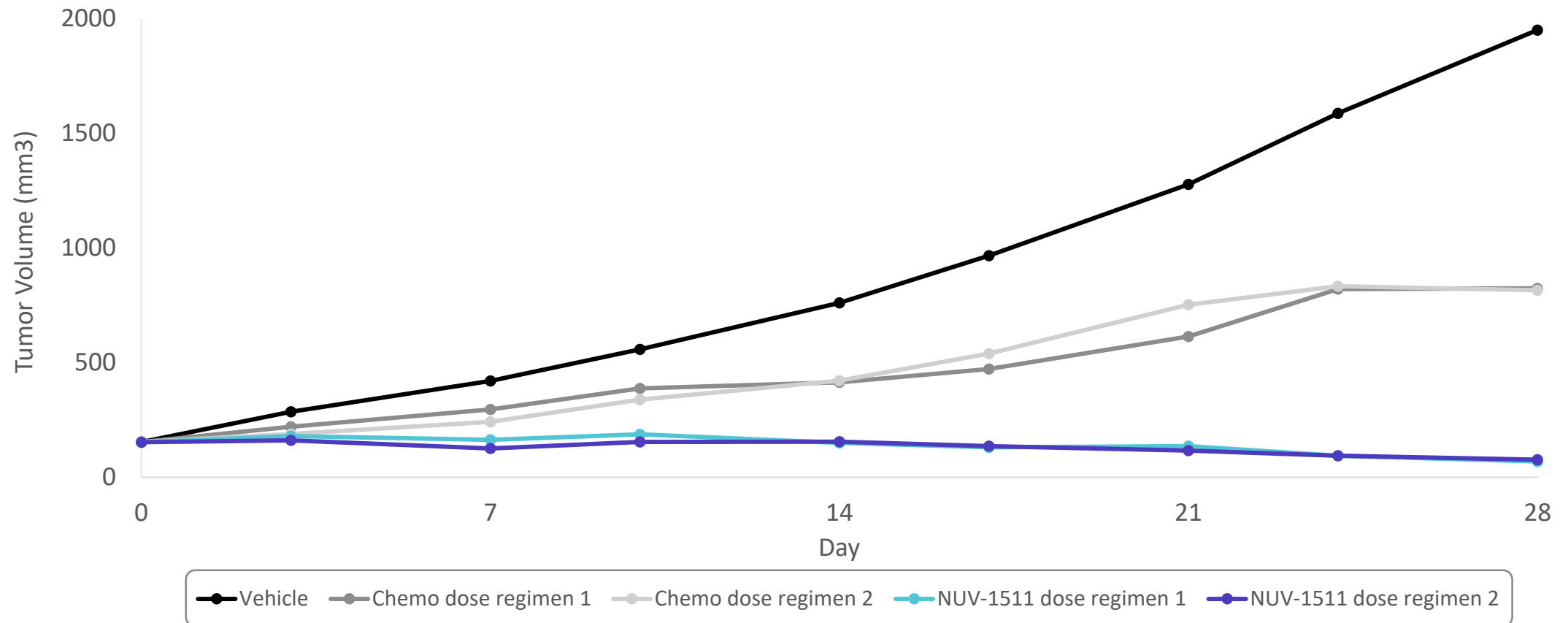


ER+ breast cancer CDX (T47D)



Intermittent dosing of NUV-1511 leads to sustained tumor inhibition for weeks

Prostate cancer CDX (LNCAP)



NUV-1511 is initially being evaluated in five indications for which there is a significant unmet need and large market potential

Nuvation Bio initiated a Phase 1/2 study evaluating NUV-1511 for the treatment of patients with:

- 1 Advanced solid tumors who previously received and progressed on or after treatment with Enhertu[®] and/or Trodelvy[®] per approved U.S. FDA labeling
- 2 Human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer
- 3 Metastatic castration-resistant prostate cancer
- 4 Platinum-resistant ovarian cancer
- 5 Advanced pancreatic cancer



NUV-868 | BETi

Advanced solid tumors

Completed Phase 1 and Phase 1b studies

Future indications

Currently evaluating next steps for program



First generation BET inhibitors have been toxic and poorly effective; NUV-868 is the most BD2-selective BET inhibitor in development

NUV-868 is the most selective BD2 vs BD1 BET inhibitor in development

- BET proteins regulate the expression of many oncogenes, including cMYC – an oncogene that has not been targetable directly with a drug
- Non-selective BD1/2-inhibitors have been associated with tolerability issues, many apparently due to BD1 inhibition¹
- NUV-868 inhibits BD2 almost 1,500 times more potently than BD1, which may improve efficacy and tolerability**

	BRD4 Affinity ²		
	BD2 (nM)	BD1 (nM)	Selectivity
NUV-868*	2	2920	1460x
ABBV-744³	1.05	340	324x
Pelabresib³	17	85	5-6x
ABBV-075¹	3	11	3.7x
MK-8628/OTX-015⁵	17	26	1.5x
BI-894999⁶	41	5	0.1x
ZEN-3694⁷	Non-selective		

LESS BD2 SELECTIVE → MORE BD2 SELECTIVE

*high plasma protein binding, > 1% free fraction



1. Fuvre et al 2020. 2. Various assays used. 3. Internal Nuvation Bio data. 4. <https://ash.confex.com/ash/2020/webprogram/Paper140138.html>. 5. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5474678/>. 6. <https://www.nature.com/articles/s41388-018-0150-2>. 7. 2016-EORTCposter-ZenithEpigenetics.pdf.

Committed team tackling the greatest unmet needs in oncology



Experienced biotech leadership team

- Founded by Dr. David Hung, previously the founder and CEO of Medivation, who successfully developed and commercialized XTANDI®



Potentially best-in-class candidates leveraging and improving validated mechanisms

- Potential for better efficacy and tolerability



Strong pro forma cash position provides path to potential profitability

- \$549.1 million as of September 30, 2024
- Secured up to \$250 million upon U.S. FDA approval of taletrectinib



Broad pipeline across multiple stages of development

- **Taletrectinib | ROS1 inhibitor:**
NDA accepted for priority review (line agnostic, full approval) in December 2024
- **Safusidenib | mIDH1 inhibitor:**
Phase 2 study ongoing
- **NUV-1511 | Drug-drug conjugate:**
Phase 1 dose escalation study ongoing
- **NUV-868 | BD2-selective BET inhibitor:**
Completed Phase 1 and Phase 1b studies



Potential to become a commercial stage organization in the U.S. as early as mid-2025

- NDA for taletrectinib accepted for priority review with PDUFA goal date of June 23, 2025
- Taletrectinib approved in China for advanced ROS1+ NSCLC

