Black Diamond Therapeutics (BDTX)

Advancing silevertinib: a potential best-in-class EGFR TKI for patients with NSCLC and GBM

BLACK DIAMOND THERAPEUTICS

September 30, 2026

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BDTX is Focused on Advancing Silevertinib: A Potential Best-in-Class CNS-Penetrant EGFR TKI for Patients with NSCLC and GBM

Silevertinib's key differentiators address significant unmet medical need



Broad EGFR mutational coverage: both classical and non-classical mutations (NCMs)

Robust CNS activity: opportunity to benefit patients with NSCLC and GBM

Anticipated Q4 2026 Catalysts



Provide updated Phase 2 results in frontline NSCLC, and FDA feedback on path to approval

Initiate randomized portion of Phase 2 trial in newly diagnosed GBM

Q2 2026 cash $110.5M; runway into H2 2028



Highly experienced team of oncology drug developers

Sufficient capital through GBM randomized Phase 2 data in 2028

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CNS – Central Nervous System; TKI – Tyrosine Kinase Inhibitor; NSCLC – Non-Small Cell Lung Cancer; GBM - Glioblastoma

Silevertinib: Clinical Results Demonstrate Potential Best-in-Class CNS Activity and Broad EGFRm Coverage to Benefit Patients Across NSCLC and GBM



Non-Small Cell Lung Cancer (NSCLC)

NCMs represent ~25% of newly diagnosed EGFRm NSCLC patients, or ~70,000 patients worldwide[1]

- Current treatments lack broad spectrum NCM coverage and/or have suboptimal brain penetrance[1,2]

Phase 2 data at ASCO 2026 demonstrated[3]:

- **15.2-month mPFS** versus 8.2 – 10.6 months with current standard of care (AstraZeneca's osimertinib and Boehringer Ingelheim's afatinib)[4]
- Responses in ~**5x more** mutations than ArriVent's firmonertinib[5], BDTX trial conducted entirely in North America
- **86% CNS-ORR** with no patients developing *de novo* brain metastases versus 35-46% CNS-ORR seen with osimertinib, afatinib and firmonertinib[5,6]



Glioblastoma (GBM)

EGFR mutations present in ~50%[7] of GBM patients, representing ~20,000 patients worldwide[8]

- Prior attempts to drug EGFR have failed because of suboptimal brain penetrance and/or inadequate mutational coverage[1,2]

Phase 0/1 and Phase 1 data have demonstrated[9,10]:

- **Best-in-class brain penetrance** in GBM tumors
- **PoC** in heavily pretreated GBM patients, including confirmed response in patient with EGFRvIII/EGFRamp

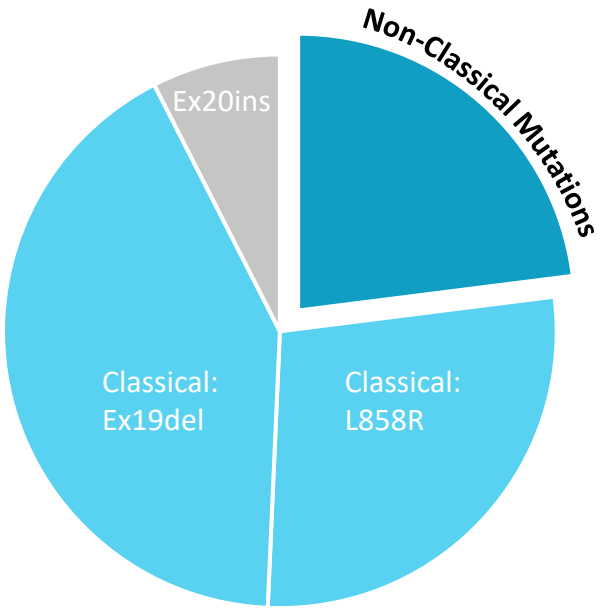
$2bn+ opportunity in 1L NCM NSCLC and EGFR+ GBM, with potential to expand to other populations/lines of therapy

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EGFRm – EGFR mutation. 1. Sung CA Cancer J Clin 2026 (GLOBOCAN 2024); Luo Lancet Respir Med 2025; Zhang Oncotarget 2016; Heymach ESMO 2024; Foundation Med AACR 2024; Soo JTO 2024; Robert Lung Cancer 2022; Ikeda Cancer Sci 2026; Hofman ESMO Open 2023; Smeltzer JTO 2025; Wang Ann Palliat Med 2024; Rotow JTO 2024. 2. Colclough Clin Can Res 2021. 3. Rotow ASCO 2026 and Yu ASCO 2026. 4. Okuma JAMA Oncology 2024, Pizzutilo ESMO Open 2024 and Kang Front Oncol 2021. 5. Kang Front Oncol 2023. 6. Priantti JCO Prec Oncol 2024. 7. O'Connor AACR 2023. 8. Ostrom Neuro-Oncology 2025; IARC GLOBOCAN 2024; Girardi Neuro-Oncology 2023; Narita Neuro-Oncology 2024; Kang Cancer Research and Treatment 2021; Le Calvez Cancer Epidemiology 2025; Han Journal of the National Cancer Center 2024; Saadeh International Journal of Biological Markers 2018; Tempus Labs analysis of 2,540 GBM patient samples; Noeuveglise ESMO Open 2022; French Neuro-Oncology 2019; Weller Lancet Oncology 2017; Chen Nature Scientific Reports 2025; Lassman Journal of Neuro-Oncology 2019. 9. Sanai SNO 2025. 10. Wen ASCO 2024

Silevertinib's Broad EGFR Mutational Coverage: Potential to Address Significant Unmet Medical Need for NSCLC Patients with NCMs

Non-Classical Mutations (NCMs) represent ~25% of newly diagnosed EGFRm NSCLC, with no established standard of care[1]



Silevertinib potently inhibits ~90% of EGFR mutations in NSCLC patients[2]

Clinical data demonstrate silevertinib's broad EGFR mutational coverage

Silevertinib demonstrated clinical responses in ~**5x more** EGFR mutations than firmonertinib, including known resistance mutations for firmonertinib[3]

Silevertinib:
Responses across **29** mutations[2]

Classical	NCM			
Ex19del	R108G	H835L	E709_T710delinsD	G719X
L858R	D191N	L861Q	E746_S752delinsV	S768I
Ex19del + C797S	H590N	H773L	H233R	E709X
L858R + C797S	G724S	E746_R748delinsKP	E746_T751delinsV	V774M
	L747_K754delinsQQ	L747S/P	L747_T751delinsP	L718X
	L833V/F	L747_A750delinsP	I740dupIPVAIK	L792X
	G779F			

Firmonertinib:
Responses across **6** mutations[4]

Classical	NCM
Ex19del	G719X
L858R	S768I
Ex19del + C797S	E709X
L858R + C797S	V774M
	L718X
	L792X

= mutation present in responder

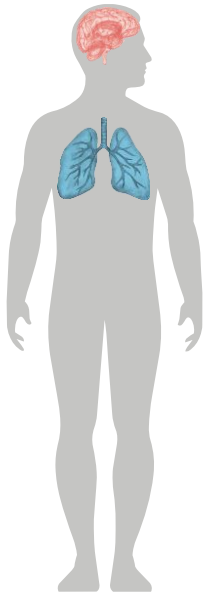
= mutation present as acquired resistance mutation following drug treatment

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1. Heymach ESMO 2024. 2. Rotow ASCO 2026 and Yu ASCO 2026. 3. Not a head-to-head comparison. 4. Le WCLC 2025 and Shi Lancet Resp Med 2021.

Brain Metastases are Highly Prevalent in EGFRm NSCLC; Silevertinib Demonstrates Potential Best-in-Class CNS Activity

Brain is the most common site of distant metastasis in EGFRm NSCLC[1]

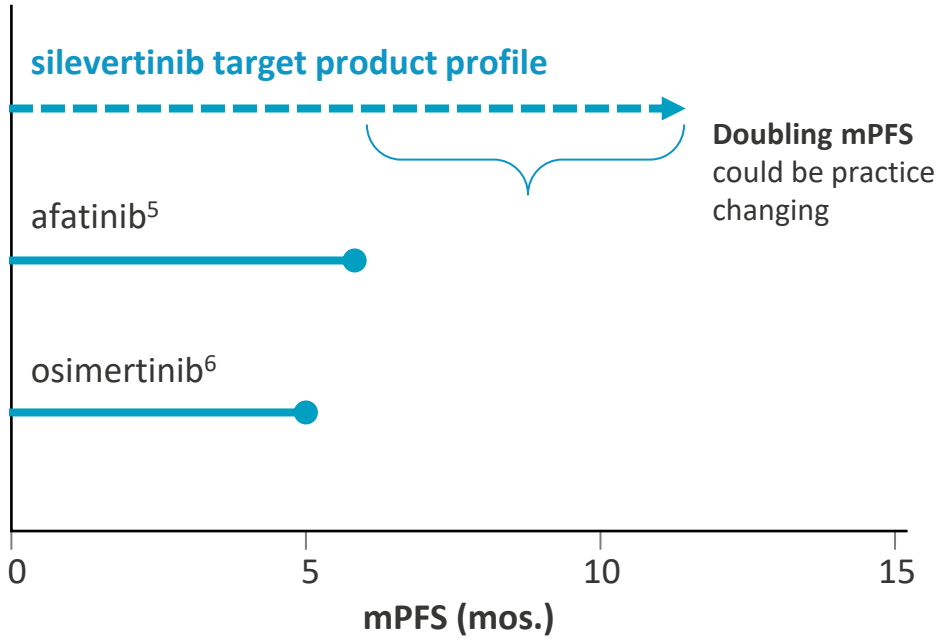


- **~40%** of patients with NCMs present with brain metastases at diagnosis[2]
- **>80%** of patients with NCMs progress in the brain[3]

Silevertinib Ph2 data demonstrate[4]:

- **86% CNS-ORR** in 1L NCM NSCLC patients with brain metastases vs. 35-46% seen with osimertinib and afatinib[5,6]
- **No patients** developed *de novo* brain metastases

Silevertinib's potential to double mPFS in frontline EGFR-NCM patients with brain metastases



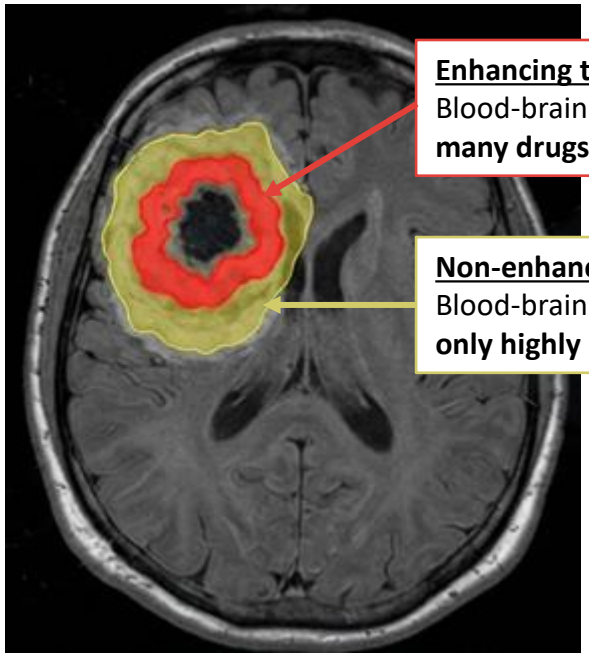
Silevertinib's potential best-in-class CNS activity offers opportunity to expedite path to approval in frontline patients with NSCLC

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1. Wang Clin Resp J. 2025. 2. Bar JTO 2022 and Wilcox Annals Onc 2025. 3. Li Cancers 2022. 4. Rotow ASCO 2026. 5. Kang Front Oncol 2023. 6. Priantti JCO Prec Oncol 2024.

Silevertinib: The Only EGFR TKI to Demonstrate Robust CNS Penetrance in All Regions of Brain Tumors, Including Where Blood-Brain Barrier is Intact

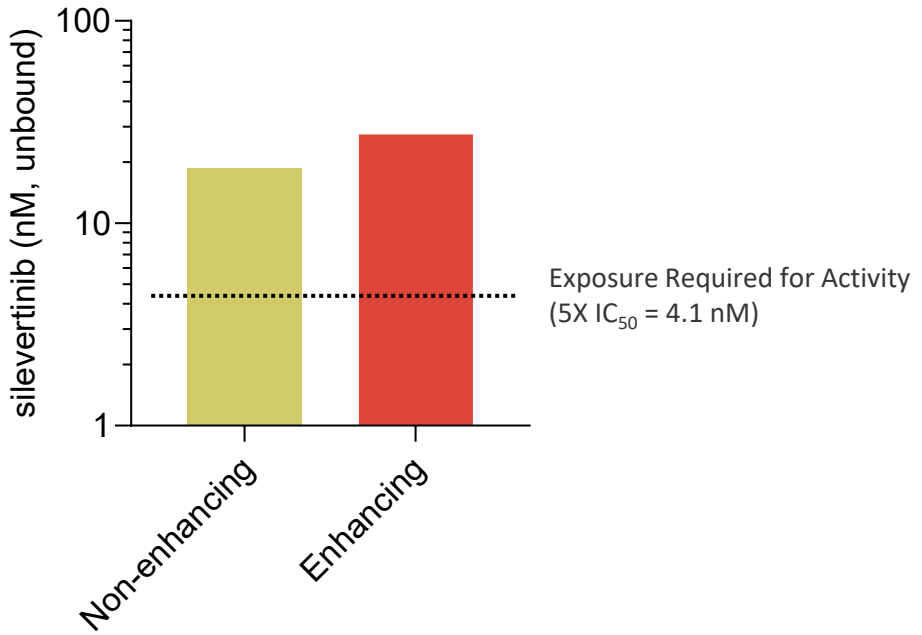
Effective treatment of brain tumors requires drug penetration into both enhancing and non-enhancing tumor regions[1]



Enhancing tumor regions:
Blood-brain barrier compromised,
many drugs can access

Non-enhancing tumor regions:
Blood-brain barrier intact,
only highly CNS penetrant drugs can access

Silevertinib exceeds target exposure in both tumor regions of GBM patients dosed in Ph0/1[2]



Silevertinib penetrates BOTH enhancing and non-enhancing regions to deliver potential best-in-class CNS activity

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No head-to-head studies have been conducted.

1. Sarkaria Neuro-Onc 2018. 2. Sanai SNO 2025. Levels of unbound silevertinib are an average of 13 patients dosed in a Ph0/1 "window of opportunity" trial.

Silevertinib:
Development in Patients with NSCLC

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Silevertinib: Key Takeaways from Phase 2 1L NSCLC Data

- Preliminary mPFS 15.2 months
- mDOR not reached
- 60% ORR (RECIST 1.1)
- 86% CNS ORR (RANO-BM), no patients developed *de novo* brain metastases

- AEs are typical for EGFR TKIs: manageable through supportive care and dose reductions
- Exposure response analyses indicate 150 mg as optimal pivotal dose

- Updated Phase 2 results in frontline NSCLC patients and FDA feedback on pivotal path expected in Q4 2026

Data presented by Julia Rotow, MD (DFCI) in an oral presentation at the ASCO Annual Meeting on May 30, 2026

Data from April 11, 2026 (11.2 mo. median follow up)

Silevertinib in EGFR-NCM NSCLC Phase 2 Trial Design

Main Inclusion Criteria:

- EGFR NCM by local NGS test
- Asymptomatic brain metastases allowed
- CNS MRI surveillance required

Main Exclusion Criteria:

- Classical EGFR mutations (del19, L858R)

Cohort 1
N=41

- Recurrent NSCLC after ≤2 prior therapies
- EGFR non-classical (NCM) mutation positive

Cohort 2
N=42

Recurrent NSCLC after ≤2 prior therapies
EGFR acquired resistance C797S mutation positive

Cohort 3
N=43

Treatment naïve patients with EGFR non-classical mutations (NCMs)

- All patients were treated with silevertinib at a daily dose of 200 mg
- At the time of April 11 data cut, median follow up time was 11.2 months

Primary endpoint:

ORR

Secondary endpoints:

PFS, DOR, OS, Safety, PK

43 Frontline Patients with NSCLC Enrolled in the US and Canada

Real world demographics:

16/43 (37%) patients with untreated brain metastases

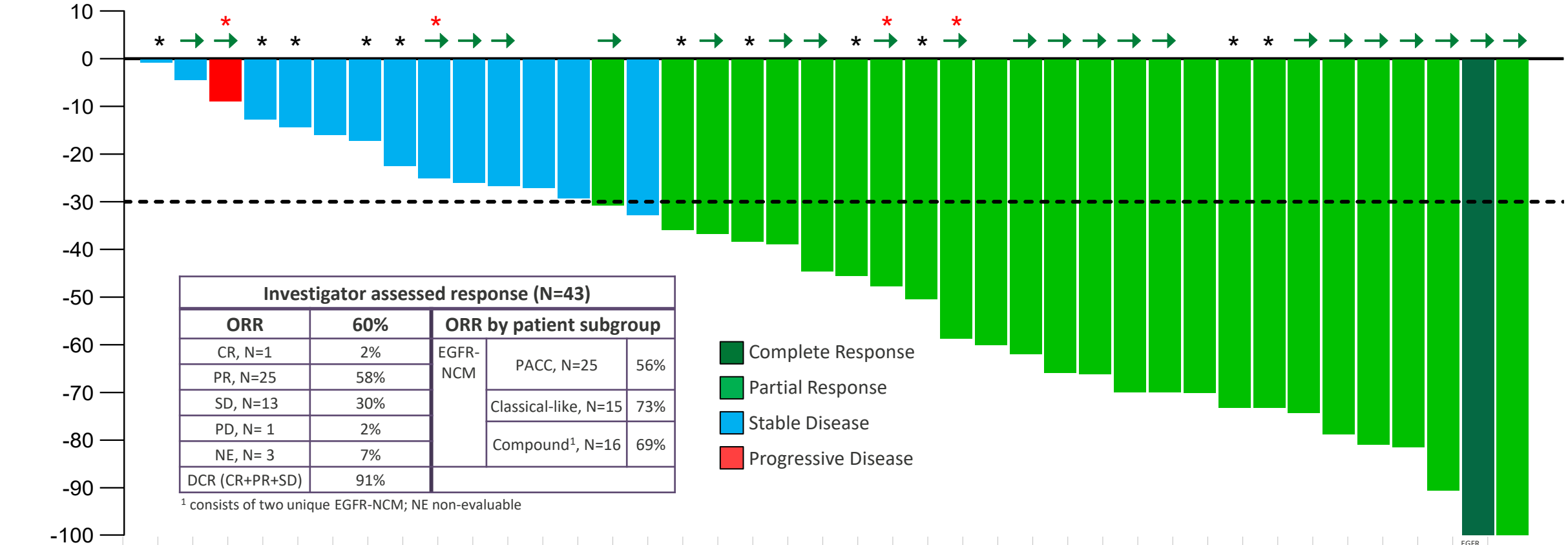
33 unique NCMs

Cohort 3 Treatment Naive 1L EGFR-NCM (N=43)	
Age in years, median (range)	70.3 (44-91)
Female, N (%)	31 (72)
ECOG 0/1, N (%)	21 (49) / 22 (51)
Non-smoker/Former current, N (%)	18 (42) / 25 (58)
Race: Asian/Caucasian/Other, N (%)	7 (16) / 32 (74) / 4 (9)
Visceral metastases, N (%)	10 (23)
Brain metastases	
All brain metastases, N (%)	19 (44)
Untreated brain metastases, N (%)	16 (37)
Untreated measurable brain metastases, N (%)	7 (16)
EGFR Mutations	
PACC[1, 2], N (%)	25 (58)
Classical-like[2], N (%)	15 (35)
Other NCM, N (%)	3 (7)
Compound[3], N (%)	16 (37)

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1. Includes at least 1 PACC mutation; PACC: P-loop and αC-helix compressing; 2. Robichaux Nature. 2021; 3. presence of 2 distinct non-classical EGFR mutations. Data from Apr 11, 2026

Silevertinib Demonstrates Potential Best-in-Class Anti-Tumor Activity



Investigator assessed response (N=43)				
ORR	**60%**	**ORR by patient subgroup**		
CR, N=1	2%	EGFR-NCM	PACC, N=25	56%
PR, N=25	58%		Classical-like, N=15	73%
SD, N=13	30%		Compound[1], N=16	69%
PD, N= 1	2%			
NE, N= 3	7%			
DCR (CR+PR+SD)	91%			

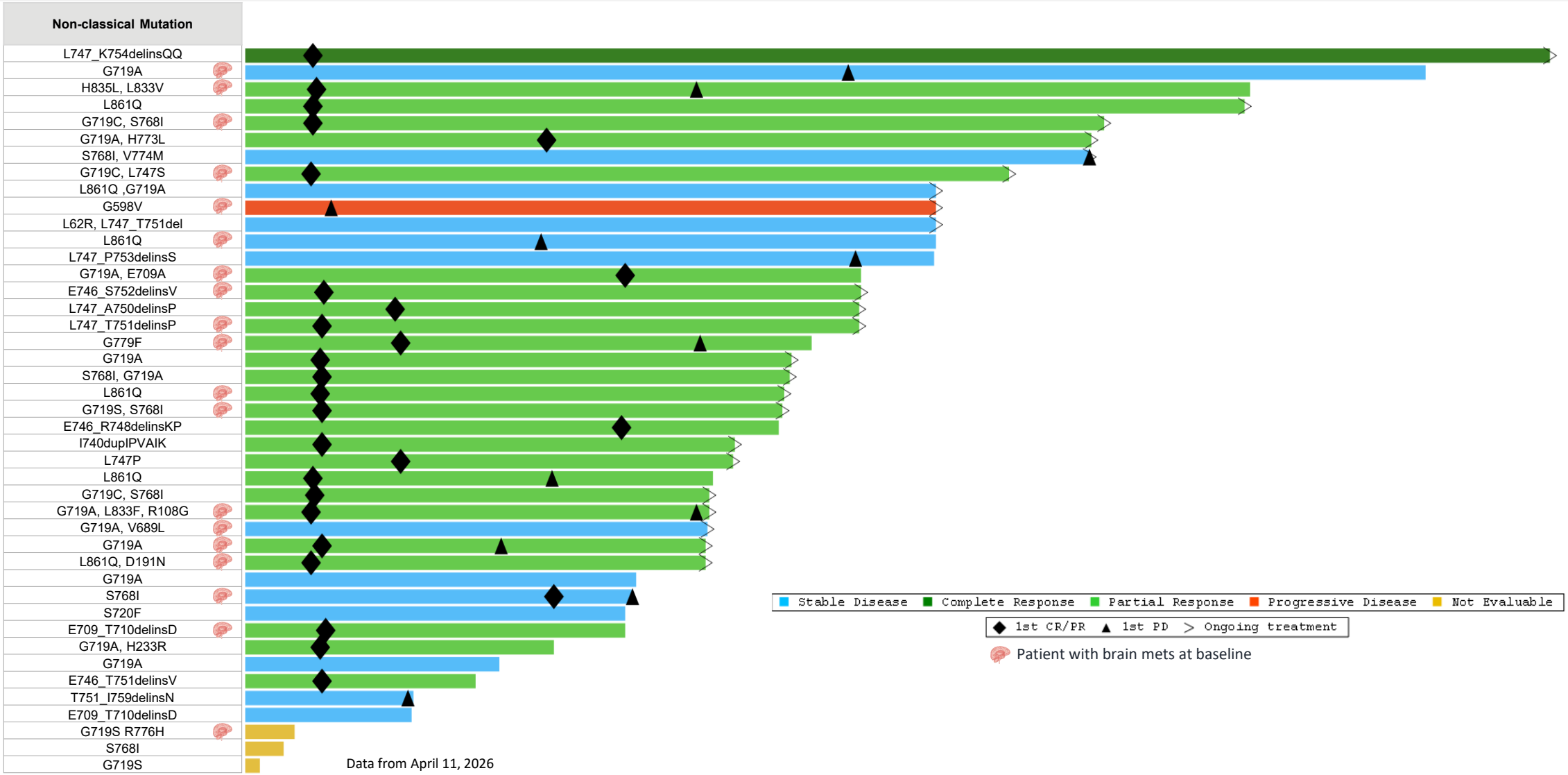
[1] consists of two unique EGFR-NCM; NE non-evaluable

Patient with brain mets at baseline → Tx ongoing * Patient on Rx beyond progression * Patient discontinued for reasons other than progression

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Data from Apr 11, 2026

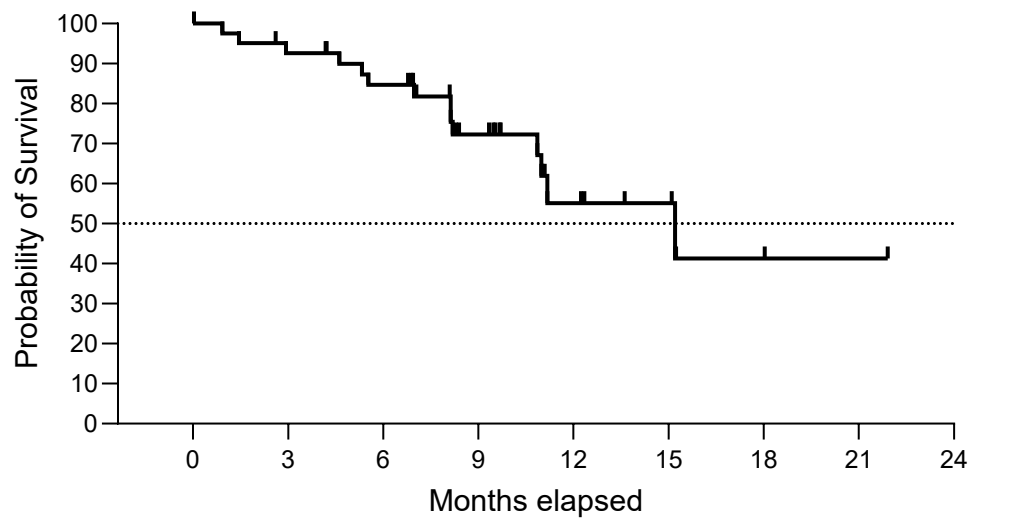
Encouraging Durability in 1L NSCLC Patients Treated with Silevertinib



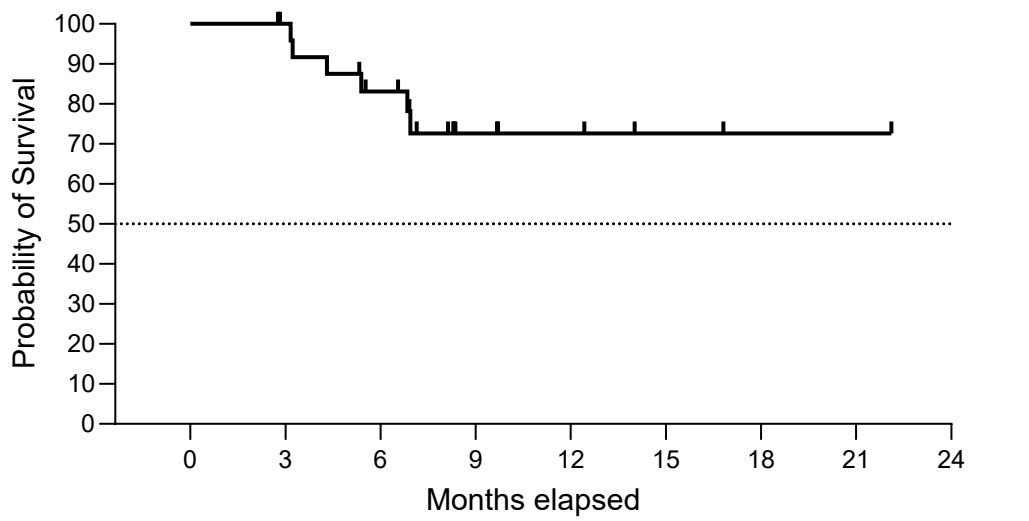
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Robust PFS and DOR in 1L NSCLC Patients Treated with Silevertinib

Silevertinib PFS in 1L EGFR-NCM



Silevertinib DOR in 1L EGFR-NCM



With median patient follow-up of 11.2 months, preliminary mPFS is 15.2 months (95%CI: 10.8, NE)

Median DOR has not been reached (95%CI: 7.0, NE); 23 patients remained on therapy with longest at 23.5 months

No patients developed de novo brain metastases[1]

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1. Patients with no brain metastases at baseline (n=24); Data from Apr 11, 2026

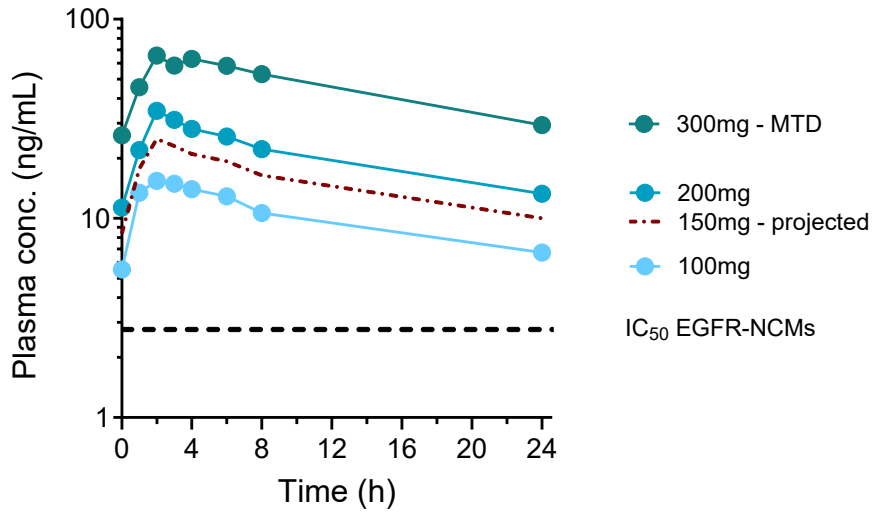
Silevertinib Demonstrated a Dose Dependent and Manageable AE Profile

Dose Dependent and Manageable AE Profile

Silevertinib TRAEs Gr ≥3; 200 mg QD (N=43)		After dose reduction (N=36)
TRAE	**Gr ≥3 n (%)**	**Gr ≥3 n (%)**
Rash	8 (19)	3 (8)
Diarrhea	8 (19)	2 (6)
Stomatitis	4 (9)	0
Paronychia	2 (5)	1 (3)
Decreased appetite	2 (5)	2 (6)
Nausea	1 (2)	1 (1)

- AEs managed by supportive care / dose reduction; consistent with other EGFR TKIs
- Most patients experienced dose interruption / reduction; only 14% of patients discontinued due to AEs
- Patients maintained clinical response after dose reduction; 134 mg/day median dose intensity

Silevertinib Demonstrates Dose-Proportional PK



- Dose-proportional PK observed in patients at 100 mg, 200 mg, and 300 mg QD[1]
- EGFR-NCM target coverage and clinical responses achieved at doses ≥100 mg QD
- Extensive exposure response analyses support 150 mg QD dose to provide optimal tolerability without sacrificing clinical activity

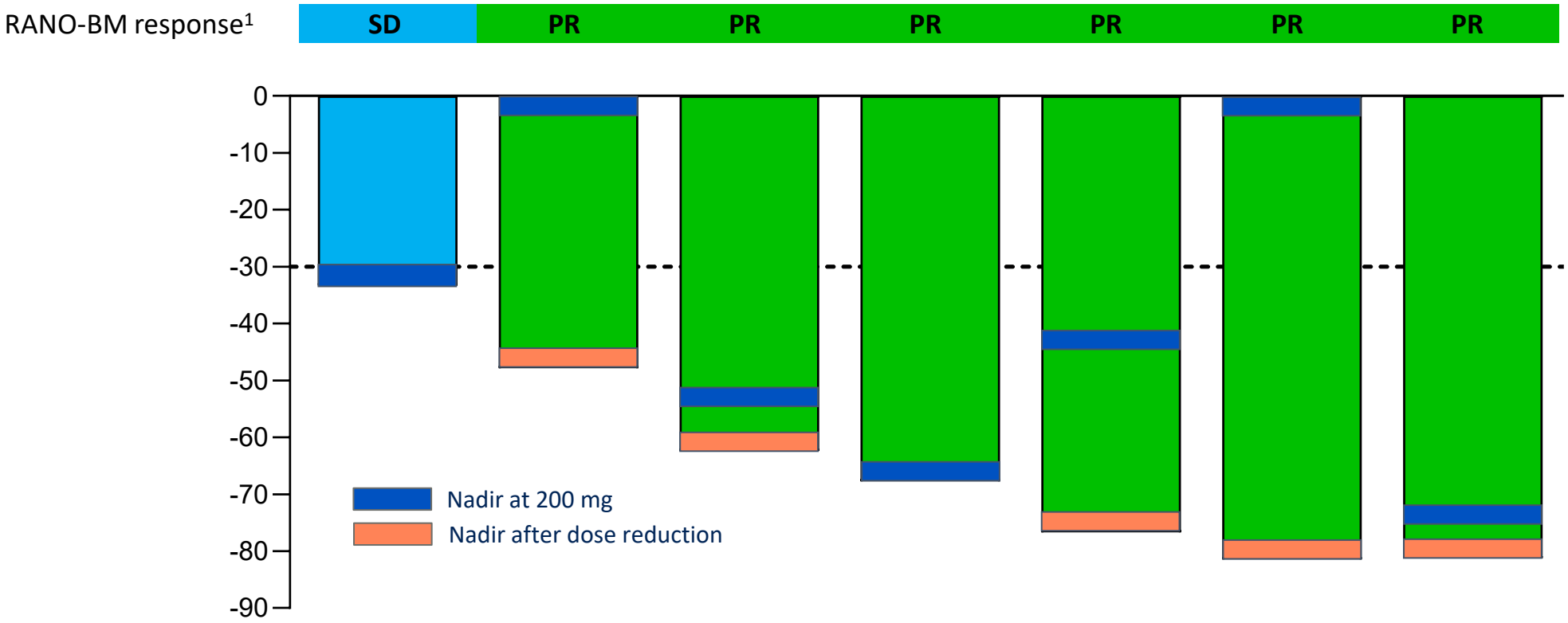
Extensive exposure response data across 200+ patients support 150 mg QD for pivotal trial

Rash group terms: rash, rash maculo-papular, rash pustular, rash erythematous, dermatitis acneiform; stomatitis terms: stomatitis, and mucosal inflammation; AE – Adverse Event; TRAE – Treatment Related Adverse Event; SAE – Serious Adverse Event; DC – Discontinuation

1 – Yu EORTC 2023; IC_{50} of EGFR NCMs tested in BaF3 cells.

Data from Apr 11, 2026

Silevertinib: 86% CNS ORR with Responses Deepening Over Time



1) Patients with measurable brain metastases at baseline (n=7). Data from Apr 11, 2026

Silevertinib Market Opportunity – Current Focus on 1L NCM NSCLC; Potential to Expand to Other EGFRm Patient Populations / Lines of Therapy

Current Focus

1L non-classical mutations

~70,000

Estimated Global Total Addressable Market (annual patients)*

Additional Market Opportunities

Adjuvant/post-adjuvant	1L L858R	Recurrent setting with EGFR resistance mutations
~27,000	~87,000	~13,000

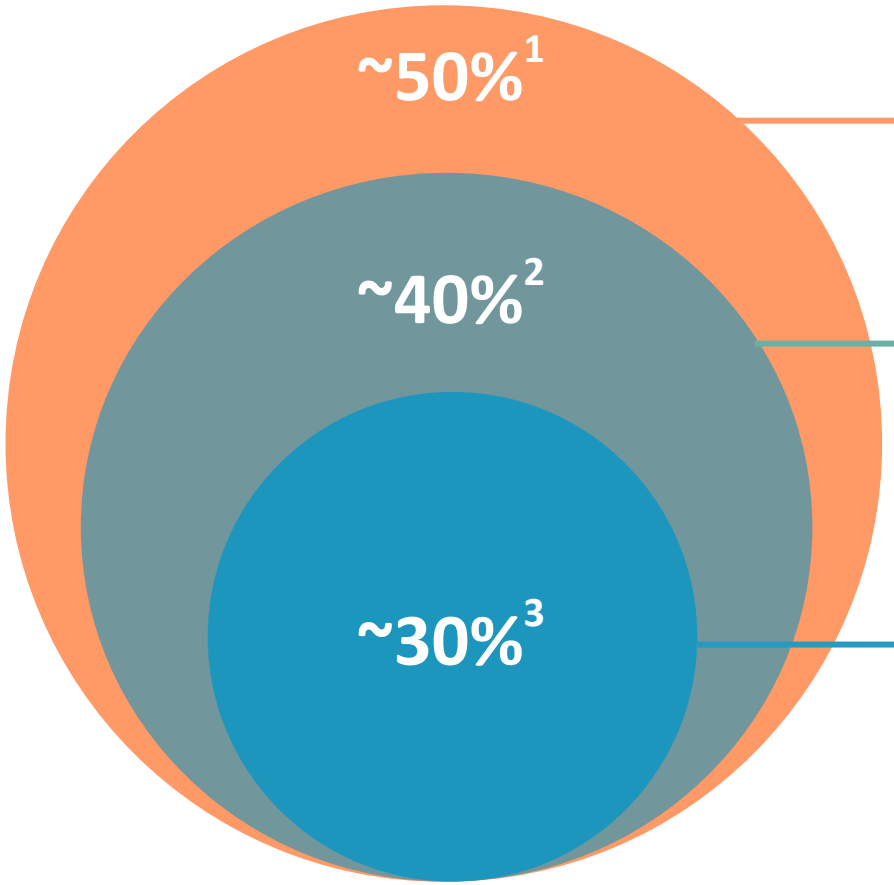
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* Sung CA Cancer J Clin 2026 (GLOBOCAN 2024); Luo Lancet Respir Med 2025; Zhang Oncotarget 2016; Heymach ESMO 2024; Foundation Med AACR 2024; Soo JTO 2024; Robert Lung Cancer 2022; Ikeda Cancer Sci 2026; Hofman ESMO Open 2023; Smeltzer JTO 2025; Wang Ann Palliat Med 2024; Rotow JTO 2024.

Silevertinib:
Development in Patients with Glioblastoma

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Silevertinib was Designed to Address the Complex EGFR Mutations Found in Patients with GBM



Of all GBM patients carry oncogenic EGFR alterations

Of all GBM patients have more than one oncogenic EGFR alteration

Of all GBM patients express EGFRvIII, which has been demonstrated to be a potent oncogenic driver

~49,000

GBM patients worldwide are diagnosed each year with EGFR mutations that have been shown in preclinical studies to be inhibited by silevertinib

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1. Saadeh, F., The International Journal of Biological Markers, 2018; 2. Tempus Labs analysis of 2,540 GBM patient samples; 3. Noeuveglise ESMO OPEN 2022, French Neuro-Oncology 2019, Weller Lancet Oncology 2017

Silevertinib: Potential to Overcome Limitations of Prior Attempts to Drug EGFR in Patients with GBM

Lessons From Past Failures		Silevertinib
Low brain exposure due to a lack of CNS penetrance	›	**Best-in-class brain penetrance to treat CNS tumors**
Heterogeneous expression of EGFR oncogenic alterations within tumors	›	**Potent inhibition of co-occurring EGFR alterations and amplification**
Paradoxical activation of EGFR GBM oncogenes induced by reversible inhibitors	›	**Covalent MOA and no paradoxical activation**
Poor tolerability driven by on target WT-EGFR activity	›	**Spares WT-EGFR in normal cells while retaining potent activity against EGFR alterations**

MOA=mechanism of action; WT=Wild-Type

Ph0/1 and Ph1 Data Have Demonstrated Best-in-Class Brain Penetrance and Preliminary Proof of Concept in Patients with GBM

Best-in-class brain penetrance

Silevertinib is the only EGFR TKI to demonstrate robust penetrance in GBM tumors, including sites where blood-brain barrier is intact.[1]

PoC in heavily pre-treated GBM patients

Prolonged stable disease in multiple patients, and confirmed response in patient with EGFRvIII / EGFRamp.[2]

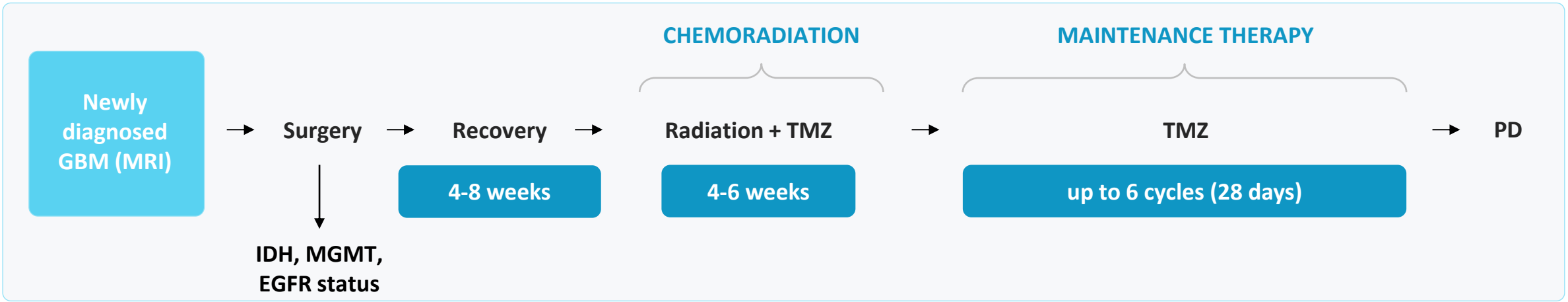
Encouraging clinical experience to date supports recently initiated Phase 2 trial in newly diagnosed GBM patients

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No head-to-head studies have been conducted.

1. Sanai SNO 2025. 2. Wen ASCO 2024.

Newly Diagnosed GBM Patient Journey: Limited Options for Patients



Only two therapies approved for GBM patients in last 20 years

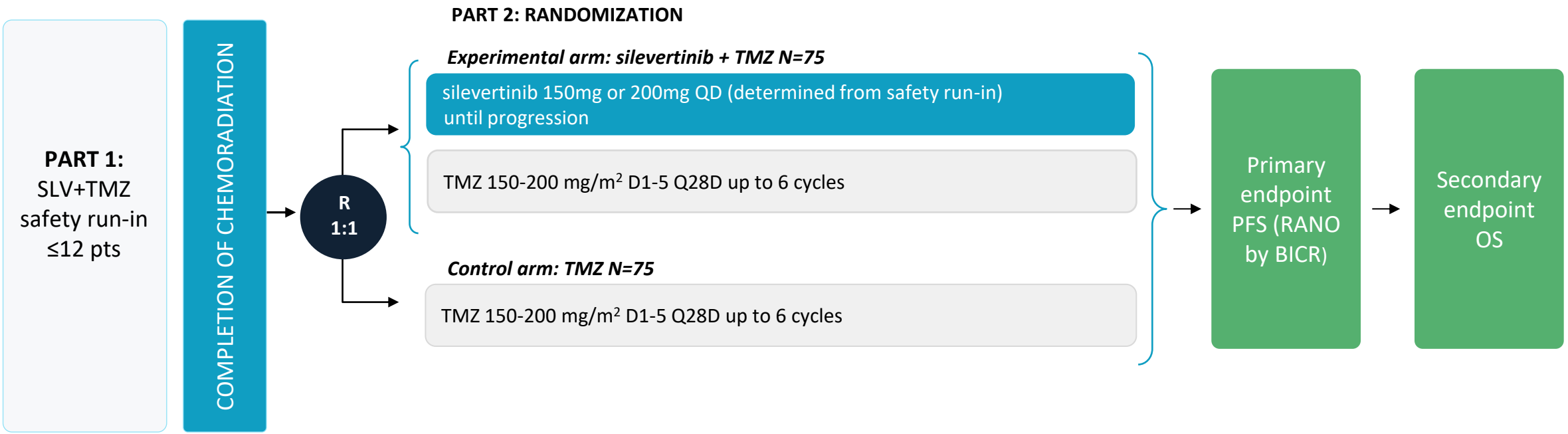
- Temozolomide (TMZ): primarily benefits methylated patients (though given to unmethylated patients as well)
- Tumor Treating Fields (TTF): device with compliance/QOL issues

Drug	N	MGMT Status	Setting	PFS	OS	Reference
TMZ	573	UM+M	CRT + MT	6.9 vs 5.0 mos; HR 0.54, p<0.001	14.6 mos vs 12.1 mos; HR 0.63, p<0.001	Stupp et al 2005
TTF	695	UM+M	MT	6.7 vs 4.0 mos; HR 0.63, p<0.001	20.9 mos vs. 16.0 mos; HR 0.63, p<0.001	Stupp et al 2017

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CRT: chemoradiation; MT: maintenance therapy after CRT; HR: hazard ratio; M: methylated; UM: unmethylated; MGMT: methylguanine methyltransferase; mos: months; PD: progressive disease

Randomized Phase 2 of Silevertinib + TMZ in Newly Diagnosed GBM Patients



Study population:
unmethylated patients with EGFRvIII

IDMC performs interim analyses for futility and PFS, and a final PFS analysis

Confirmation of progression (RANO) by Blinded Independent Committee Review (BICR)

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SLV: silevertinib; TMZ: temozolomide; ND – newly diagnosed; BICR: Blinded Independent Central Review; IDMC: Independent Data Monitoring Committee

Silevertinib Market Opportunity in GBM – Current Focus on EGFRvIII; Potential to Expand to All EGFR Variants

Current Focus

Newly Diagnosed
EGFRvIII
unmethylated

~20,000

Estimated Global Total Addressable Market (annual patients)*

Additional Market Opportunities

Newly Diagnosed
All EGFR alterations
unmethylated

Additional ~15,000

Newly Diagnosed
All EGFR alterations

Additional ~14,000

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* Ostrom Neuro-Oncology 2025; IARC GLOBOCAN 2024; Girardi Neuro-Oncology 2023; Narita Neuro-Oncology 2024; Kang Cancer Research and Treatment 2021; Le Calvez Cancer Epidemiology 2025; Han Journal of the National Cancer Center 2024; Saadeh International Journal of Biological Markers 2018; Tempus Labs analysis of 2,540 GBM patient samples; Noeuveglise ESMO Open 2022; French Neuro-Oncology 2019; Weller Lancet Oncology 2017; Chen Nature Scientific Reports 2025; Lassman Journal of Neuro-Oncology 2019; Higa Cancer Medicine 2023.

Silevertinib: Key Takeaways and Next Steps

NSCLC

- ✓ Opportunity to capture ~25% of the 1L EGFRm NSCLC market
- ✓ Robust anti-tumor activity and durability achieved in Phase 2
- ✓ Potential best-in-class CNS activity to address highest unmet need in NSCLC
- ✓ **FDA feedback on path to approval in 1L NSCLC expected Q4 2026**

GBM

- ✓ Opportunity to capture ~50% of the newly diagnosed GBM market
- ✓ Robust CNS penetrance and PoC achieved in Phase 0/1 and Phase 1
- ✓ **Randomized portion of Phase 2 trial expected to initiate in Q4 2026**