Black Diamond Therapeutics, Inc.

Developing MasterKey Therapies to Defeat Cancer Resistance

BLACK DIAMOND THERAPEUTICS

May 21, 2026

Forward-Looking Statements

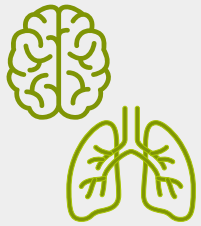
This presentation contains forward looking statements of Black Diamond Therapeutics, Inc ("we," "us," "our") within the meaning of the Private Securities Litigation Reform Act of 1995. Forward looking statements include all statements that are not historical facts, and in some cases, can be identified by terms such as "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "potential," "continue," "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future. Forward looking statements contained in this presentation include, but are not limited to, statements regarding our future financial or business performance, conditions, plans, prospects, trends or strategies and other financial and business matters, the continued development and advancement of silevertinib, including the ongoing Phase 2 clinical trials and the timing of clinical updates for silevertinib in patients with non-small cell lung cancer ("NSCLC") and in patients with glioblastoma ("GBM"), the potential of silevertinib to address the unmet medical need for newly diagnosed GBM and newly diagnosed NSCLC patients with non-classical EGFR mutations and benefit patients with NSCLC across multiple lines of therapy, and the potential future development plans for silevertinib in NSCLC and GBM, the competitive landscape and market for silevertinib or any of our other current or future product candidates, including statements relating to the estimated percentage of newly diagnosed NSCLC patients with non-classical EGFR mutations and the potential addressable patient population, a potential partnership for silevertinib, our ability to maintain our intellectual property portfolio, the timing and success of our development and commercialization of our product candidates, including our ability to establish and maintain collaborations or strategic relationships, and our expected cash runway. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by law, we assume no obligation to update these forward looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward looking statements, even if new information becomes available in the future. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward looking statements, see the section entitled "Risk Factors" in our most recent annual report on Form 10-K filed with the Securities and Exchange Commission (the "SEC"), as well as discussions of potential risks, uncertainties, and other important factors in our other subsequent filings with the SEC. In addition, we have not conducted any head to head studies comparing our product candidates to any third party drug products or candidates, whether investigated or approved. Information regarding other drug products in this presentation is meant to provide context for illustrative purposes only. Because there are no head to head studies, no conclusions should be made based on cross study comparisons. Recipients are cautioned not to place undue reliance on these forward looking statements, which speak only as of the date such statements are made and should not be construed as statements of fact. This presentation also contains information using industry publications that generally state that the information contained therein has been obtained from sources believed to be reliable, but such information may not be accurate or complete. While we are not aware of any misstatements regarding the information from these industry publications, we have not independently verified any of the data from third party sources nor have we ascertained the underlying economic assumptions relied on therein.

Black Diamond Therapeutics At-a-Glance

Clinical-stage company **advancing MasterKey therapies** designed to expand the addressable patient population

Experienced team with deep understanding of cancer biology and oncology drug development

Pipeline of oral, brain penetrant drug candidates selectively **targeting families of oncogenic mutations**



Silevertinib: potential **First and Best-in-Class 4th-gen EGFRi in Ph2 for NSCLC,** Ph2 trial in GBM initiated in Q2 2026

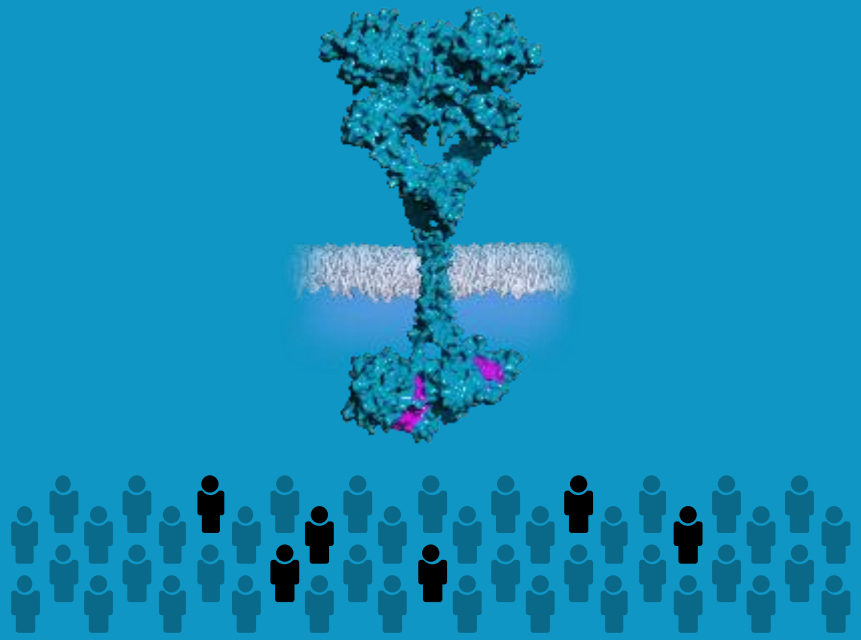
Multiple clinical catalysts including silevertinib Phase 2 PFS data in 1L NSCLC patients at ASCO 2026

Lean organization with runway into H2 2028; ended Q1 2026 with $118.3M

MasterKey: One Solution for Many Mutations

Traditional Approach:

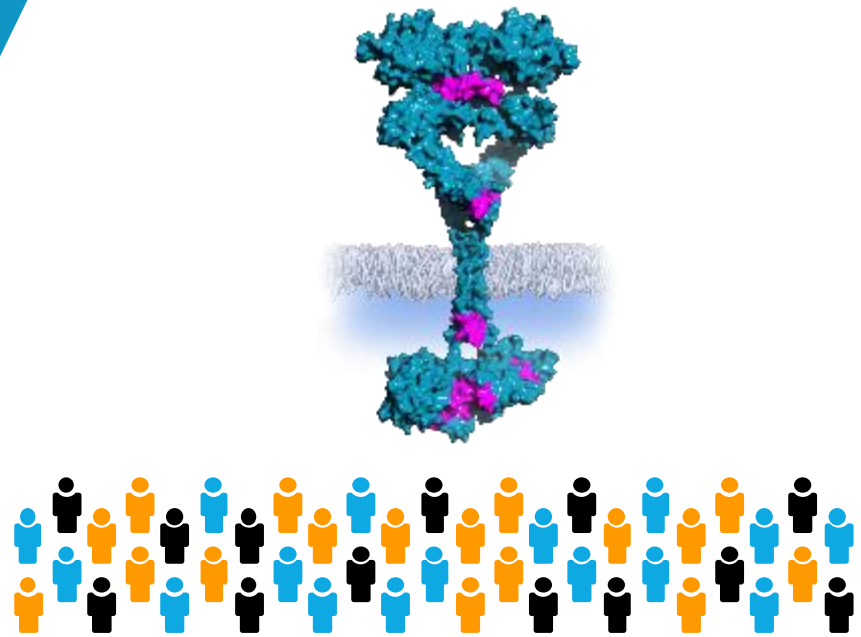
Targeting single mutations in individual tumor types



Limited addressable patient population

Black Diamond Approach:

Targeting families of oncogenic mutations



Expanded addressable patient population

Potent against broad mutation families (including drug resistance mutations)	Brain-penetrant to treat CNS disease	Selective targeting to deliver well-tolerated therapies

BLACK DIAMOND THERAPEUTICS

Advancing Pipeline Across Multiple Oncology Indications

Target	Drug Candidate	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3
EGFR	**silevertinib**	1L NSCLC			**Ph2 preliminary DOR/PFS data at ASCO 2026** **FDA feedback on pivotal development path expected H2 2026**	*Exploring partnering opportunities for pivotal development*
		2L/3L NSCLC			**Final Ph2 data at ASCO 2026** **FDA Fast Track Designation for C797S+ Patients**	
		Newly Diagnosed GBM			**Initiated randomized Ph2 trial Q2 2026** **Interim PFS data expected H1 2028**	
RAF	**BDTX-4933**	RAF/RAS mutant solid tumors			**Licensed to Servier***	
FGFR2/3	**BDTX-4876**	Achondroplasia and solid tumors			**Partnering opportunity**	

*BDTX eligible for up to $710M in development and commercial milestones + royalties

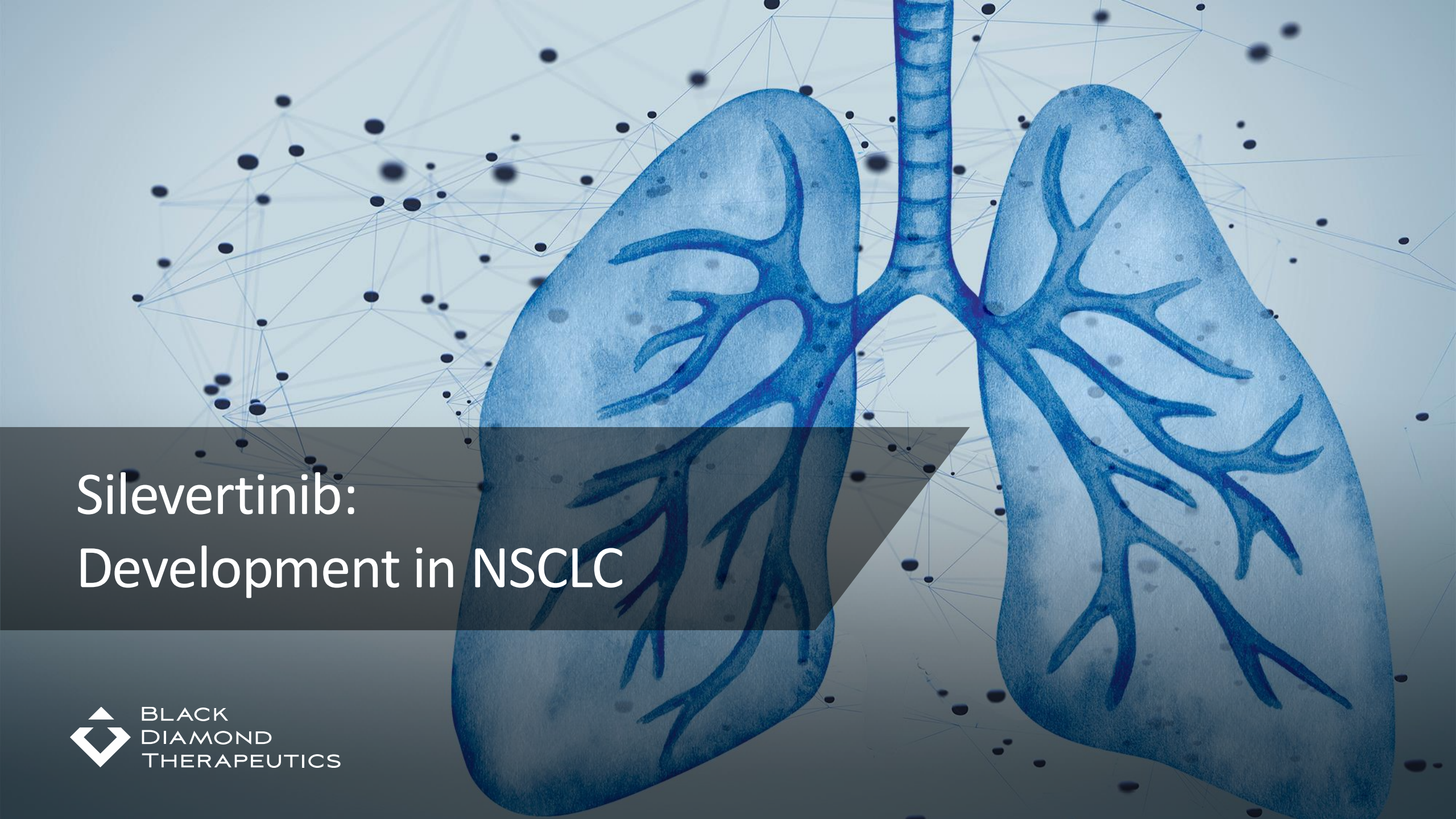
BLACK DIAMOND THERAPEUTICS

Silevertinib: Potential First and Best-in-Class 4th Generation EGFR TKI

MasterKey	**Targets broad spectrum of EGFR classical, non-classical, and C797S resistance mutations in NSCLC, as well as EGFR oncogenic alterations in GBM**
Spares WT-EGFR	**Selective for mutations versus WT-EGFR to deliver favorable tolerability profile**
Covalent	**Oral small molecule with covalent MOA for potency and durability**
Brain-Penetrant	**Demonstrated pharmacologically relevant exposure in GBM tumor tissue; 86% CNS ORR in frontline NSCLC**
Robust Clinical Activity	**60% ORR and 15.2mo mPFS in frontline NSCLC (43 EGFR-NCM patients in Phase 2), more than 200 patients treated across NSCLC and GBM**
Significant Commercial Potential	**$2bn+ opportunity in 1L non-classical EGFRm NSCLC and EGFR+ GBM, with potential to expand to other patient populations/lines of therapy**

BLACK DIAMOND THERAPEUTICS

NCM: non-classical mutations

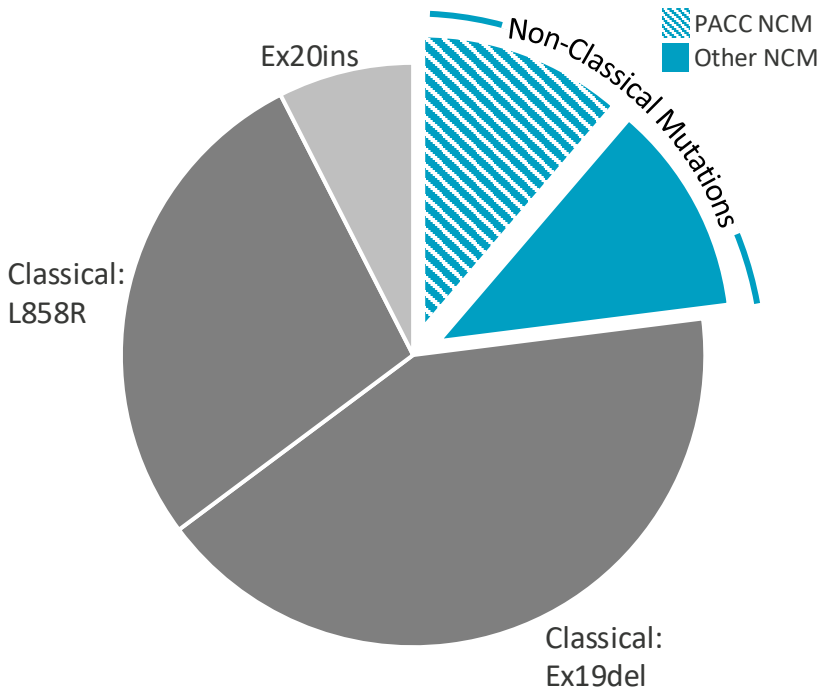


Silevertinib: Development in NSCLC

Black Diamond Therapeutics

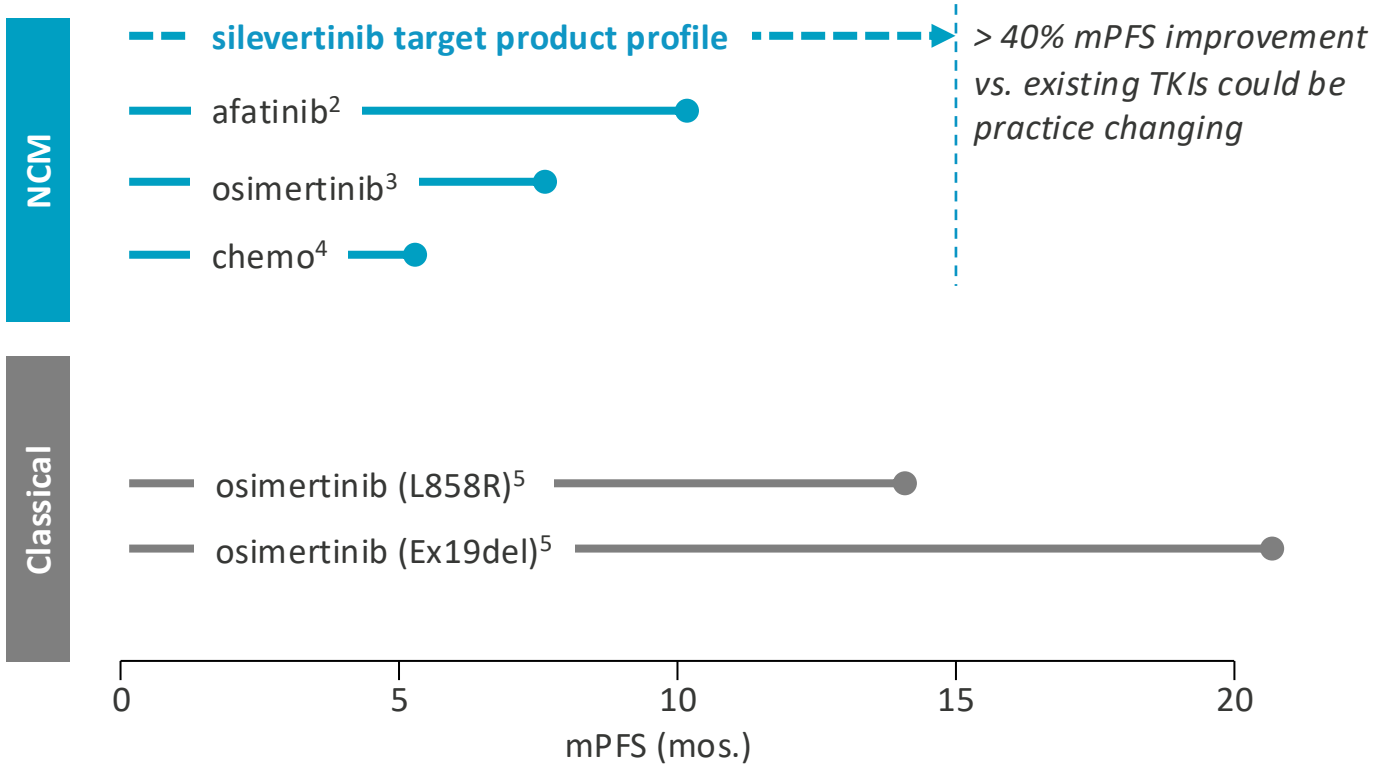
Silevertinib: Practice Changing Potential for ~25% of 1L EGFRm NSCLC Patients

NSCLC Diagnosis by EGFR Mutation[1]



EGFR-NCMs represent ~25% of newly diagnosed cases of EGFRm NSCLC…

mPFS with Currently Available Therapies



…and **current therapies fall short** of delivering optimal benefit to EGFR-NCM patients

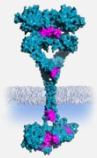
BLACK DIAMOND THERAPEUTICS

1. Heymach et al ESMO 2024. PACC subset is derived from real world data from Guardant Health and from silevertinib Ph2 1L cohort. 2. ACHILLES-2025: Miura et al JCO 2025. 3. Average mPFS from UNICORN-2024: Okuma et al JAMA Oncology 2024 and ARTICUNO: Pizzutilo et al ESMO Open 2024, mPFS for all NCM represents data for Group A TKI naïve patients, mPFS for other NCMs is for n=27 patients, for whom all but 2 were TKI-naive. 4. Chemo mPFS calculated in reference to relative rwTTD for osi versus chemo (non-targeted agents) as presented in Heymach et al ESMO 2024. 5. FLAURA: Soria et al NEJM 2018.

Broad Spectrum Potency and CNS Penetrance are Critical to Optimizing Benefit to NSCLC Patients with EGFR-NCMs

Critical success factors for treating EGFR-NCM NSCLC patients:

Broad spectrum potency



- There are >50 unique EGFR-NCMs[1]
- ~ 40% of EGFR-NCM patients present with more than one mutation (compound)[2]

CNS penetrance

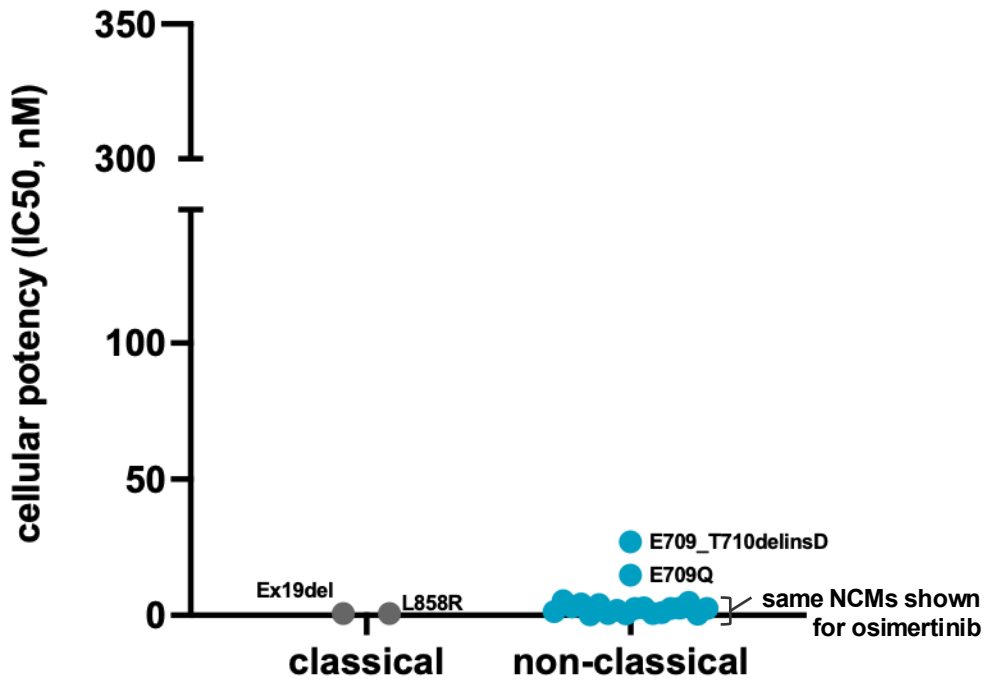
- ~40% of EGFR-NCM patients present with brain metastases at diagnosis[3]
- Patients frequently progress via brain metastases[3]

Black Diamond Therapeutics	Other EGFR TKIs[4]	
silevertinib	**afatinib**	**osimertinib**
✓	✓	✗
✓	✗	✓

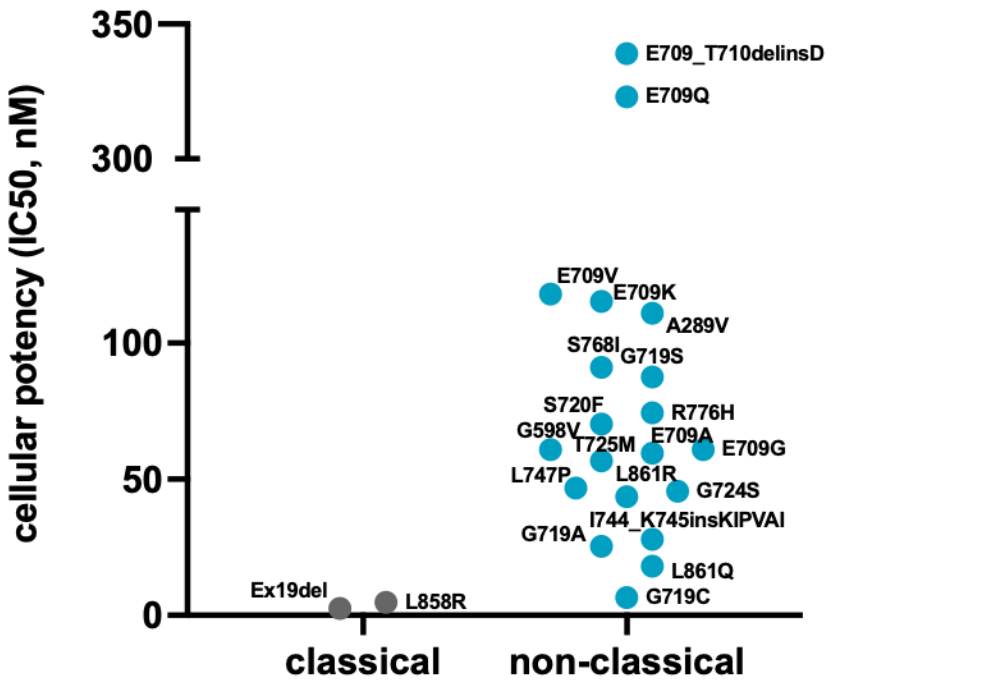
1. Heymach et al ESMO 2024. 2. Li et al Cancers 2022. 3. Kang et al Front Oncol 2023, Wilcox et al Annals Oncology 2025, and Li et al Cancers 2022. 4. Heymach et al ESMO 2024, Colclough et al Clin Can Res 2021 (afatinib and osimertinib), data on file (silevertinib). Brain penetration considered positive for Kpuu>0.2. Potency is considered positive if IC50 for TKI is <25nM. No head-to-head clinical study has been conducted between silevertinib and other EGFR targeted therapies in NSCLC.

Silevertinib Potently Targets the Full Spectrum of EGFR Classical and NCM Drivers

Silevertinib potently inhibits NCMs



Osimertinib exhibits poor potency against most NCMs

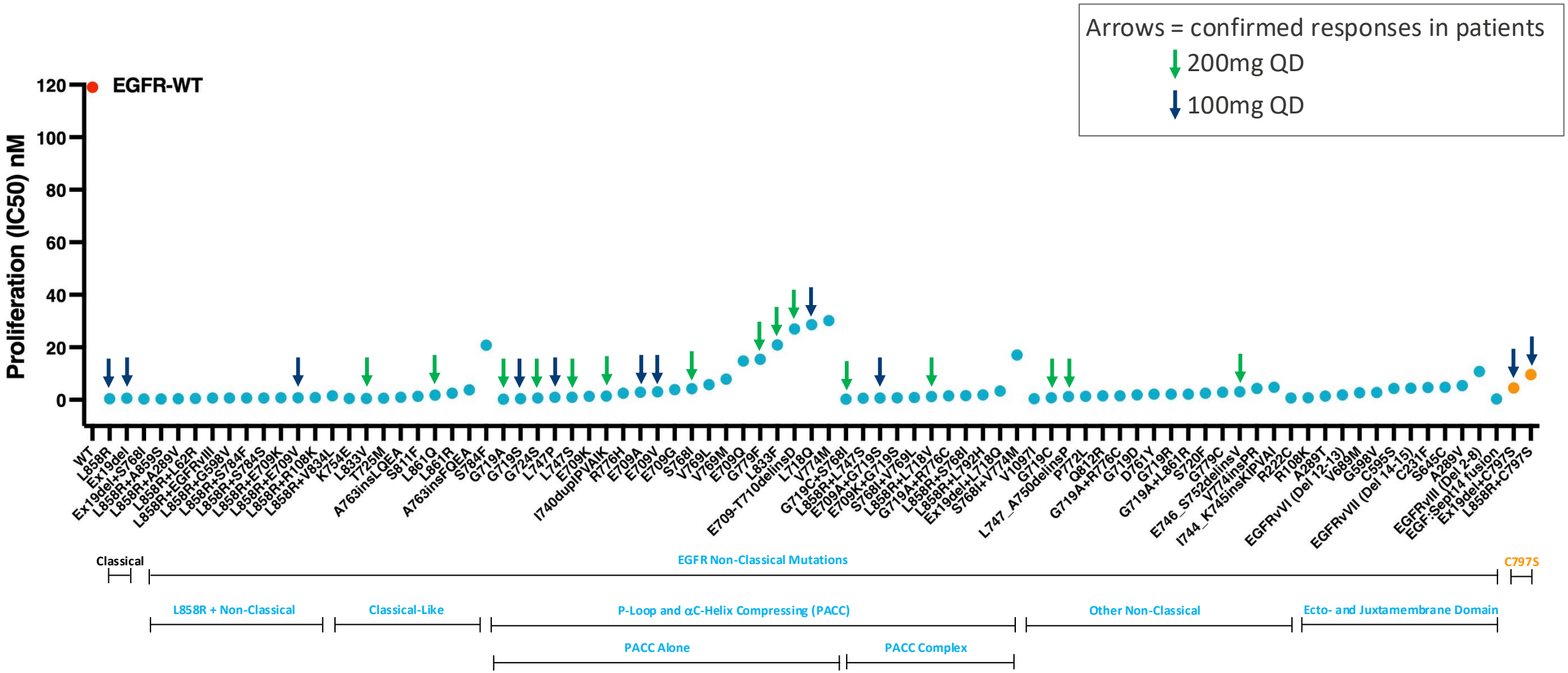


BLACK DIAMOND THERAPEUTICS

Heymach et al ESMO 2024. Data reflect phenotypic IC50 values from cellular proliferation assays using Ba/F3 cells transformed with indicated mutation. IC50 values for osimertinib and silevertinib were attained in head-to-head experiments.

Silevertinib Achieves Confirmed Responses Across Dozens of Unique Mutations

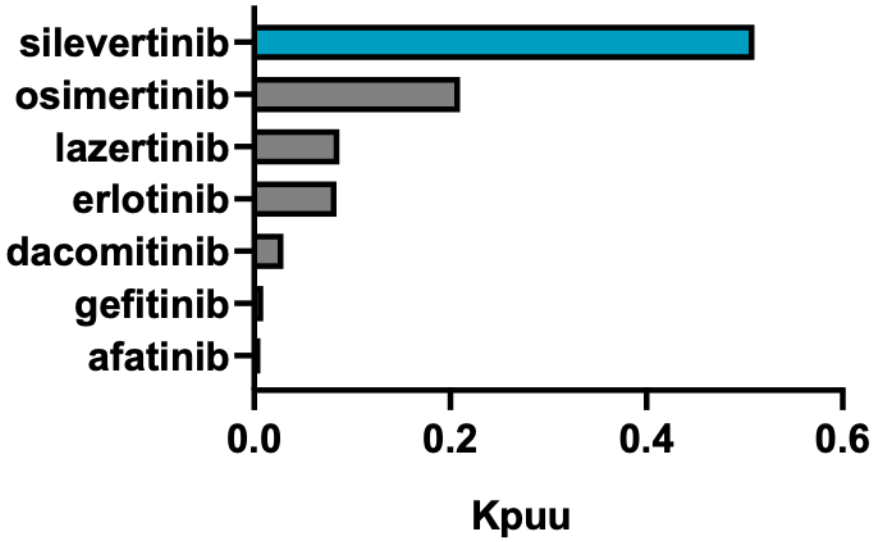
Most mutations shown below cannot be addressed by osimertinib



IC50 data adapted from BDTX AACR 2024 oral presentation. Confirmed responses in frontline and recurrent setting patients from BDTX-1535-101 trial (Ph1 and Ph2, data on file).

Silevertinib Demonstrates Best-in-Class Brain Penetrance Among EGFR TKIs

Best brain penetration properties among EGFR TKIs[1]



Best CNS-ORR in defined 1L EGFR-NCM patient population[2]

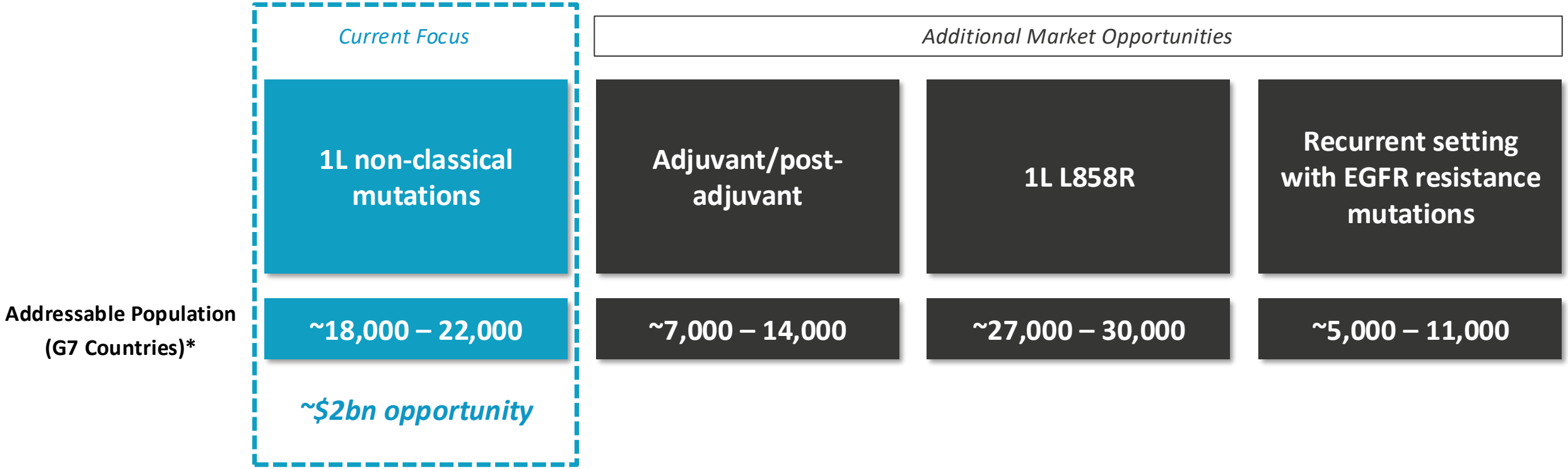
silevertinib	firmonertinib	osimertinib	afatinib
CNS ORR = 86%[2]	CNS ORR = 43%[4]	CNS ORR = 36%[5]	CNS ORR = 33%[6]

Robust CNS activity critical for driving prolonged PFS and OS

1. Kpuu from Colclough et al Clin Can Res 2021 and data on file (silevertinib). Kpuu for firmonertinib not disclosed. CNS ORR: 2. No head-to-head studies have been conducted; cross-study data reflect different study designs, populations, and other features. 3. Silevertinib – 3Dec2026 BDTX presentation 4. Firmonertinib – Le et al WCLC 2025. 5. Osimertinib – UNICORN (Uncommon): Bar et al JTO 2022. 6. Afatinib – Schuler et al JTO 2015.

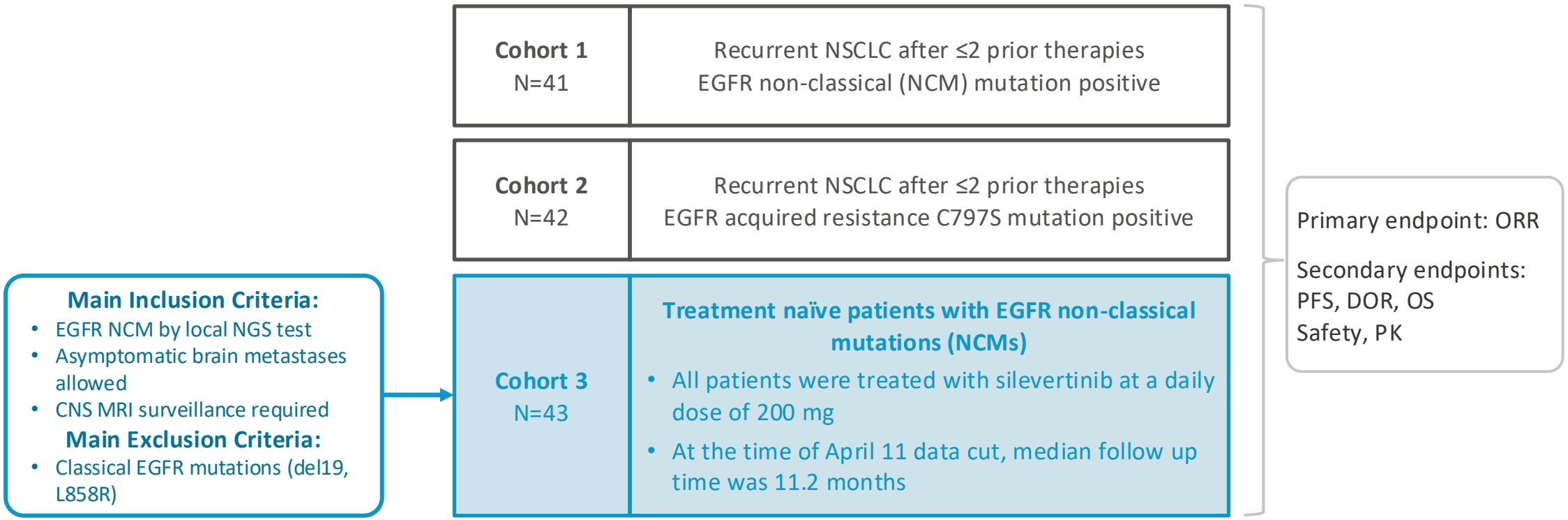
BLACK DIAMOND THERAPEUTICS

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



* Data Monitor Pharma Intelligence; Zhang Oncotarget 2016; Heymach ESMO 2024; Kantar Treatment Architecture; Rotow JTO 2023; BDTX Internal Data Analysis; Foundation Med AACR 2023; Bertoli Int J Mol Sci 2019; Piotrowska Annals of Oncology 2022

Silevertinib in EGFR-NCM NSCLC Phase 2 Design



Silevertinib: Key Takeaways from Phase 2 1L NSCLC Data

- 60% ORR (RECIST 1.1), 86% CNS ORR (RANO-BM)
- Preliminary mPFS 15.2 months; mDOR not reached
- 23 of 43 (53%) patients remained on therapy, longest at 23.5 months
- No patients developed *de novo* brain metastases
- Dose dependent and manageable adverse event (AE) profile

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

Data from April 11, 2026: 43 patients with 33 unique EGFR NCMs and 44% with baseline brain metastases; 11.2 mo. median follow up

Silevertinib 1L NSCLC Summary and Next Steps

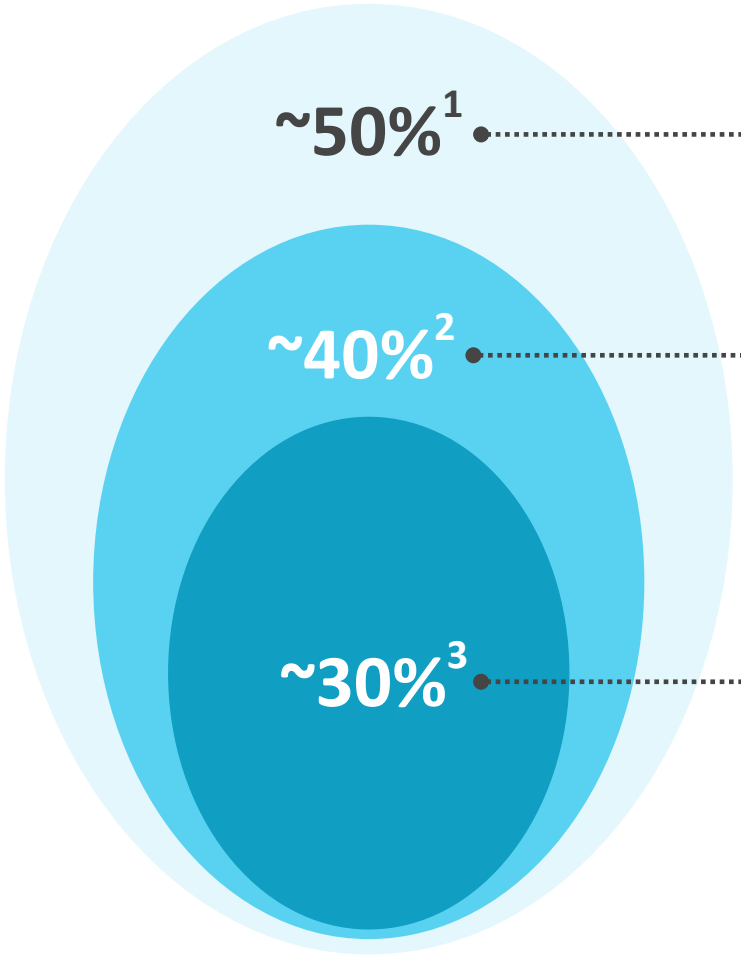
- Robust anti-tumor activity and durability achieved in Phase 2
- Potential best-in-class CNS activity, a significant unmet medical need in NSCLC
- FDA feedback on pivotal development path in 1L NSCLC expected in H2 2026
- Opportunity to capture up to ~25% of 1L EGFRm NSCLC market

Silevertinib presents practice changing potential for treatment naïve patients with EGFR NCMs

Silevertinib: Development in Glioblastoma

Black Diamond Therapeutics

Treatment of EGFR-Driven GBM Requires Inhibition of Complex EGFR Mutations, Particularly EGFRvIII: Potent Preclinical Inhibition by Silevertinib



~50%[1] Of all GBM patients carry oncogenic EGFR alterations

~40%[2] Of all GBM patients have more than one oncogenic EGFR alteration

~30%[3] Of all GBM patients express EGFRvIII, which has been demonstrated to be a potent oncogenic driver

~7,000

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

BLACK DIAMOND THERAPEUTICS

1. Saadeh, F., et al., The International Journal of Biological Markers, 2018 2. Real world evidence data from Tempus Labs analysis of 2,540 GBM patient samples. 3. EGFRvIII expression based upon Noeuveglise et al ESMO OPEN 2022, French et al Neuro-Oncology 2019, Weller et al Lancet Oncology 2017

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

Lessons From Past Failures	Silevertinib
Low brain exposure due to a lack of CNS penetrance	**Brain-penetrant to treat CNS tumors**
Heterogenic expression of EGFR oncogenic alterations within tumors	**Potent MasterKey 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**

BLACK DIAMOND THERAPEUTICS

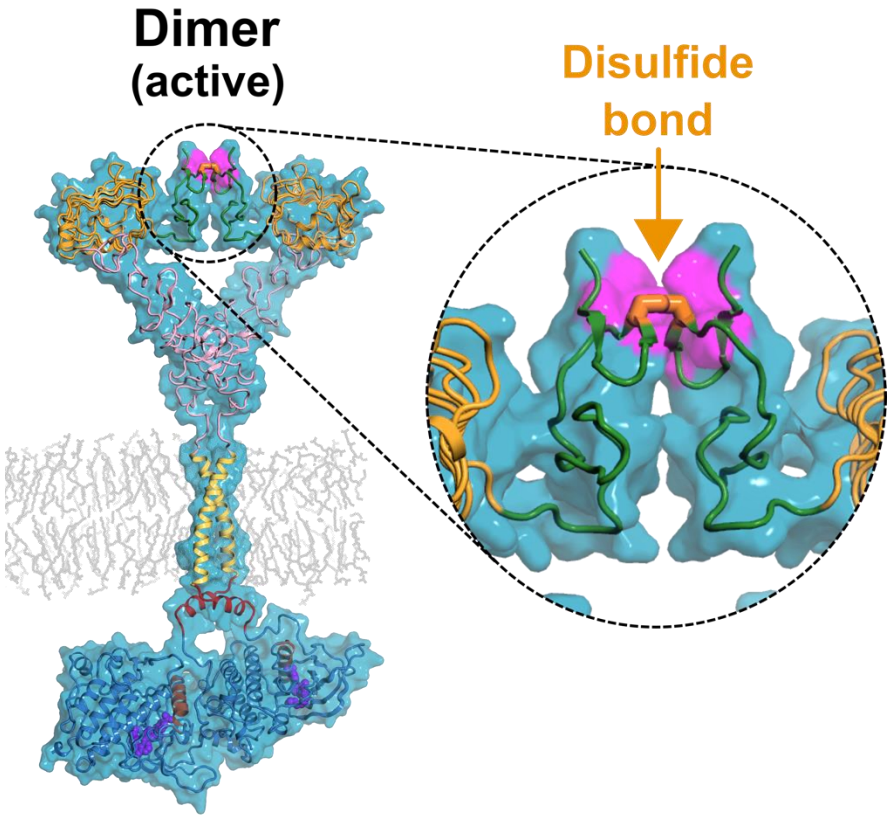
MOA=mechanism of action; CNS=Central Nervous System; WT=Wild-Type; GBM=Glioblastoma Multiforme; NSCLC=Non-Small Cell Lung Cancer

Silevertinib: Potential to Address Limitations of Other EGFR Therapies

		Black Diamond Therapeutics	Other EGFR Targeted Therapies					
		silevertinib	afatinib	dacomitinib	depatuximab	osimertinib	erlotinib	gefitinib
Brain Penetration		✓	✗	✗	✗	✓	✗	✗
Potency against EGFR variants in GBM	EGFRvIII	✓	✓	✓	✓	✗	✗ *paradoxical activation*	✗ *paradoxical activation*
	Other EGFR Alterations	✓	✓	✓	✗	✗	✗ *paradoxical activation*	✗ *paradoxical activation*
	EGFR-Amp	✓	✓	✓	✓	✗	✗	✗

Potency and paradoxical activation for EGFR variants for erlotinib, gefitinib, afatinib, dacomitinib, osimertinib from O'Connor et al – BioRxiv 2019. Potency for EGFR variants for depatuximab-M from Marin et al Neuro-Oncology 2021. Brain penetration for erlotinib, gefitinib, afatinib, dacomitinib, and osimertinib from Colclough et al Clin Can Res 2021. Brain penetration for depatuximab-M from Marin et al Neuro-Oncology 2021. Potency for EGFR variants and brain penetration for silevertinib – data on file. No head-to-head clinical study has been conducted between silevertinib and other EGFR targeted therapies in GBM. Brain penetration considered positive for Kpuu>0.2. Potency is considered positive if IC50 for TKI is <25nM or if antibody is shown to bind to EGFR variant.

EGFRvIII: Covalent Homodimers Promote Potent Oncogenic Activity in GBM



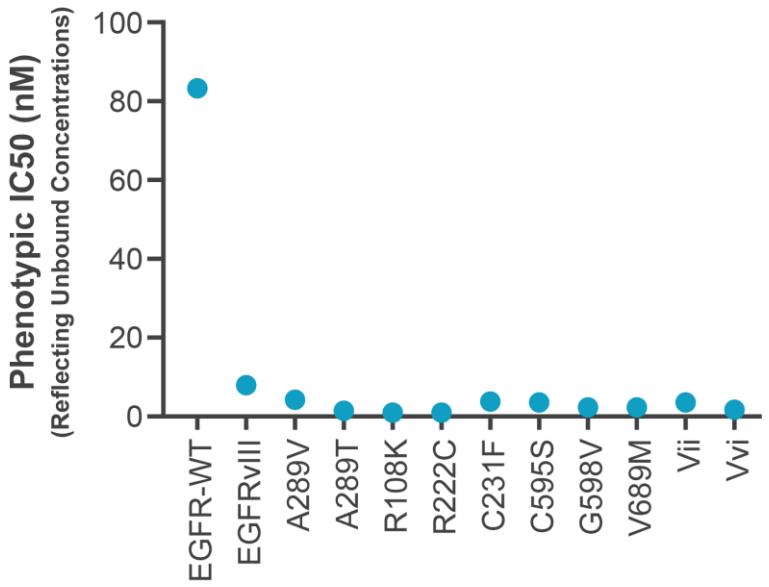
- The EGFRvIII covalent homodimer is highly oncogenic[1]
- EGFRvIII is present as a compound mutation in nearly 90% of cases[2]; compound mutations are considered to be *the most oncogenic and actionable* based on experience in EGFR-NCM NSCLC
- EGFRvIII is present in approximately 30% of all GBM patients[3,4,5], regardless of MGMT methylation status[6]

BLACK DIAMOND THERAPEUTICS

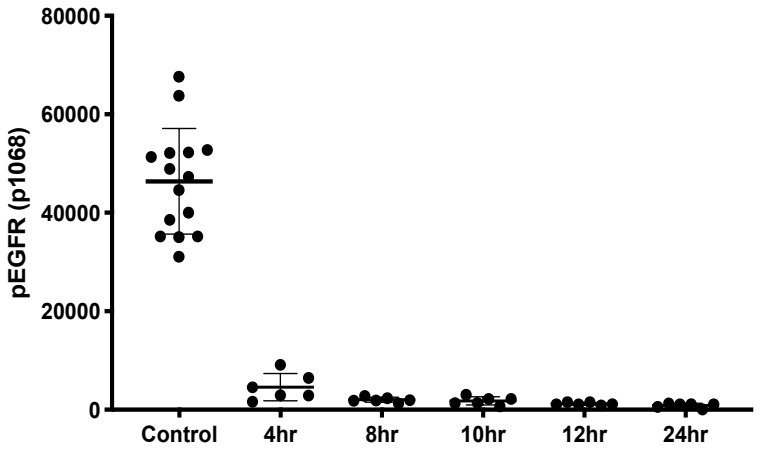
1. O'Connor et al bioRxiv 2019. 2. Brennan et al Cancer Cell 2012. 3. Noeuveglise et al ESMO OPEN 2022. 4. French et al Neuro-Oncology 2019. 5. Weller et al Lancet Oncology 2017. 6. Felsberg et al Clin Can Res 2017.

Silevertinib Demonstrates Potent Preclinical Inhibition of EGFRvIII and Other Alterations that are Co-Expressed with EGFRvIII

Silevertinib potently inhibits EGFRvIII and co-expressed EGFR mutations present in GBM

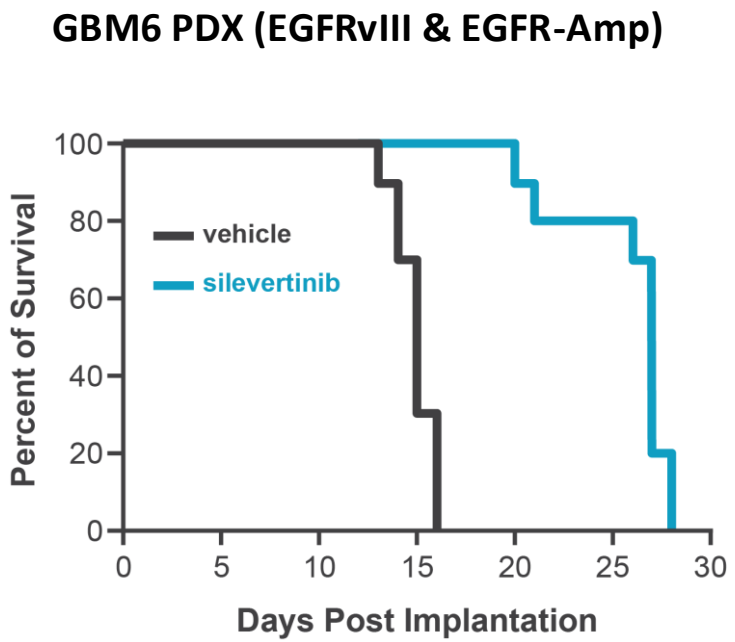


Silevertinib durably inhibits EGFRvIII activity in vivo following a single oral dose



Durable inhibition of pEGFR following single oral 50mg/kg dose of silevertinib

Silevertinib improves survival in an intracranial EGFRvIII PDX model



Day 6 – Day 17

Dosing period

BLACK DIAMOND THERAPEUTICS

BDTX data on file and presented at AACR 2023 Annual Meeting. Phenotypic IC50 reflects cellular antiproliferative IC50 corrected for protein binding. GBM6 PDX study conducted at UCSF neuro oncology core facility; 50mg/kg silevertinib dosed orally over the indicated dosing period.

Encouraging Results for Silevertinib in GBM Trials to Date Support Initiation of a Randomized Phase 2 Trial in Newly Diagnosed GBM Patients

Phase 1 Dose Escalation in 2L+

Confirmed ***tolerability***

Encouraging ***clinical activity***

Data at ASCO 2024

- 41* patients with recurrent disease
- Generally well tolerated @ 200mg
- Preliminary efficacy/RANO response

Phase 0/1 IST

Confirmed ***brain exposure***

Data at EANO 2025

- 21 patients with recurrent disease
- Demonstrated brain exposure
- Up to 48 ND pts currently enrolling

Randomized Phase 2 in ND patients

PFS Primary Endpoint
OS Secondary Endpoint

Interim Analysis (PFS) expected H1 2028

- 150 newly diagnosed patients
- Silevertinib + TMZ vs. TMZ
- Randomization after surgery/radiation

BLACK DIAMOND THERAPEUTICS

Wen et al ASCO 2024, Sanai et al ASCO 2024, Sanai et al EANO 2024, Sanai et al SNO 2024, Sanai et al AACR 2025, and Sanai et al EANO 2025
*27 dose escalation patients presented at ASCO 2024, an additional 14 patients were dosed at 200mg primarily to assess PK and safety.
ND = Newly Diagnosed

Silevertinib is Ready for Phase 2 Development in ND GBM Patients

	BDTX Phase 1 (n=17)*		Ivy Phase 1 (n=21)^
Adverse Event	**Any Grade**	**Grade ≥3**	**Any Grade**
Rash or Acne	82%	6%	NA
Diarrhea	41%	0%	NA
Stomatitis	24%	0%	NA
Paronychia	12%	0%	NA
ALT Increase	6%	6%	NA
Dry Skin	0%	0	NA
TRAE Grade≥3	35%		28.6%
SAEs	6%		4.8%
Dose interruption	29%		28.6%
Dose reduction	6%		0%
AE Leading to DC	18%		0%

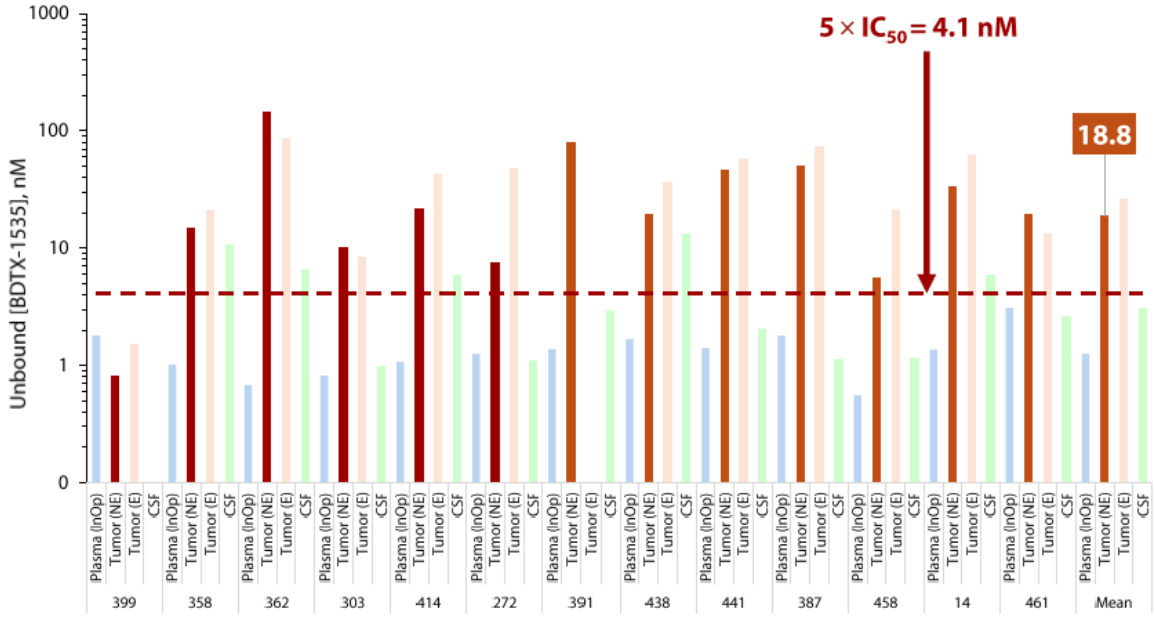
- Silevertinib has been generally well-tolerated; administered to >60 GBM Phase 1 patients (38 at 200mg QD), with the longest on therapy for >16 months
- Silevertinib demonstrated encouraging activity, including RANO response, in a heavily pre-treated patient population (BDTX Phase 1 trial data presented at ASCO 2024)
- Combination of TMZ and silevertinib unlikely to have drug-drug interactions and showed additive anti-tumor activity (preclinical data)
- TMZ and EGFR-TKIs have been combined in GBM patients previously[1], and side-effect profile is manageable
- Phase 0/1 trial (Ivy IST) demonstrates pharmacologically relevant exposure of silevertinib in GBM tumor tissue

^ Sanai et al EANO 2025: 21 patients in treatment phase at 200mg
* 3 patients at 200mg from dose escalation + 14 patients at 200mg from PK/safety cohort; BDTX data on file.
1. Prados et al Cancer Chemotherapy Pharmacology 2008 and Brown et al Journal of Clinical Oncology 2008
ND = Newly Diagnosed

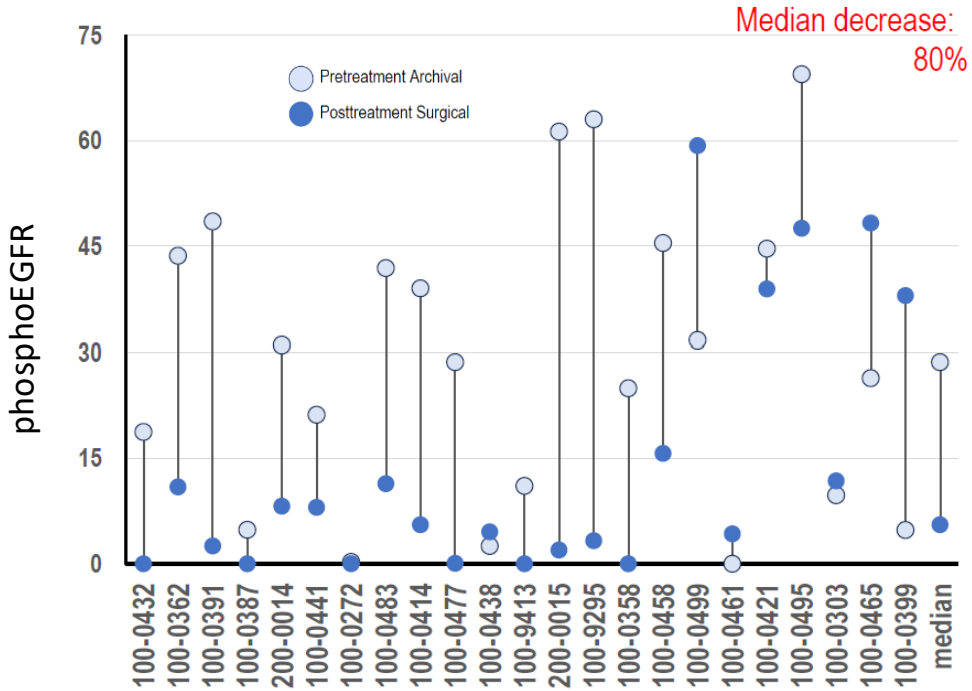
BLACK DIAMOND THERAPEUTICS

Phase 0/1 IST in Recurrent GBM Patients: Silevertinib Exceeds Targeted Exposure in Non-Contrast Enhancing Regions of Brain Tumors

Exposure in GBM tumors exceeds IC50 for targeted mutations (measured in patients dosed 5 days @ 200mg QD)



Decreased pEGFR vs. pretreatment archival tissue

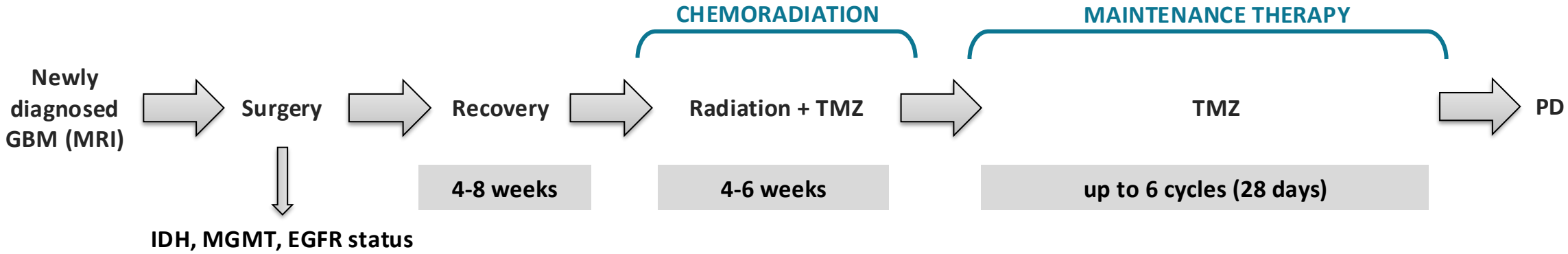


Ivy Brain Tumor Center

BLACK DIAMOND THERAPEUTICS

Sanai et al EANO 2025. NE = non-enhancing, E = enhancing, CSF = cerebral spinal fluid

Newly Diagnosed GBM Patient Journey: Limited Options for Patients



Only two therapies approved for GBM patients in last 20 years

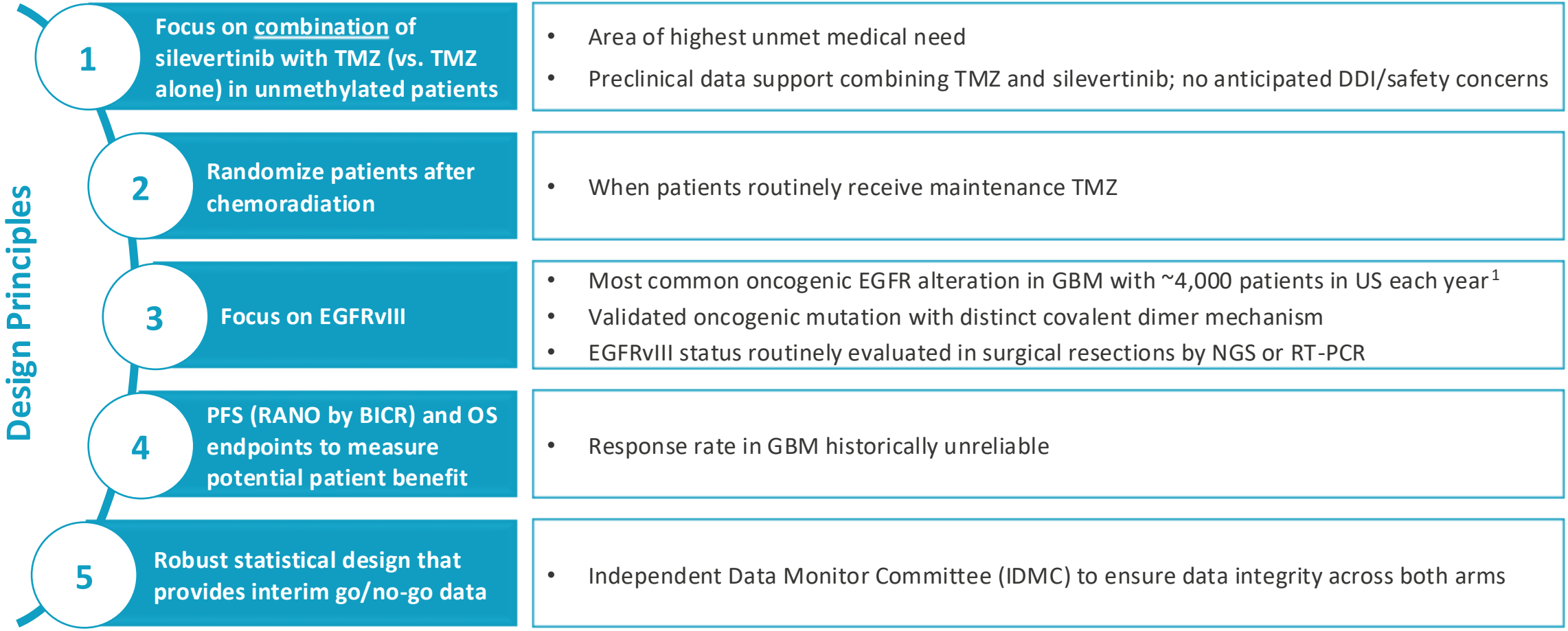
- Temozolomide (TMZ): primarily benefits methylated patients (though given to unmethylated patients as well)
- Tumor Treating Fields (TTF): device with compliance/QOL issues

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

BLACK DIAMOND THERAPEUTICS

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

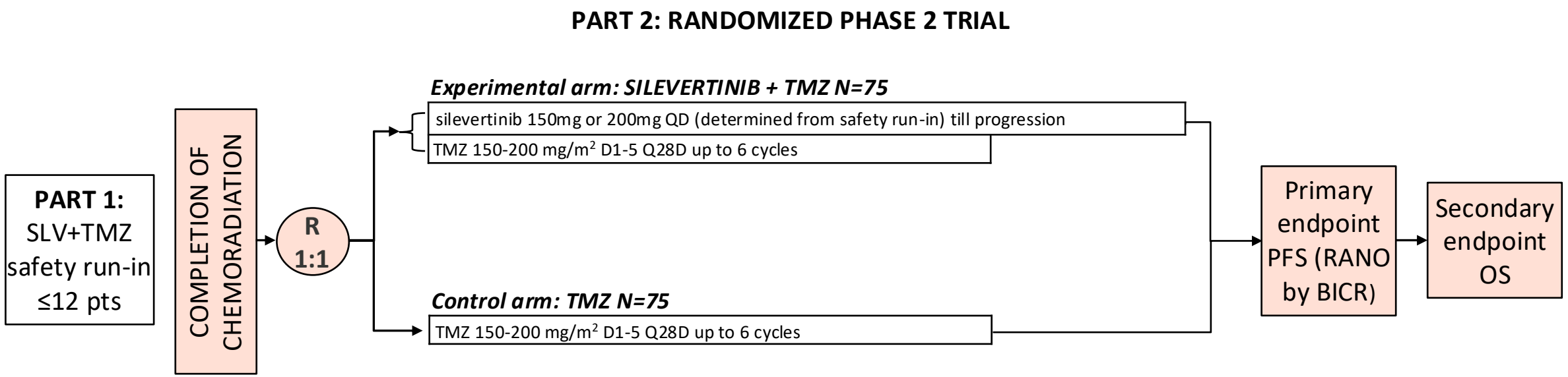
Design Principles: Randomized Phase 2 Trial in Newly Diagnosed GBM



DDI: Drug-Drug Interaction

1. Based upon EGFRvIII expression in 30% of all GBM (Noeuveglise et al ESMO OPEN 2022, French et al Neuro-Oncology 2019, Weller et al Lancet Oncology 2017), with all EGFR alterations in GBM comprising 50% of all GBM and representing 7000 patients in US each year.

Randomized Phase 2 of Silevertinib + TMZ in Newly Diagnosed GBM

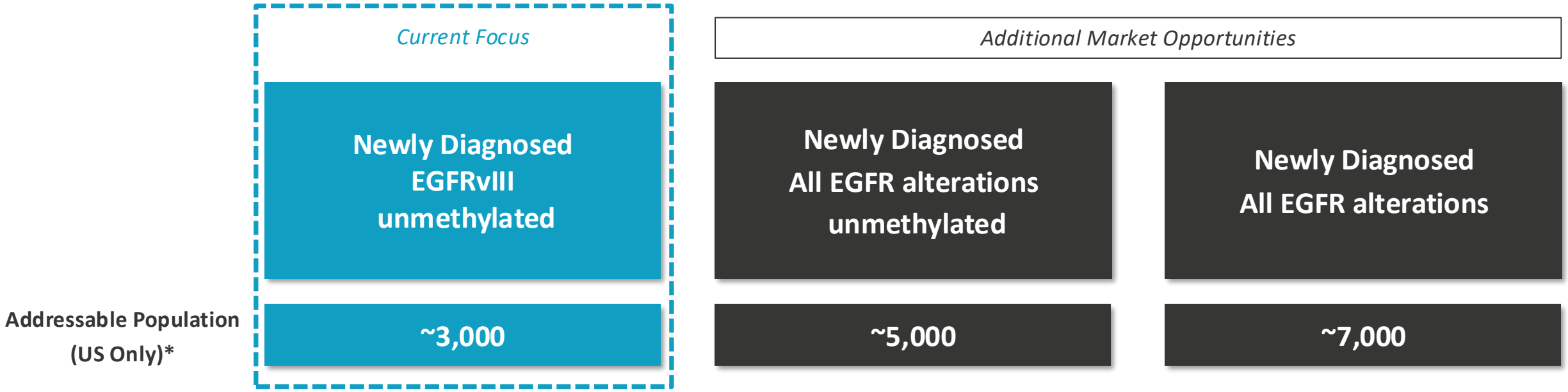


- Study population: unmethylated patients with EGFRvIII
- IDMC will perform interim analyses for futility and early efficacy, and a final analysis for PFS efficacy
- Confirmation of progression (RANO) by Blinded Independent Committee Review (BICR)

BLACK DIAMOND THERAPEUTICS

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



* Saadeh, F., et al., The International Journal of Biological Markers, 2018; Real world evidence data from Tempus Labs analysis of 2,540 GBM patient samples; EGFRvIII expression based upon Noeuveglise et al ESMO OPEN 2022, French et al Neuro-Oncology 2019, Weller et al Lancet Oncology 2017; Chen et al Nature Scientific Reports 2025 showing methylation in approximately a third of patients

Silevertinib: Key Takeaways and Next Steps

NSCLC

- ✓ Opportunity to capture ~25% of the 1L EGFRm NSCLC market
- ✓ Robust efficacy and durability achieved in Ph2
- ✓ Potential best-in-class CNS activity to address a significant unmet need in NSCLC
- ✓ FDA feedback on pivotal development path in 1L NSCLC expected H2 2026

GBM

- ✓ Opportunity to capture ~50% of the 1L EGFRm GBM market
- ✓ Proof of concept achieved in Ph0/1 and Ph1
- ✓ Randomized Ph2 trial in newly diagnosed GBM patients initiated in May 2026