Black Diamond Therapeutics, Inc.

Developing MasterKey Therapies to Defeat Cancer Resistance

BLACK DIAMOND THERAPEUTICS

November 2024

Forward-Looking Statements

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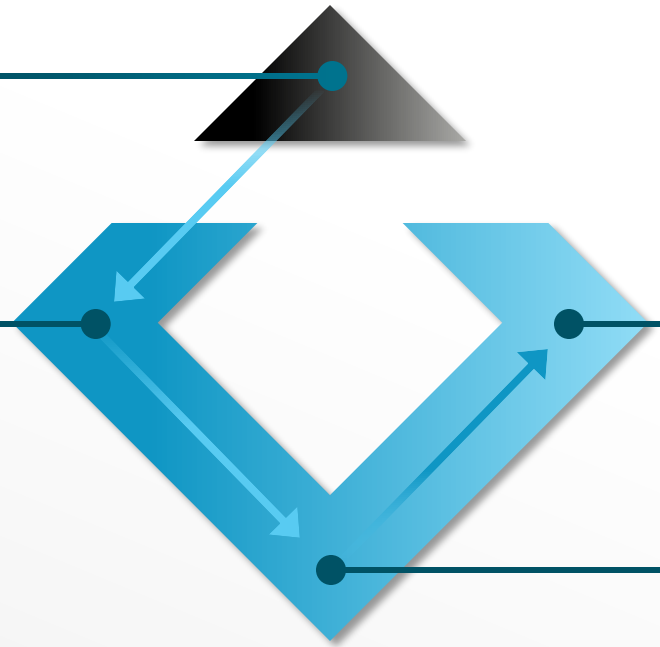
Cancer is a Complex and Ever-Evolving Disease

Current targeted therapies were designed against a **limited subset of oncogenic mutations**

Increasing adoption of liquid biopsies reveals a **broader set of oncogenic mutations**



We are Developing MasterKey Therapies to Defeat Cancer Resistance

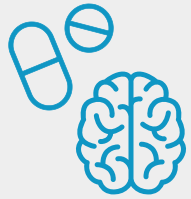
Our oral therapies are designed so that **patients have the opportunity for a longer, healthier, active life**

MasterKey approach aims to **provide one solution for many mutations and expand addressable patient population**

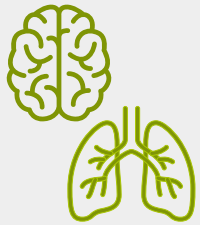
Black Diamond Therapeutics At-a-Glance

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**



Lead asset BDTX-1535: **robust Phase 2 data in recurrent NSCLC**, with additional opportunity in GBM

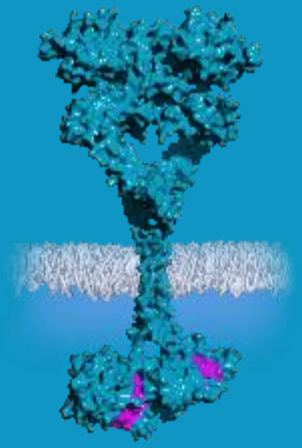
Multiple clinical catalysts including BDTX-1535 Phase 2 data in 1L NSCLC patients in Q1 2025

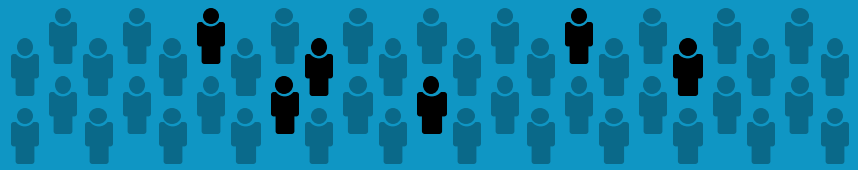
Strong balance sheet, with runway into Q2 2026; ended Q3 2024 with $112.7M in cash

MasterKey: One Solution for Many Mutations

Traditional Approach:

Targeting single mutations in individual tumor types

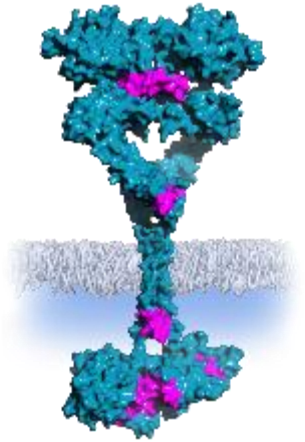


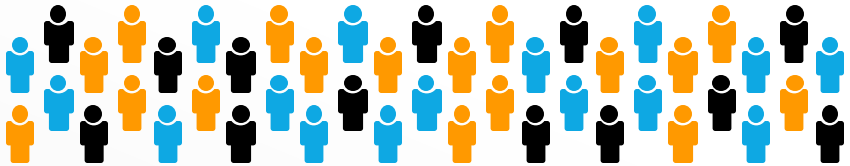


Limited addressable patient population

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

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Advancing Wholly Owned Pipeline Across Multiple Oncology Indications

Target	Drug Candidate	Indication	Pre-clinical / Phase 1 / Phase 2 / Phase 3
EGFR	BDTX-1535	2L/3L NSCLC	Initial Phase 2 data disclosed September 2024
		1L NSCLC	Initial Phase 2 data expected Q1 2025
		GBM	Phase 1 and "window of opportunity" data presented at ASCO and EANO 2024
RAF	BDTX-4933	RAF/RAS mutant solid tumors	Partnering opportunity
FGFR2/3	BDTX-4876	Achondroplasia or solid tumors	Partnering opportunity

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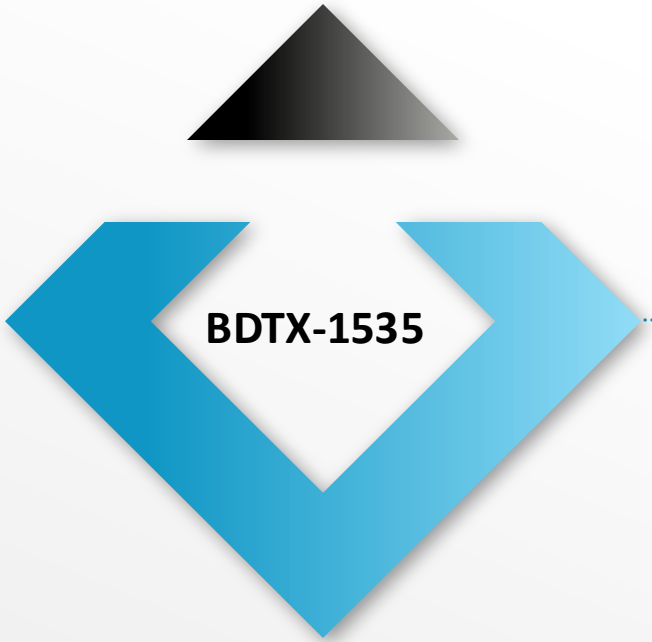
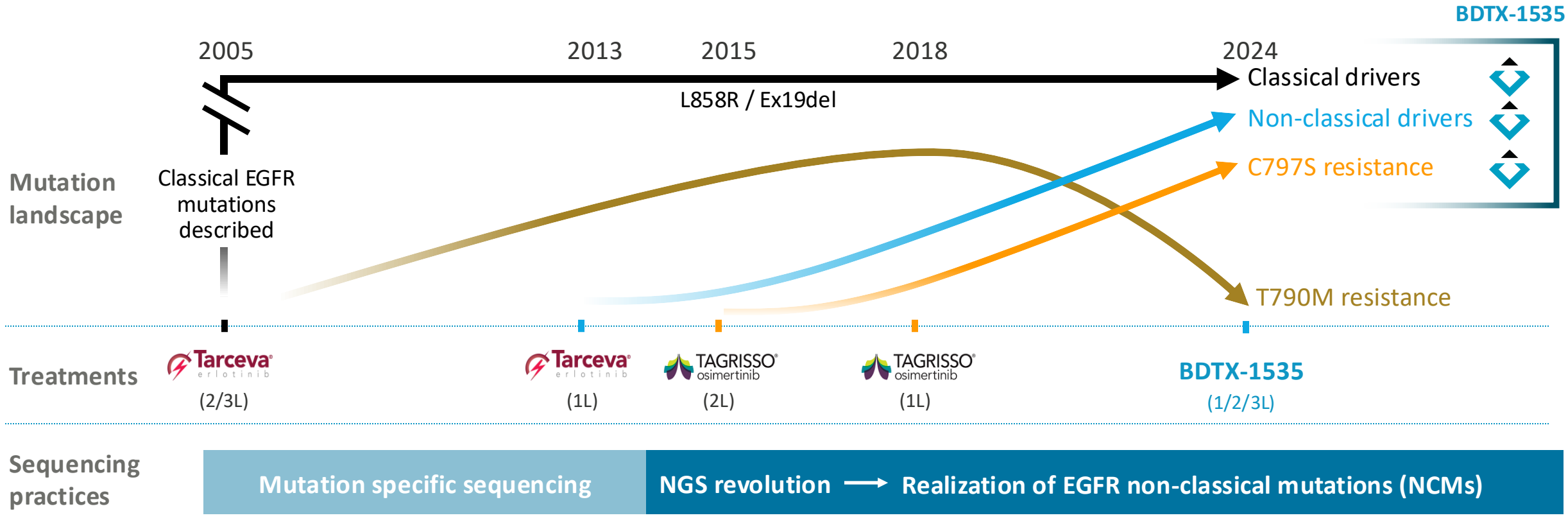
BDTX-1535: Potential First and Best-in-Class 4th Generation EGFR TKI for Patients with EGFRm NSCLC



MasterKey	Targets a broad spectrum of EGFR classical, non-classical, and C797S resistance mutations
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	Designed to treat CNS tumors and brain metastases
Robust clinical activity	Phase 2 cohorts ongoing in both recurrent and frontline EGFRm NSCLC

The EGFR Mutational Landscape in NSCLC has Evolved, Revealing a Broad Spectrum of Unaddressed Non-Classical Oncogenic Driver & Drug Resistance EGFR Mutations

Evolution of the EGFR mutation landscape over the past 20 years



BDTX-1535: opportunity to address unmet need for non-classical drivers and C797S resistance mutations

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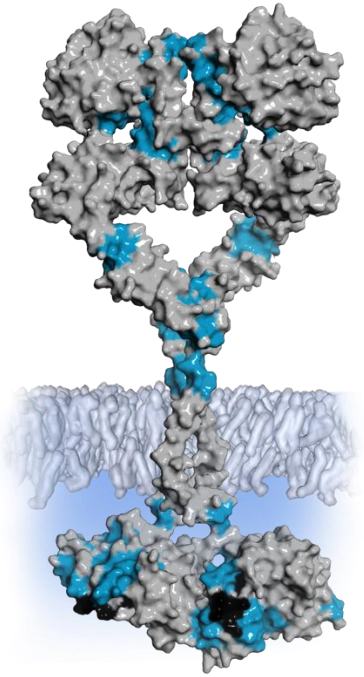
20-30% of Newly Diagnosed EGFRm NSCLC Patients Carry Non-Classical Mutations (NCMs); Not Adequately Addressed by Current Therapies[1]

Classical and non-classical driver mutations are distributed across EGFR structure



Ectodomain-Juxtamembrane *(non-classical)*

50+ mutations

R108X
R222X
A289X
C598X
S645X
…

PACC[2] & others *(non-classical)*

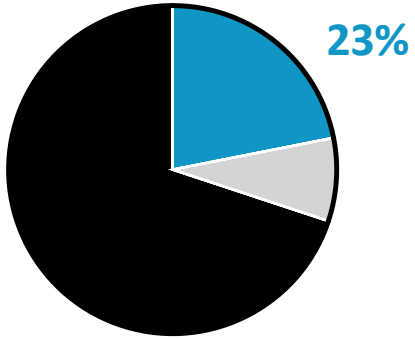
60+ mutations

E709X
G719X
T725M
L754E
L747X
S768I
V769X
L861X
L833X
…

- Non-Classical
- Classical: L858R and Exon19del

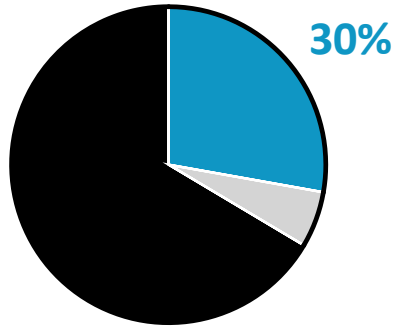
23-30% of newly diagnosed EGFRm NSCLC express non-classical mutations

GUARDANTINFORM™



Black Diamond Therapeutics analyses of 94,939 sequencing reports from treatment naïve NSCLC

PROJECTGENIE
Genomics Evidence Neoplasia Information Exchange



Adapted from Du et al. 2023. Analysis of the AACR GENIE database of 22,050 cases of NSCLC

Current therapies do not adequately address non-classical EGFR mutations[1]

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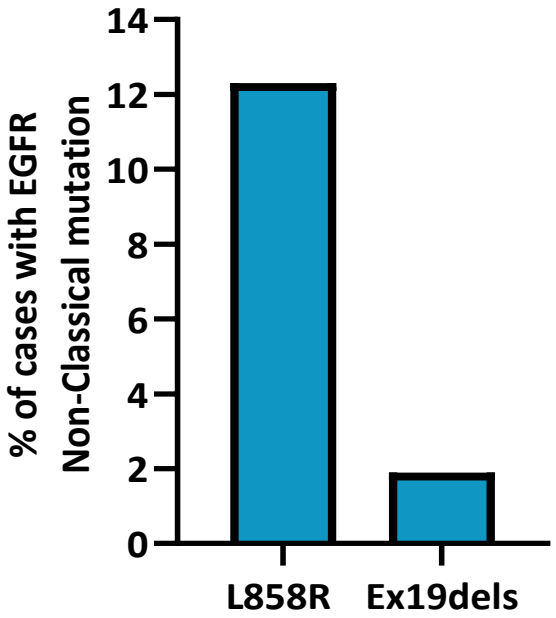
1. Borgeaud M. JTO 2024
2. Robichaux J, Nature 2021
BDTX AACR and ESMO 2024 presentations

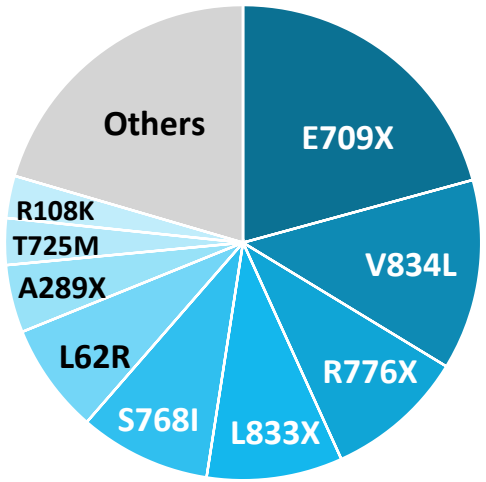
Real World Data Demonstrate Frontline L858R Patients Presenting with EGFR-NCMs Discontinue Quickly Following Osimertinib Therapy

EGFR-NCMs frequently present as compound mutations together with the classical L858R mutation

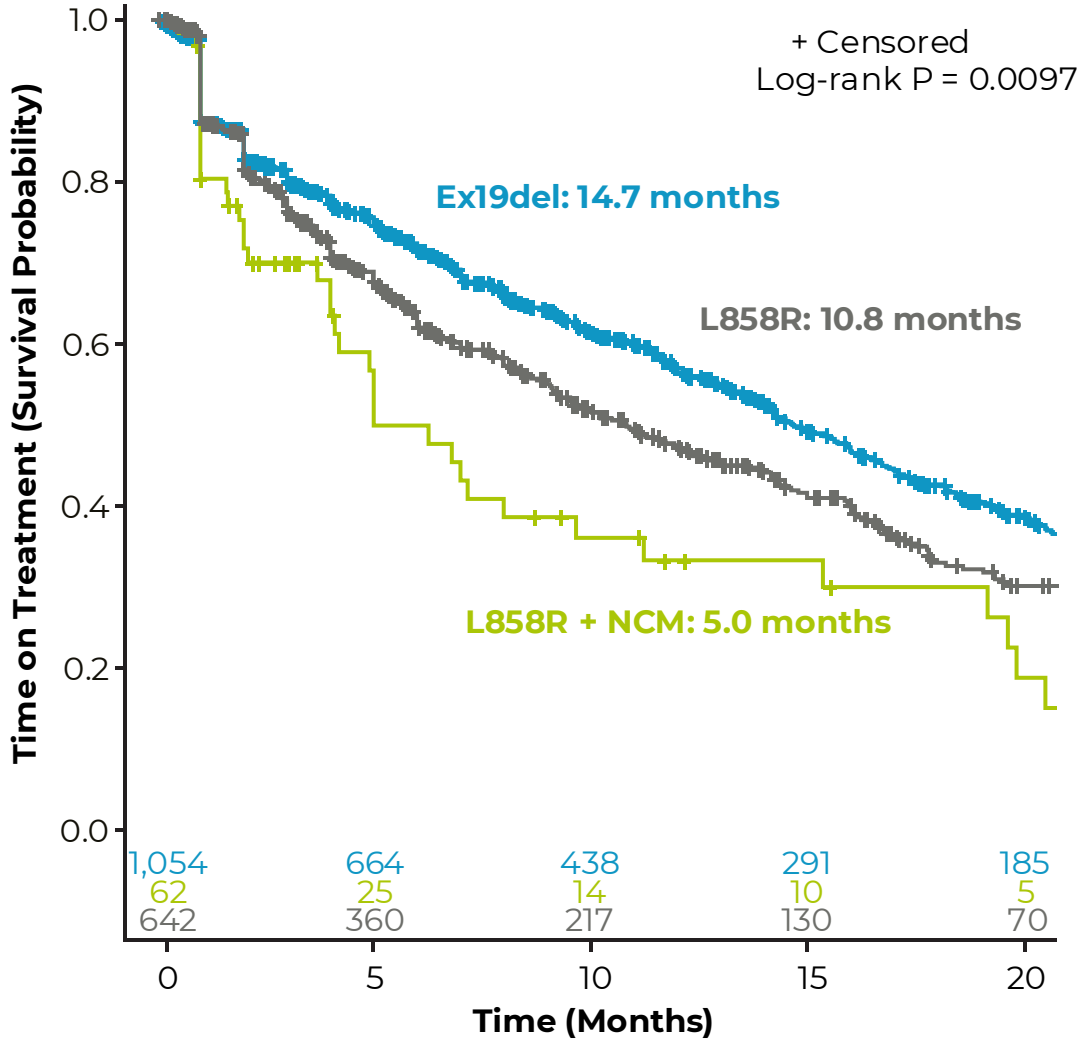
NCMs more frequently co-occur with L858R vs Ex19del



A spectrum of NCMs co-occur together with L858R



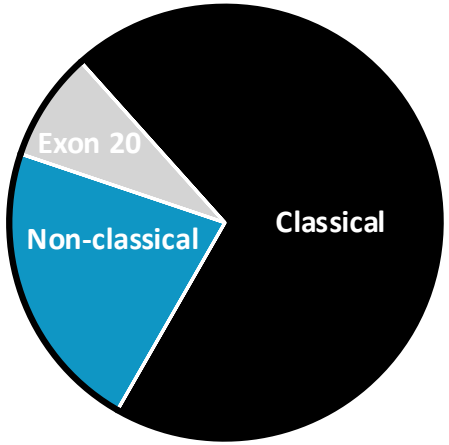
Poor performance for osimertinib in the context of L858R + NCM NSCLC



In Recurrent EGFRm NSCLC, Patients Most Frequently Present with PACC-NCM and C797S Resistance Mutations

PACC-NCMs and C797S are major mechanisms of on-target EGFR resistance in patients post osimertinib[1]

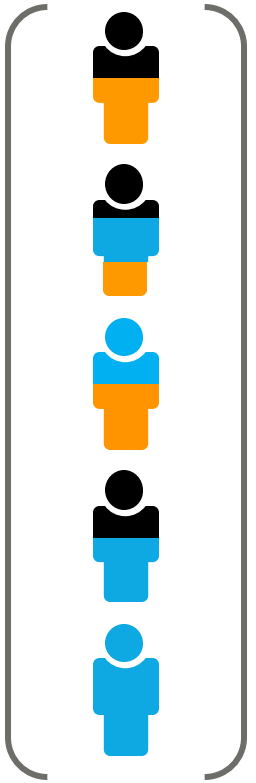
Newly Diagnosed EGFRm NSCLC



osimertinib therapy

Under selective pressure, patients acquire / accumulate EGFR resistance mutations

Recurrent



Classical mutation

Non-classical mutation (including PACC-NCM)

C797S Resistance

Dardenne et al. AACR 2024. Heymach et al. ESMO 2024.

1. Rotow JK, et al. *Journal of Thoracic Oncology*, 2023.

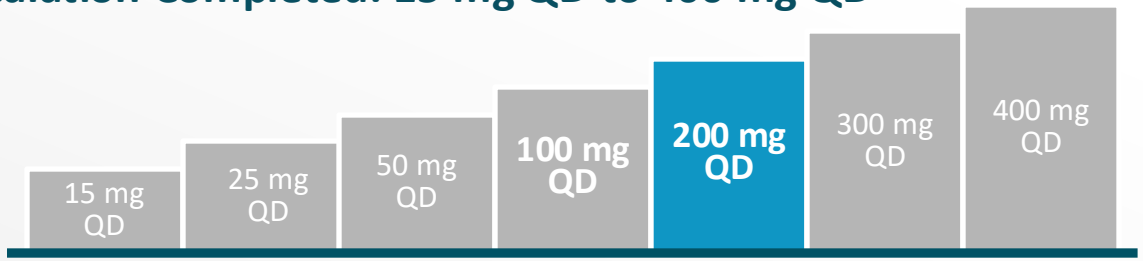
BDTX-1535 Phase 1 Dose Escalation: Summary

Mutation Matched Phase 1 Study Inclusion Criteria

Recurrent NSCLC Cohort			Recurrent GBM Cohort	
EGFR mutations at the time of progression: – Non-classical driver, OR – Acquired resistance C797S	Progression after EGFR TKI	Exclusion of EGFR T790M, Ex20ins, KRAS mutations, cMET amplification	EGFR alterations at resection/diagnosis	Wild-type isocitrate dehydrogenase (IDH)

Dose Escalation Completed: 15 mg QD to 400 mg QD

- **Primary objective:** PK and safety
- **Secondary objective:** Anti-tumor activity



- Target coverage and clinical activity at ≥ 100 mg, MTD at 300 mg

Ph 1 NSCLC Key Data Takeaways

- **Once-daily dosing delivers sufficient exposure to inhibit EGFR mutations**
- **Manageable EGFR TKI tolerability profile at 200 mg (similar to osimertinib)**
- **Radiographic responses and durable anti-tumor activity across multiple mutation families**
- **ctDNA reduction confirms loss of mutant alleles, which is predictive of clinical benefit[1]**
- **Data at EORTC 2023**

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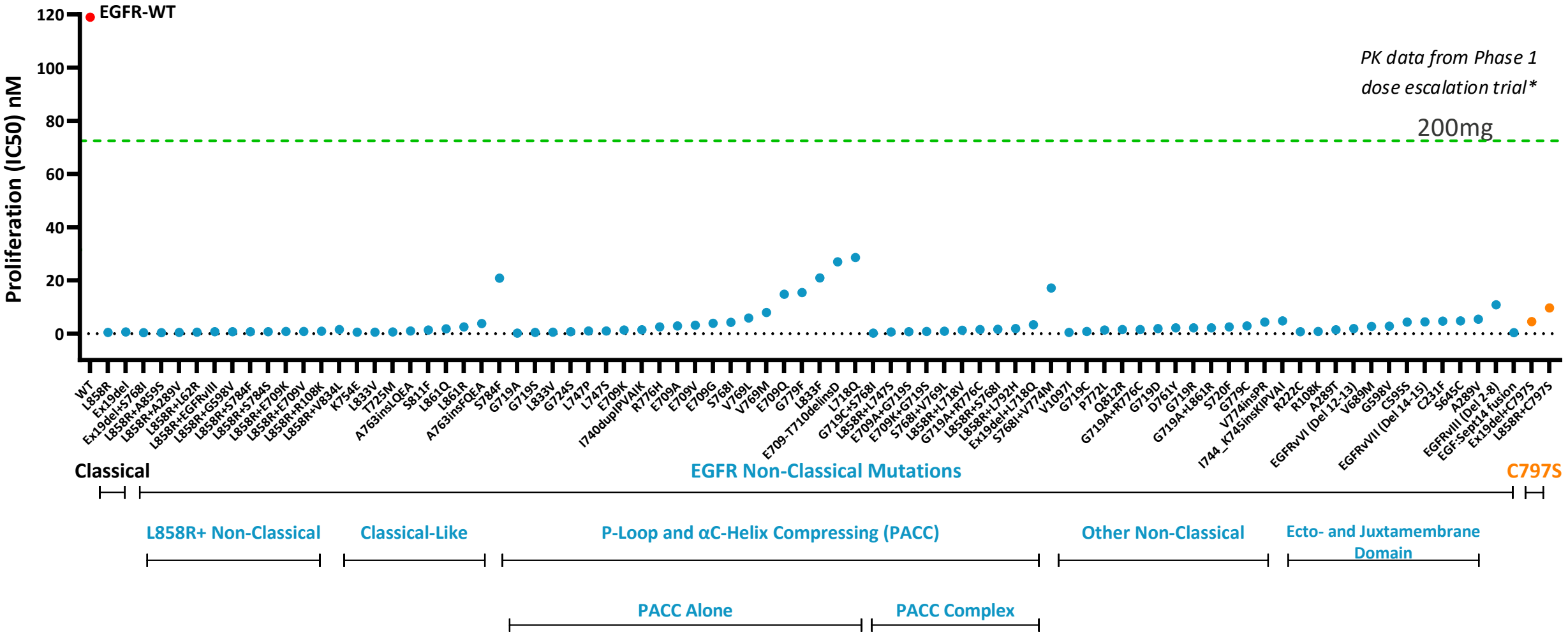
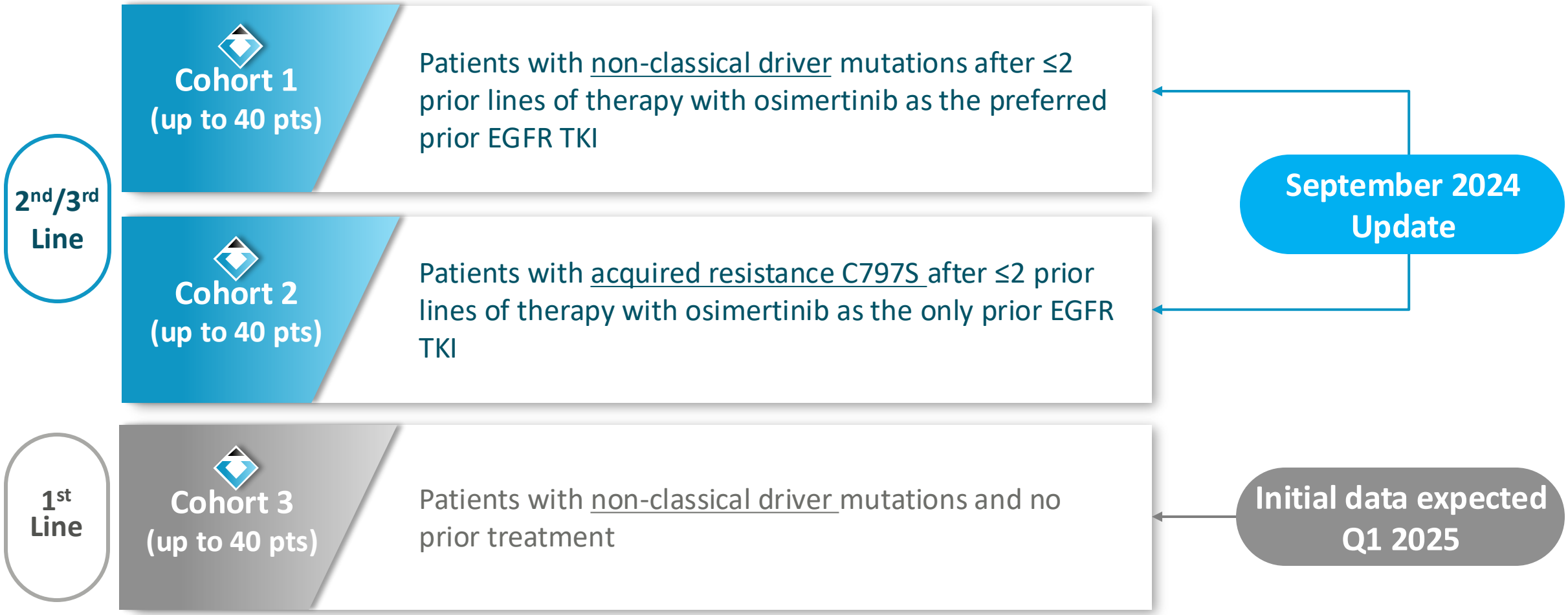
1. Thompson, JC., et al., British Journal of Cancer, 2023.

BDTX-1535 Achieves Coverage of the EGFR Mutation Spectrum at the Well-Tolerated Oral Dose of 200mg QD



*Cmax doses plotted for human PK. PK data adapted from poster at EORTC/AACR/NCI International Conference on Molecular Targets and Cancer Therapeutics, October 2023 BDTX AACR 2024 oral presentation

BDTX-1535 Preliminary Phase 2 Data in Recurrent Setting



Preliminary Phase 2 Data: Initial Safety and Efficacy Data Cuts

Safety/PK Assessment for Dose Selection

Focus on PK, Safety, Tolerability

- Data cut on June 15, 2024
- 40 patients randomized to 100 mg or 200 mg, across Cohorts 1 and 2
  - 20 patients at 100mg
  - 20 patients at 200mg

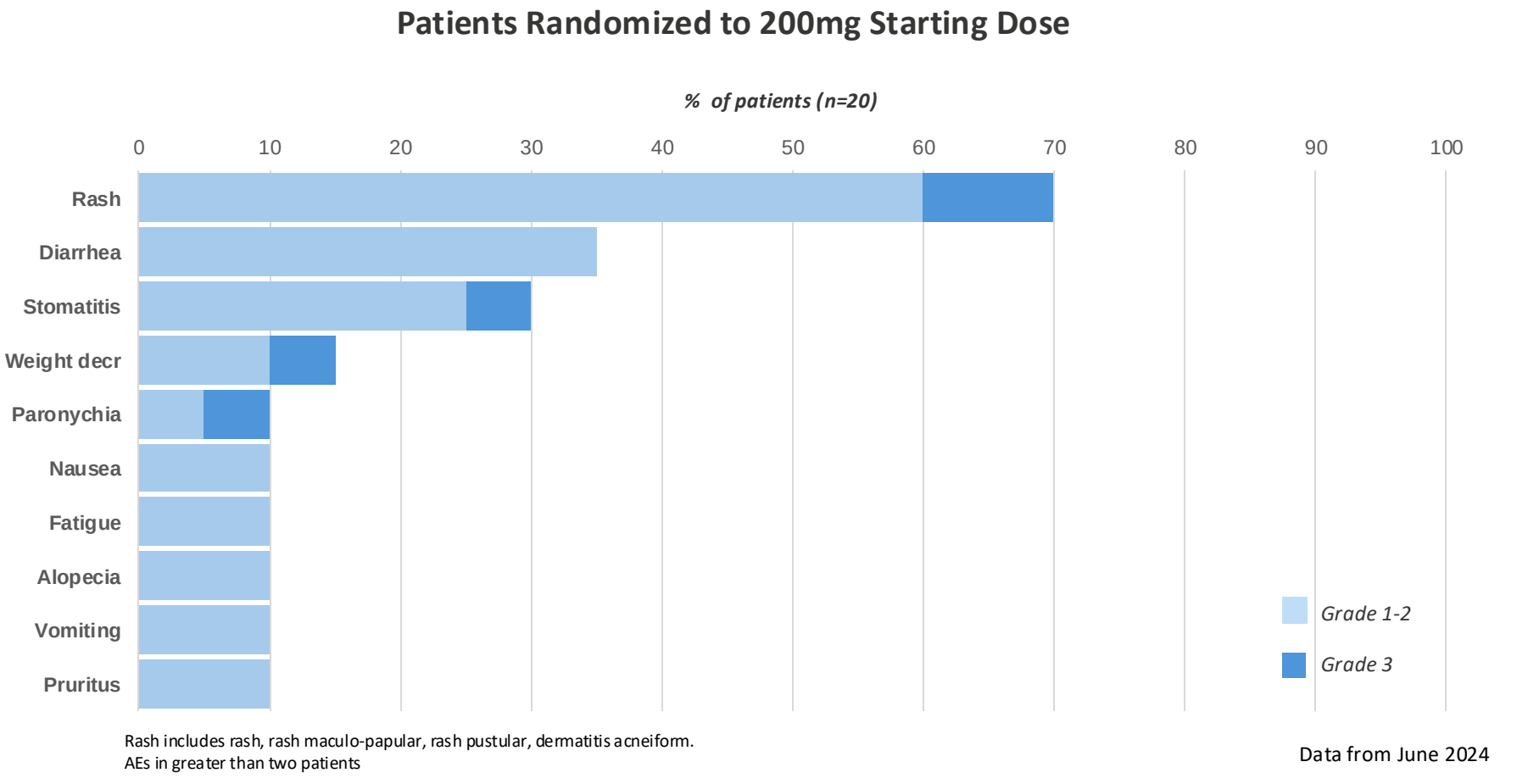
Preliminary Efficacy Assessment

Focus on Response Rate and Durability

- Data cut on August 17, 2024
- 27 patients at 200 mg eligible for first post-baseline assessment

BDTX-1535: Favorable Tolerability Profile

Treatment Related Adverse Events (TRAE) ≥ 10% Patients



Data Summary

- No grade 3/4 diarrhea
- No liver enzyme elevation
- No QTc prolongation
- 1/20 patient discontinued
- 4/20 patients dose reduced

August 17, 2024 no new safety/ tolerability signals observed

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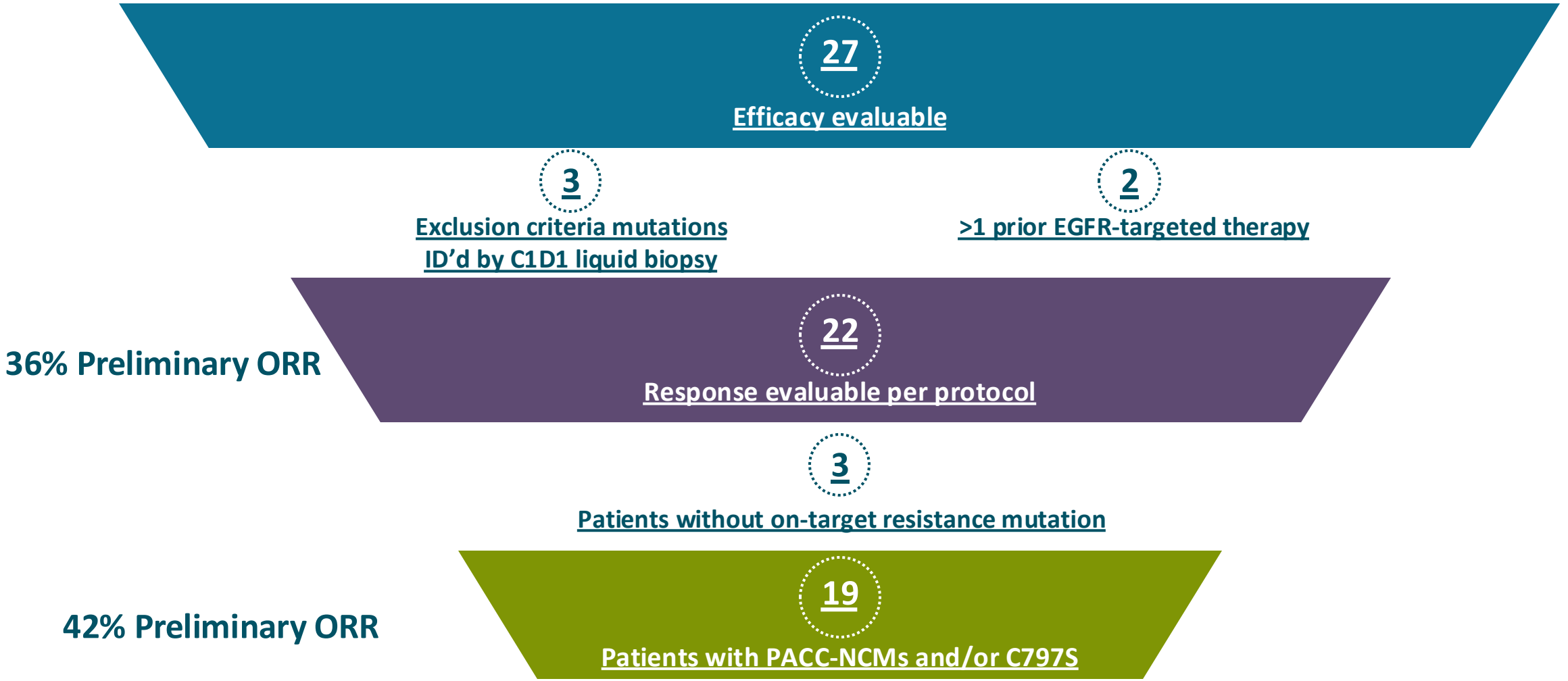
BDTX-1535: 200 mg Patient Demographics and Baseline Characteristics

Baseline Characteristics	Efficacy evaluable patients (N=27)
Age, median (range)	62 (41, 82)
Female	19 (70%)
ECOG PS 1	16 (59%)
CNS metastases at baseline	6 (22%)
Visceral metastases at baseline	9 (33%)
Prior lines of anticancer treatment*	
1	14 (52%)
2	12 (44%)
Mutation Stratification	
Cohort 1 (NCMs)	15 (56%)
Cohort 2 (C797S)	12 (44%)

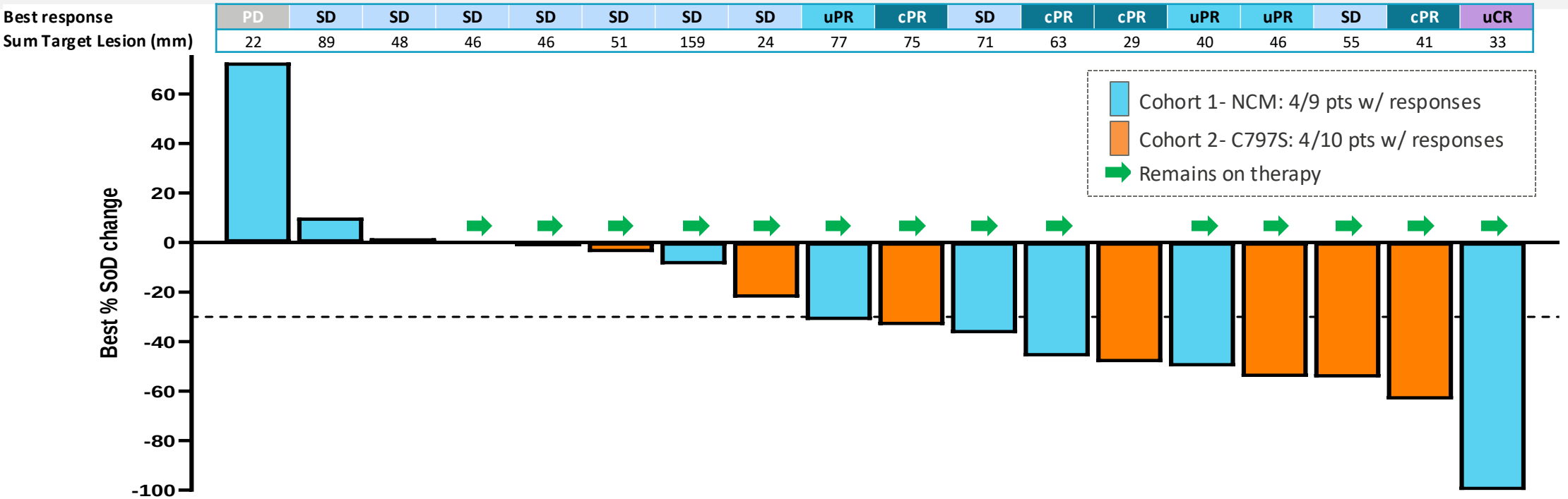
*1 patient had 3 prior lines prior lines of treatment (incl. amivantamab)

Phase 2: 200 mg patients from Aug. 17 data cut-off



BDTX-1535 Phase 2 Preliminary Waterfall Plot

Preliminary ORR 42% in patients with PACC-NCM and/or C797S



	Patient ID	2199	2124	2160	2197	2169	2158	2181	2184	2198	2179	2172	2115	2097	2208	2207	2195	2110	2152
mEGFR*	Classical	L858R		L858R					E19del		L858R		L858R	Ex19del			Ex19del	L858R	
	NCM	E709A	E19delinsD	R108K	K745N Ex19Ins-IPVAIK K745N	L747_P753 delinsS	L747_A750 delinsP	G719A S768I		L747_P753 delinsS L718V G930R	Y1016C	G719A S768I	L718V		V774M S768I	L747_A755 delinsSKD		L833V	G719S S768I
	C797S			C797S		C797S	C797S		C797S		C797S			C797S		C797S	C797S	C797S	
	Prior 1L Duration, months	O 19.6	O 1.5	O 25.8	O 20.8	O 22.8	O 23.5	O+Cis+Pem 1.4	Osi 19.0	O+B 67.5	C+pac 1.3	O 5.1	O 24.9	O 38.3	A 13.9	O 14.1	O 15.8	O 50.0	O 8.5
	Prior 2L Duration, months				O+C+Pem 6.4			O+C+Pac 6.9		O+C+Pem 4.0	Osi 16.8	O+C+Pem 3.0	HER3-Dxd 0.8					O+C+Pem+B 26.6	C+Pac 1.8
	Off-Pathway Detected	RTK		MAPK	PI3K	RTK		TK/MAPK											

*Retrospective liquid and tissue biopsy NGS testing; Pt 2118 withdrew consent prior to first scan (see patient in swimmer plot)

O-osimertinib; A- afatinib; C- carboplatin, Cis – cisplatin, Pem- pemetrexed; Pac- paclitaxel; B- bevacizumab; HER3-Dxd- patritumab deruxtecan;

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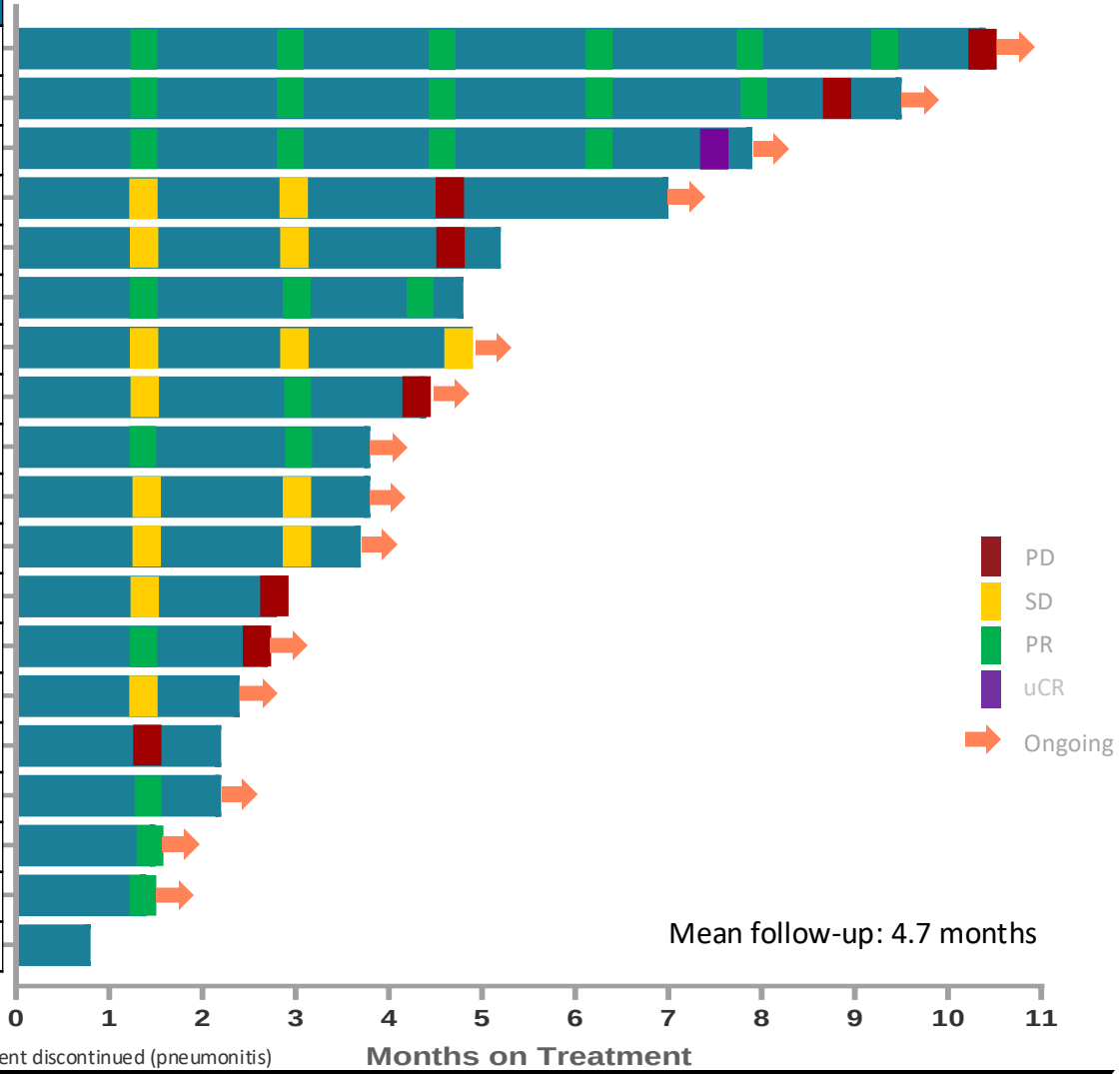
BDTX-1535 Phase 2 Preliminary Swimmer Plot

Encouraging durability with 14 out of 19 patients still on therapy

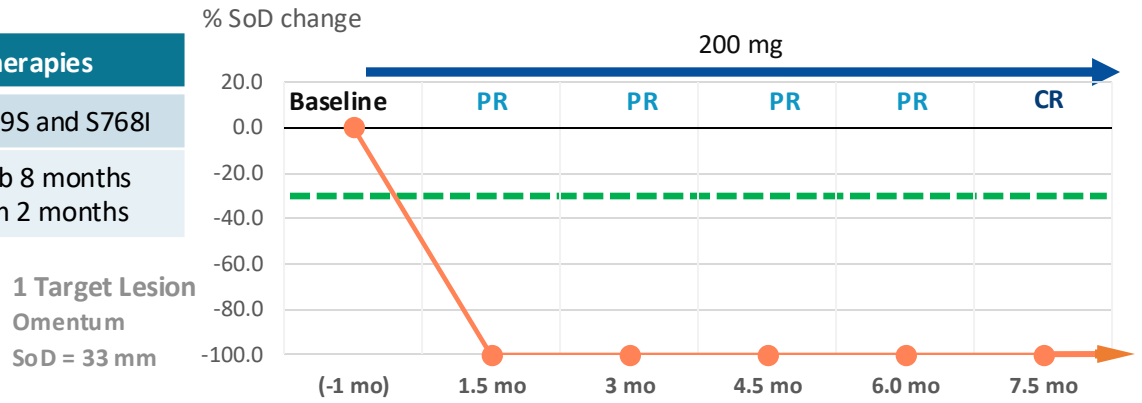
Pt ID	EGFR Mutation(s)			Prior Therapy		Best response
	Classical	Non-classical	C797S	1st	2nd	
2110	L858R	L833V	C797S	Osi	Osi+C+pem+bev	cPR
2115	L858R	L718V		Osi	HER3-DXd	cPR
2152		G719S; S768I		Osi	C+pac	uCR
2158		L747_A750delinsP	C797S	Osi		SD
2160	L858R	R108K	C797S	Osi		SD
2097	Exon 19del		C797S	Osi		cPR*
2169		L747_P753delinsS	C797S	Osi		SD
2172		G719A; S768I		Osi	Osi+C+Pem	SD
2179	L858R	Y1016C	C797S	C+pac	Osi	cPR
2181		G719A; S768I		Osi+C+pem	Osi+C+pac	SD
2184	Exon 19del		C797S	Osi		SD
2124		E709_T710delinsD		Osi		SD
2195	Exon 19del		C797S	Osi		SD
2197		K745_E746insIPVAIK K745N		Osi	Osi+pem+C	SD
2199	L858R	E709A		Osi		PD
2198		L718V; L747_P753delinsS; G930R		Osi+bev	Osi+C+pem	uPR
2207		L747_A755delinsSKD	C797S	Osi		uPR
2208		V774M; S768I		Afatinib		uPR
2118		L747_T751del; V834L	C797S	Osi	C+pem/CPI	WC



N=19 in swimmer plot, including Pt 2118 who withdrew consent (WC) prior to first scan *Patient discontinued (pneumonitis)

Patient 2152: Unconfirmed Complete Response and Remains on Therapy

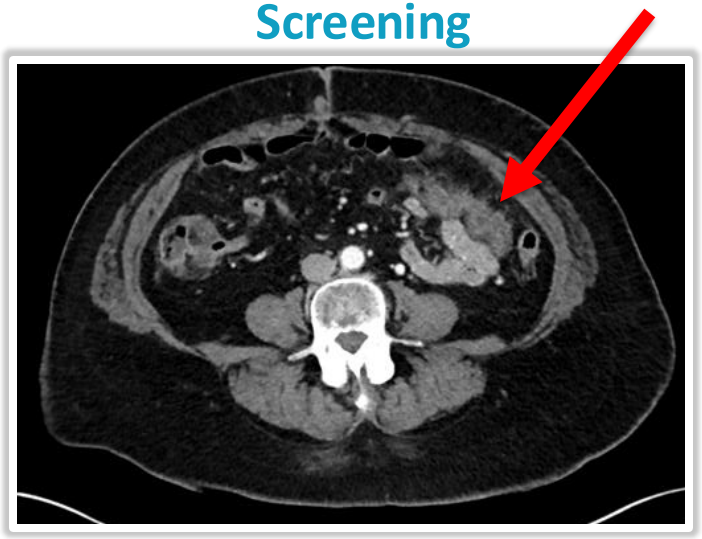
Mutations and Prior Therapies	
Mutations:	2 NCMs: G719S and S768I
Prior Therapies:	1L osimertinib 8 months 2L carbo/pem 2 months



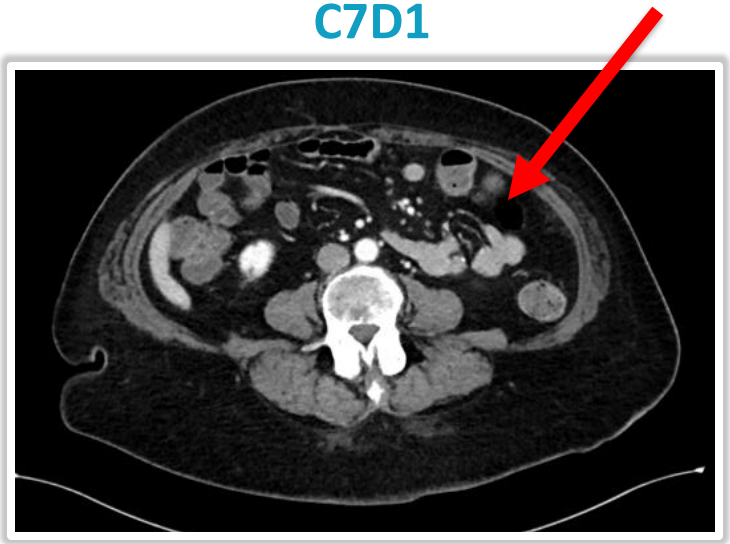
5 Non-Target lesions

Pleura	Present	Present	Absent
LN- pleura	Present	Present	Absent/Normal
Mesentery	Present	Present	Absent
Brain	Present	Present	Absent
Brain	Present	Present	Absent

Screening



C7D1

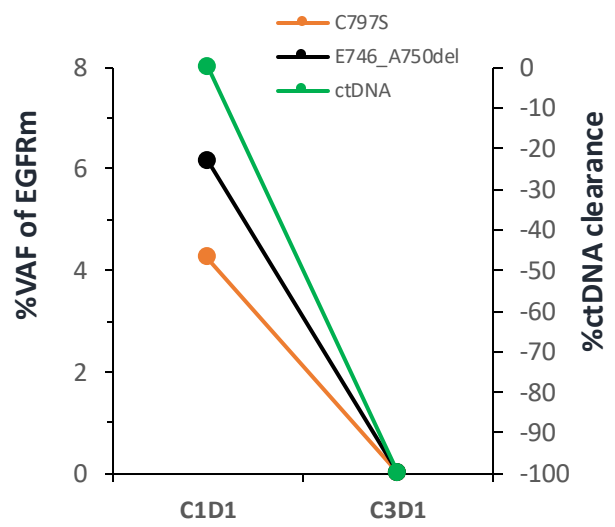


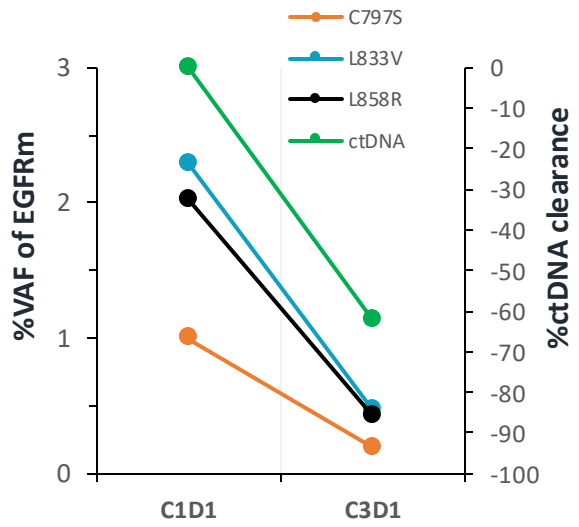
Source: Data on File as of Aug 17, 2024

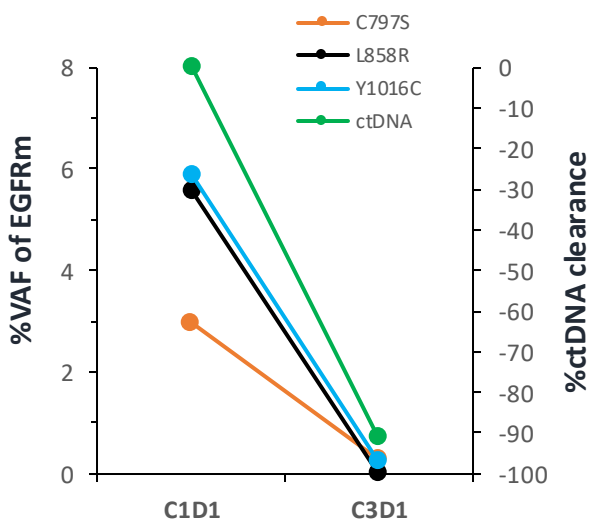
LN= lymph node, SoD = Sum of diameters per RECIST 1.1

BDTX-1535 Eradicates EGFRm Alleles and Drives ctDNA Clearance

Patient ID	2097	2110	2179
	PR	PR	PR







Eradication of targeted variant alleles and reduction of ctDNA are early predictors of PFS[1]

Of 8 patients with PRs, ctDNA testing on 3 patients shown above, insufficient DNA on 2 patients, and pending testing on 3 patients

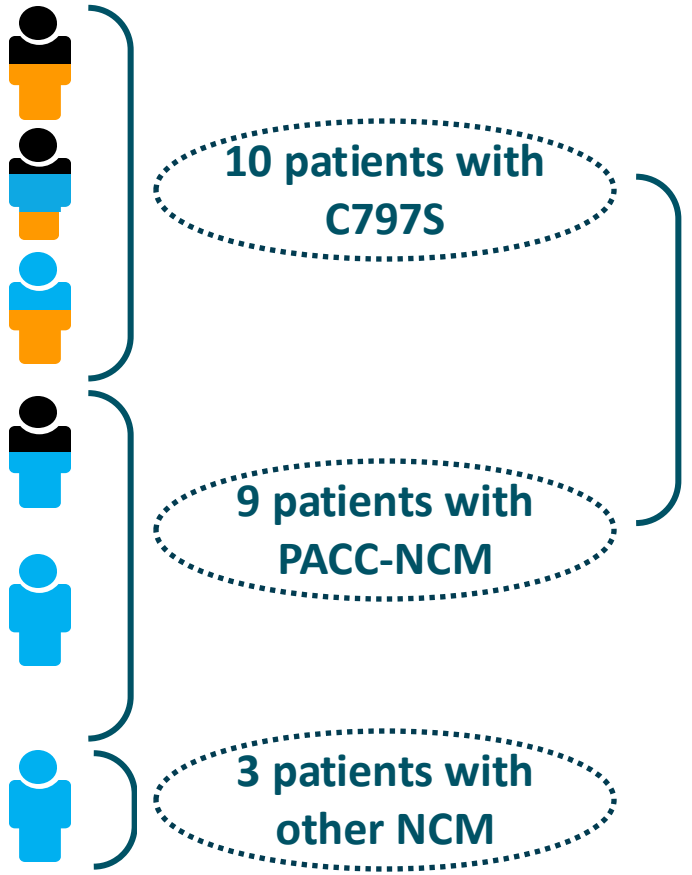
1. *Thompson, JC., et al., British Journal of Cancer, 2023*

BDTX-1535 Phase 2 Clinical Activity Across Broad Spectrum of EGFR Mutations Found in Recurrent Post EGFR TKI Patients

Pts w/ PR

Patient ID	Classical[#]	PACC NCMs	other NCMs*	C797S
2195	Exon 19del			C797S
2184	Exon 19del			C797S
2097	Exon 19del			C797S
2110	L858R		L833V	C797S
2160	L858R		R108K	C797S
2179	L858R		Y1016C	C797S
2158			L747_A750delinsP^	C797S
2169			L747_P753delinsS ^	C797S
2207			L747_A755delinsSKD^	C797S
2118			L747_T751del^; V834L	C797S
2115	L858R	L718V		
2199	L858R	E709A		
2152		G719S; S768I		
2172		G719A; S768I		
2181		G719A; S768I		
2124		E709_T710delinsD		
2197		K745_E746insIPVAIK	K745N	
2208		V774M; S768I		
2198		L718V	L747_P753delinsS^; G930R	
2203			L747P_P753delinS^	
2101			L861Q^	
2188			L861R^; L62R	

All mutations identified with common practice NGS



Preliminary ORR of 42% in 19 patients with PACC-NCM or C797S mutations

*[#] includes Ex19del (E746_A750) and L858R; *Includes atypical Ex19dels with variable sensitivity to osimertinib (Heymach et al ESMO 2024)*
^osimertinib-sensitive mutations (Robichaux et al Nature 2021, Heymach et al ESMO 2024)

Preliminary Phase 2 Data: Key Takeaways and Next Steps in Recurrent NSCLC

Safety/PK Assessment for Dose Selection

Data supporting 200 mg/daily

- Well-tolerated
- 24-hour target coverage across EGFR mutations

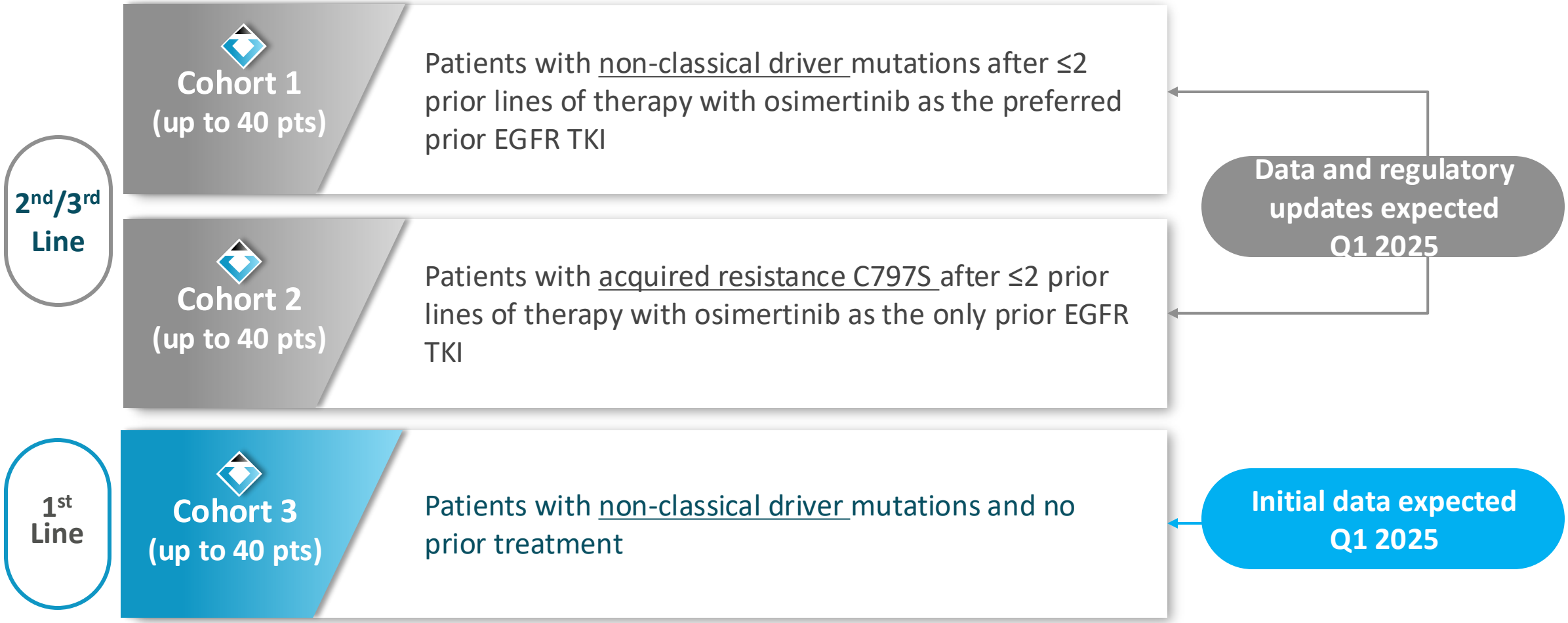
200 mg dose selected for pivotal development

Preliminary Efficacy Assessment

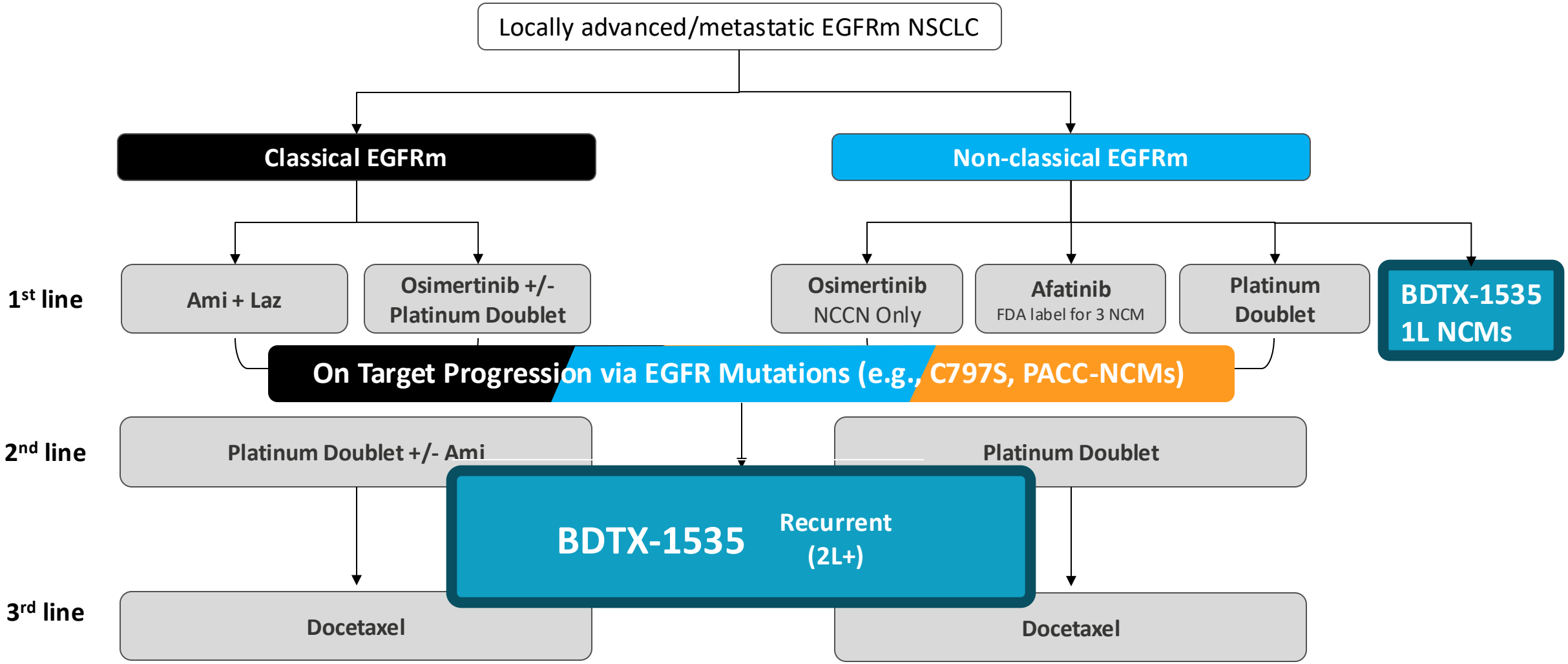
- Robust activity across a broad spectrum of EGFR mutations
- Preliminary ORR of 42% in well-defined population (PACC-NCM and/or C797S)
- Encouraging durability with 14 of 19 patients still on therapy

Q1 2025: expect to report updated results and regulatory feedback on registration path

BDTX-1535 Phase 2 Status



Current Treatment Landscape for EGFRm NSCLC



Ami: Amivantamab Laz: Lazertinib

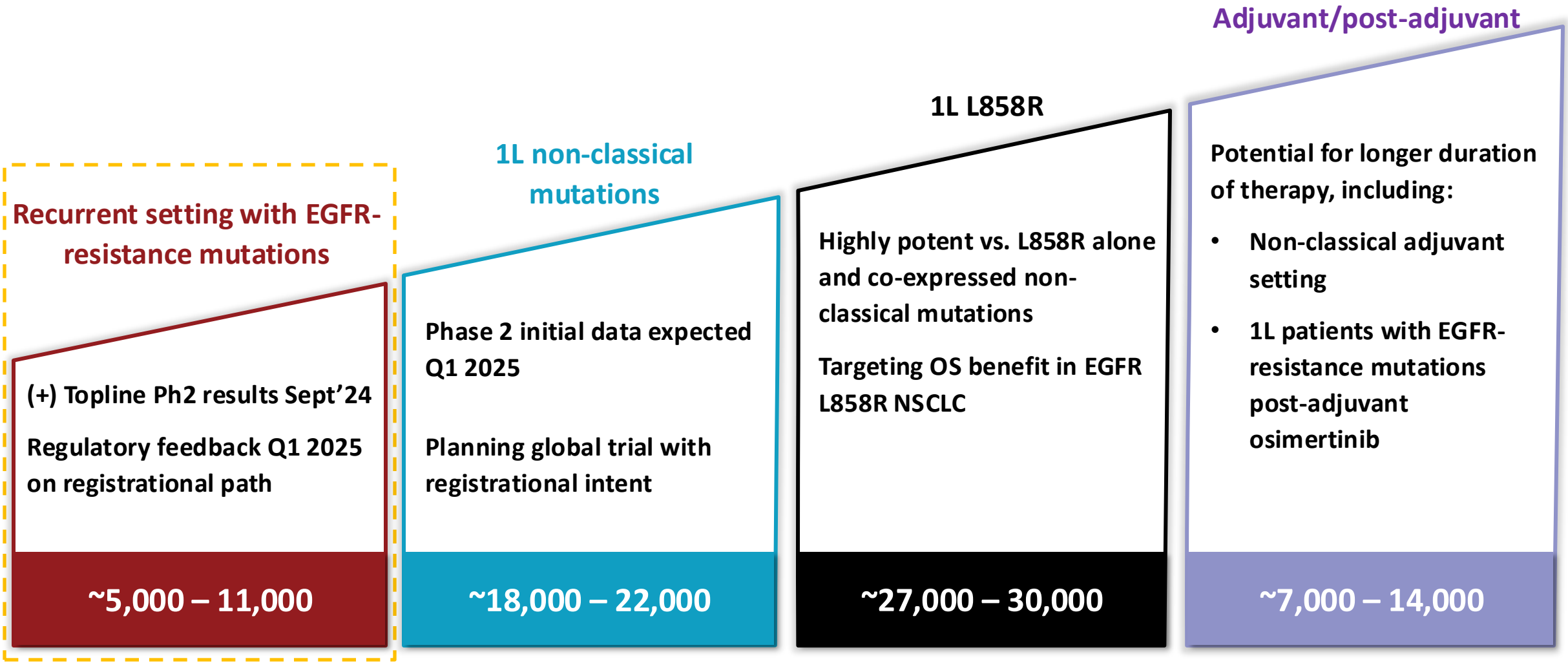
BDTX-1535: Well-Positioned Versus Chemo-Based Combination Regimens

BDTX-1535 monotherapy		Chemo-based combination regimens
Oral once daily	Route of administration	Infusion
Generally well-tolerated	Safety and tolerability	High rates of grade 3 AEs
Classical + non-classical	Mutation coverage	Classical
Continuity in oral therapy post-osi	Patient QoL	Burdensome

osi = osimertinib

No head to head study has been conducted between BDTX-1535 monotherapy and chemo-based combination regimens.

BDTX-1535: Broad Potential to Benefit EGFRm NSCLC Patients Across Multiple Lines of Therapy



Estimated Addressable Patients in G7 Countries

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

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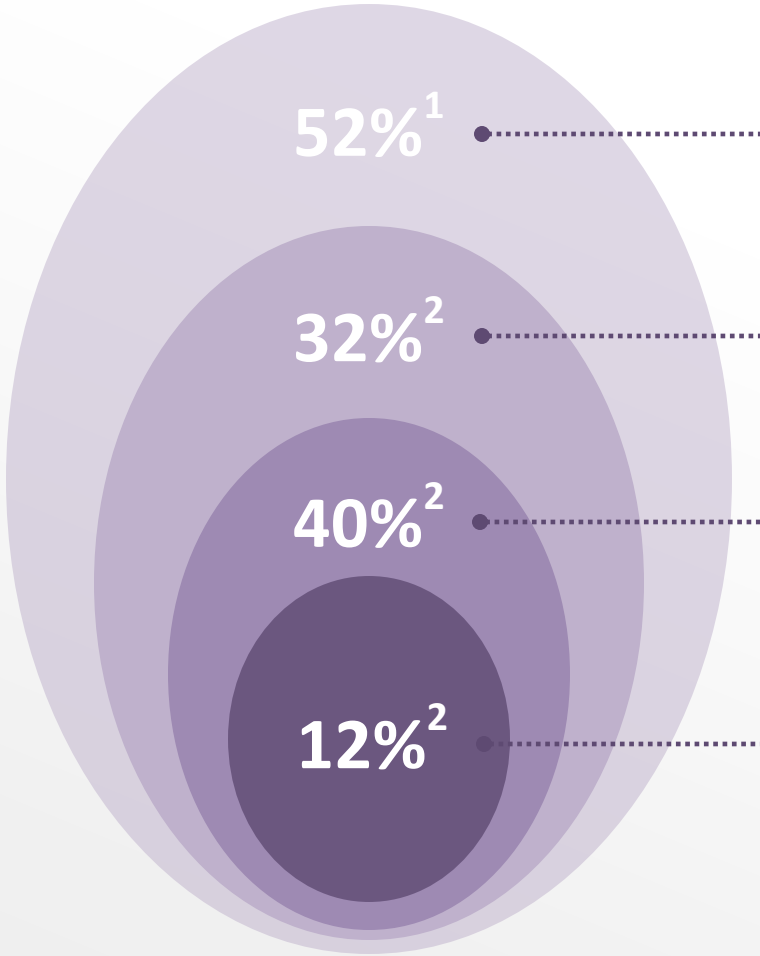
BDTX-1535: Opportunity in Glioblastoma

Black Diamond Therapeutics

Treatment of EGFR-Driven GBM Requires Inhibition of Complex EGFR Mutations: Potent Preclinical Inhibition by BDTX-1535



Of all GBM samples carry oncogenic EGFR alterations

Of all GBM samples had EGFR extracellular-domain (ECD) mutations, according to real-world evidence

Of all ECD-driven tumors were complex, containing 2 or more ECD mutations

Of complex ECD-driven tumors were highly heterogeneous, with 3 or more ECD mutations

~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 BDTX-1535

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

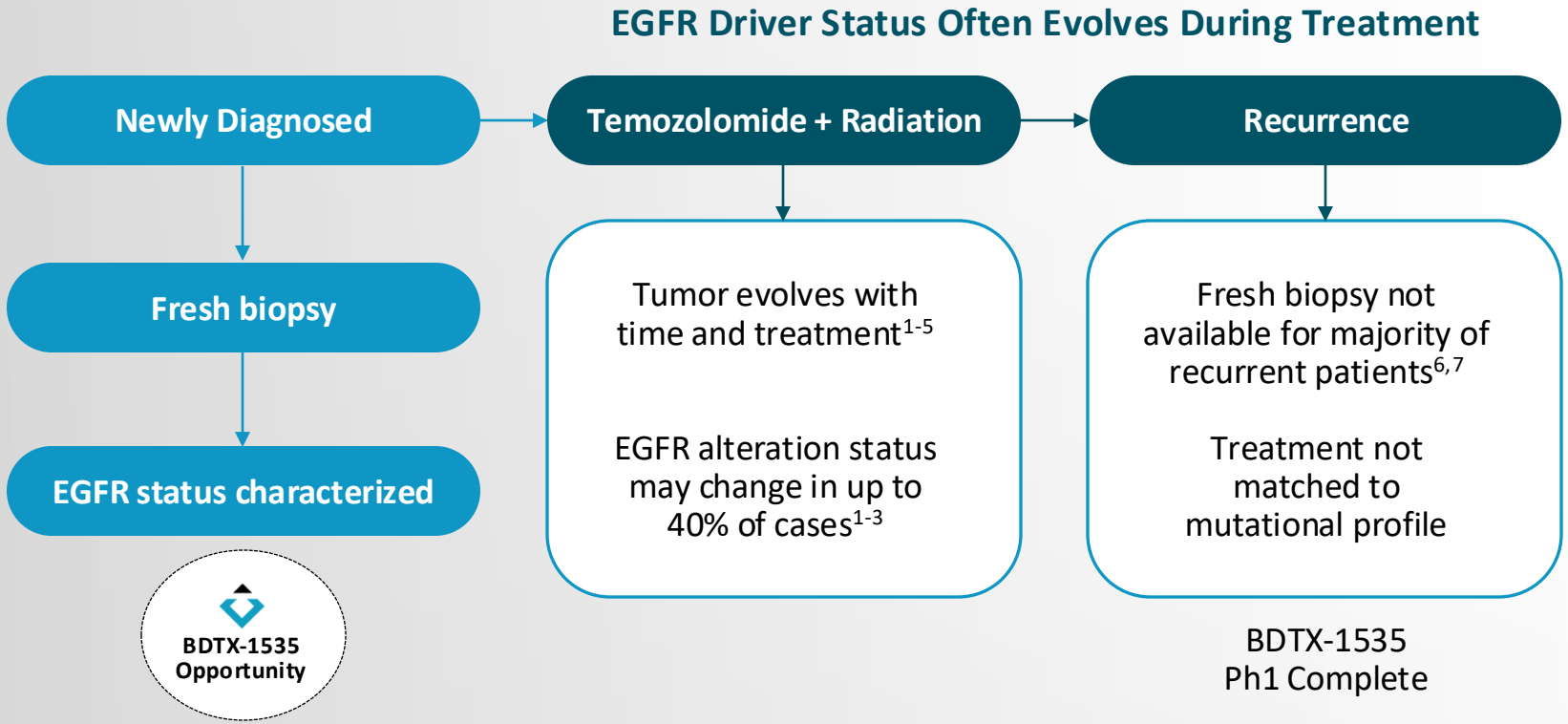
BDTX-1535: Potential to Overcome Limitations of Prior Attempts to Drug EGFR in GBM

Lessons From Past Failures	BDTX-1535
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**
Low brain exposure due to a lack of CNS penetrance	**Brain-penetrant to treat CNS tumors**

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

BDTX-1535 Opportunity in Newly Diagnosed EGFRm GBM Patients

GBM Treatment Paradigm

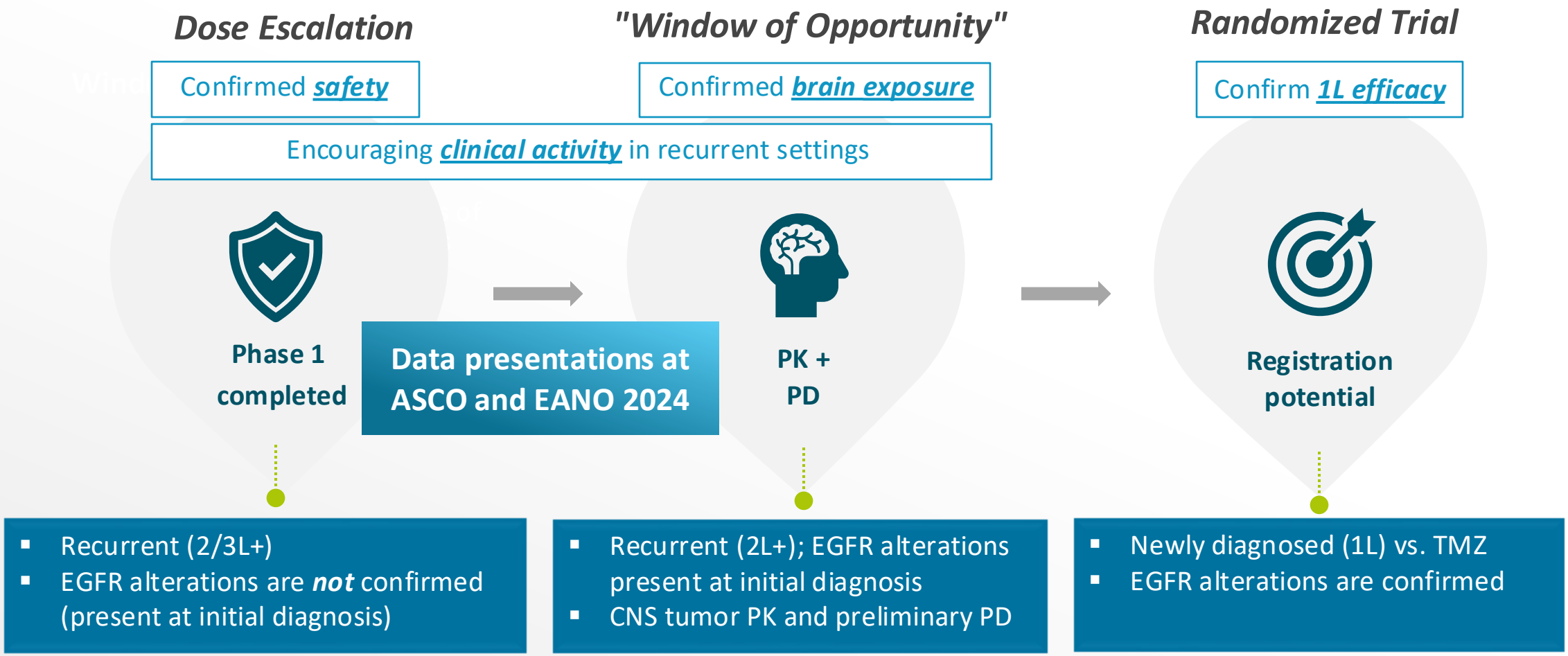


Opportunity for BDTX-1535 in Newly Diagnosed Patients

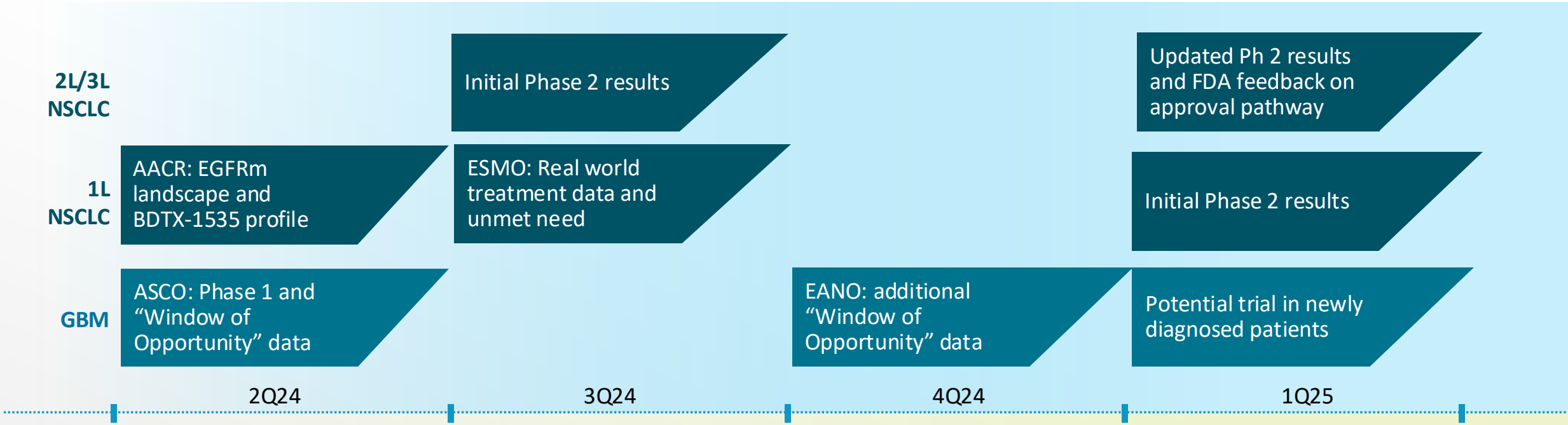
- Fresh biopsy tissue used for testing
- Up-to-date test results guide treatment
- Treatment matches tumor alterations

1. Kim, Cancer Cell 2024; 2. Schäfer, J. Transl. Med. 2019; 3. Wang, Nat. Genet. 2016; 4. Johnson, Science 2014; 5. López, Acta Neuropathol. 2019; 6. Weller, Neuro-Oncology 2013; 7. Audureau, J. Neurooncol. 2018

BDTX-1535 GBM Development Path Designed for Sequential De-Risking



BDTX-1535: Key 2024/2025 Milestones



Financial Summary

$112.7M

as of September 30, 2024

Cash runway into Q2 2026

Thank You

Partnership: partnership@bdtx.com

Investors: investors@bdtx.com

Media: media@bdtx.com

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