Black Diamond Therapeutics, Inc.

Developing MasterKey Therapies to Defeat Cancer Resistance

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Today's Agenda

Opening Remarks

Mark Velleca, M.D., Ph.D, Chief Executive Officer

EGFR Mutation Landscape

Christine Lovly, M.D., Ph.D, Vanderbilt University

Phase 2 BDTX-1535 Update

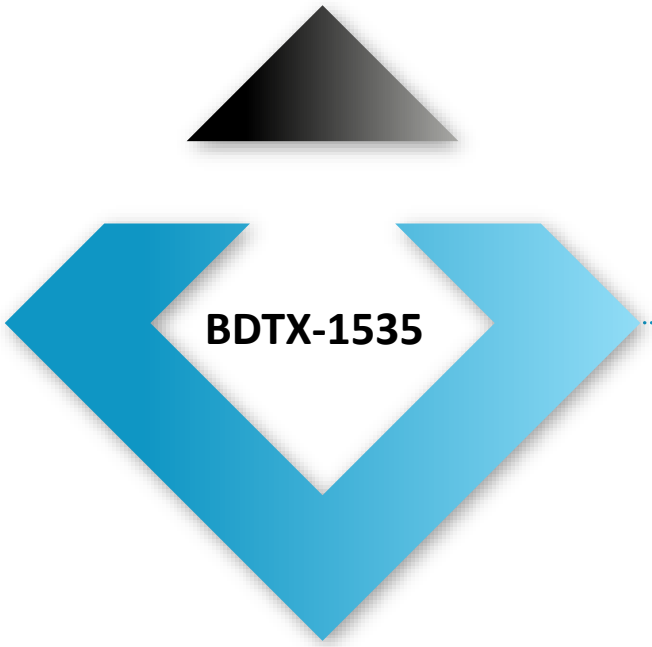
Sergey Yurasov, M.D., Chief Medical Officer

Clinical Perspective

Danny Nguyen, M.D., City of Hope

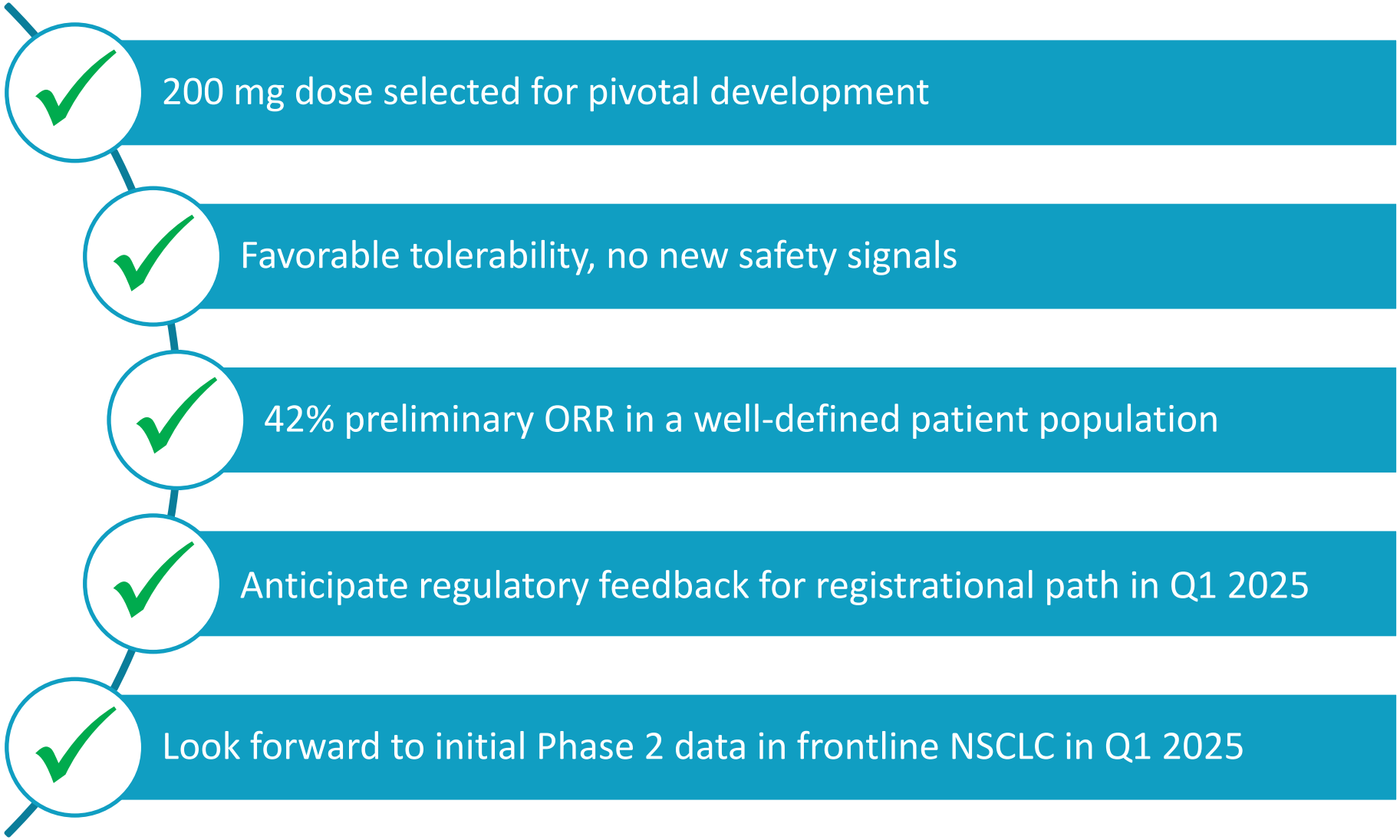
Q&A

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**

BDTX-1535 in Recurrent NSCLC: Key Ph 2 Learnings and Next Steps



Christine Lovly, MD, PhD

Associate Professor of Medicine and Ingram Associate Professor of Cancer Research

Vanderbilt University Medical Center and Vanderbilt Ingram Cancer Center

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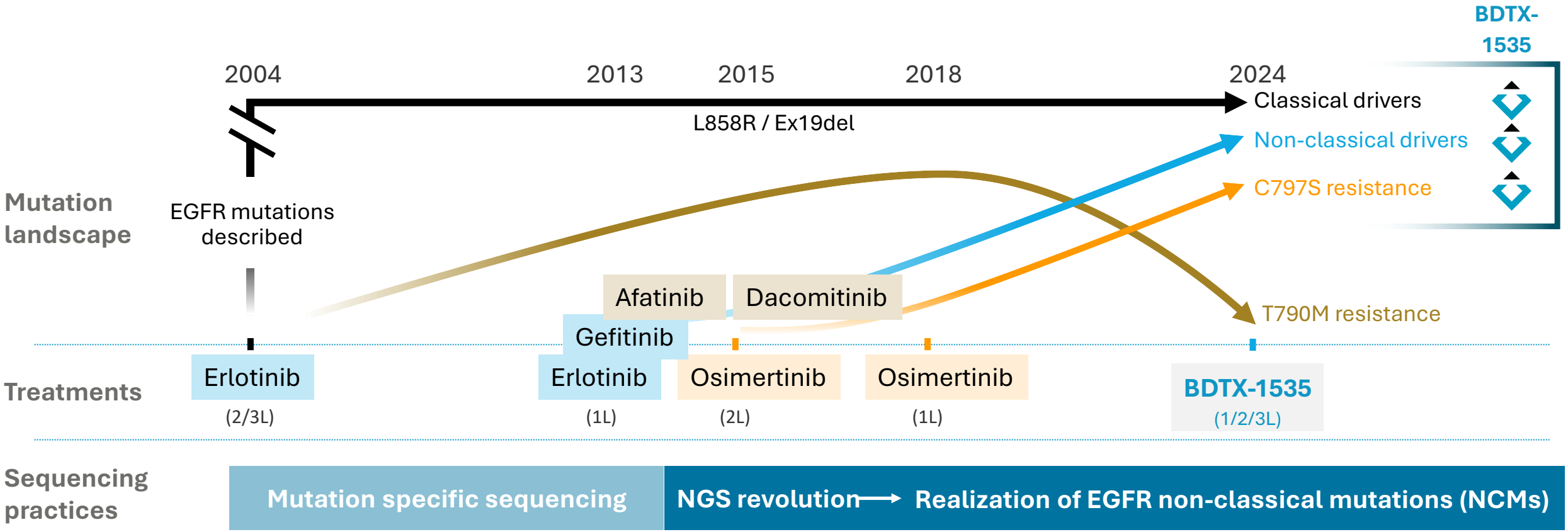
The EGFR Mutational Landscape in NSCLC has Evolved, Revealing a Broad Spectrum of "Non-Classical" Oncogenic Driver & TKI-resistant EGFR Mutations

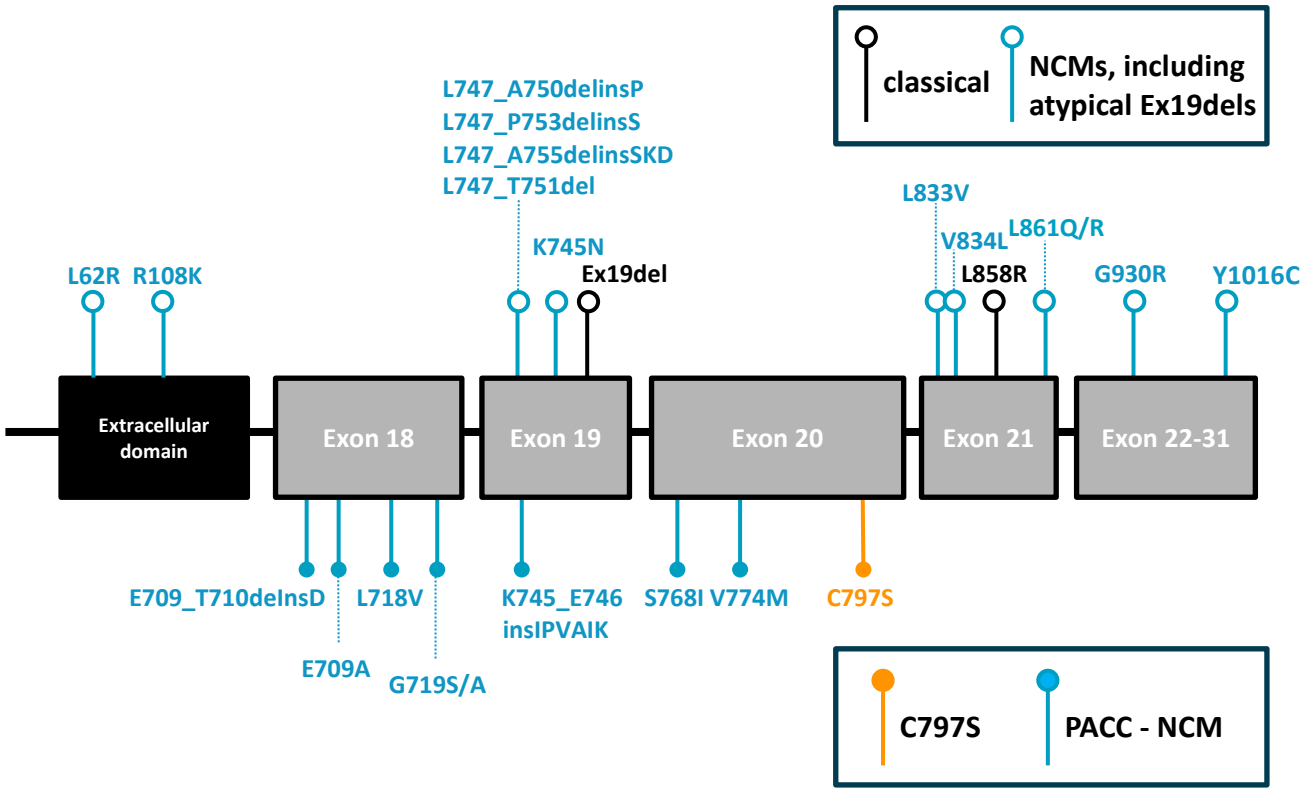
Evolution of the EGFR mutation landscape over the past 20 years



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

EGFR Non-Classical Mutations (NCM) Comprise Multiple Structure-Function Groups, with PACC Mutations Representing One Frequent Structural Class

EGFR non-classical mutations affect multiple oncogenic hotspots, with PACC[1] mutations in the kinase domain one important class



1-PACC: P-loop and αC-helix compressing; Robichaux et al. Nature. 2021.
All mutations shown were detected in patients from BDTX-1535 Phase 2 trial

PACC - NCM mutations are defined by structure and have decreased sensitivity to osimertinib *in vitro*

- PACC mutations comprise >30 unique mutations and are characterized by decreased sensitivity to osimertinib vs. classical mutations (Robichaux et al. *Nature* 2021)
- Together with C797S, PACC-NCMs comprise ~20% of recurrent EGFRm NSCLC
- Recurrent NSCLC tumors presenting with PACC/C797S mutations expected to retain EGFR onco-addiction.

BDTX-1535 Phase 2 Trial Reveals a Broad Spectrum of EGFR Mutations Found in Patients Who had Received Prior EGFR TKI Therapy

Pt 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	

10 patients with C797S

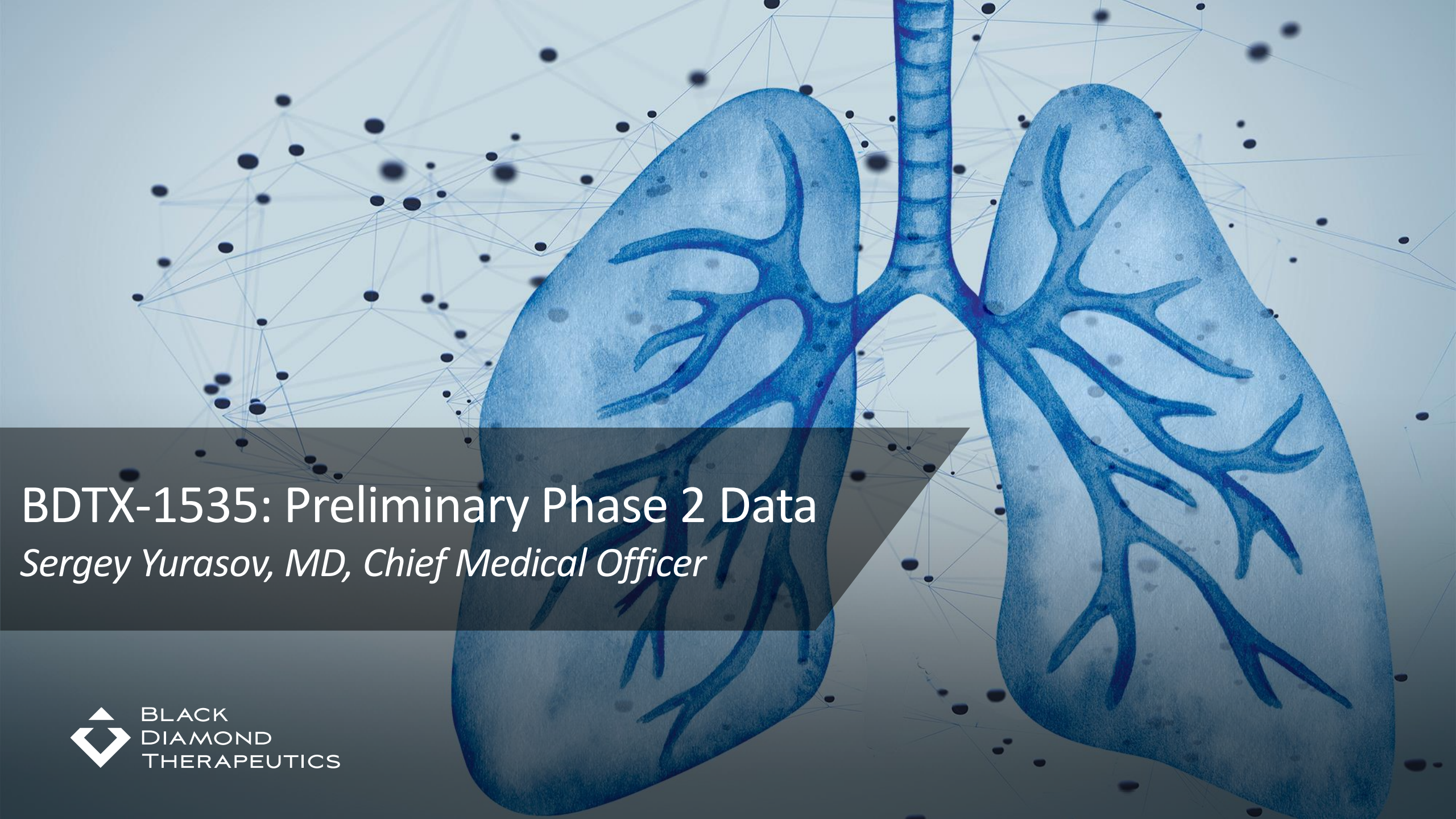
9 patients with PACC-NCM

3 patients with other NCM

19 of 22 patients with PACC-NCM or C797S mutations

All mutations identified with standard tumor biomarker testing (via NGS) currently done in oncology clinics

*# 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)



BDTX-1535: Preliminary Phase 2 Data

Sergey Yurasov, MD, Chief Medical Officer

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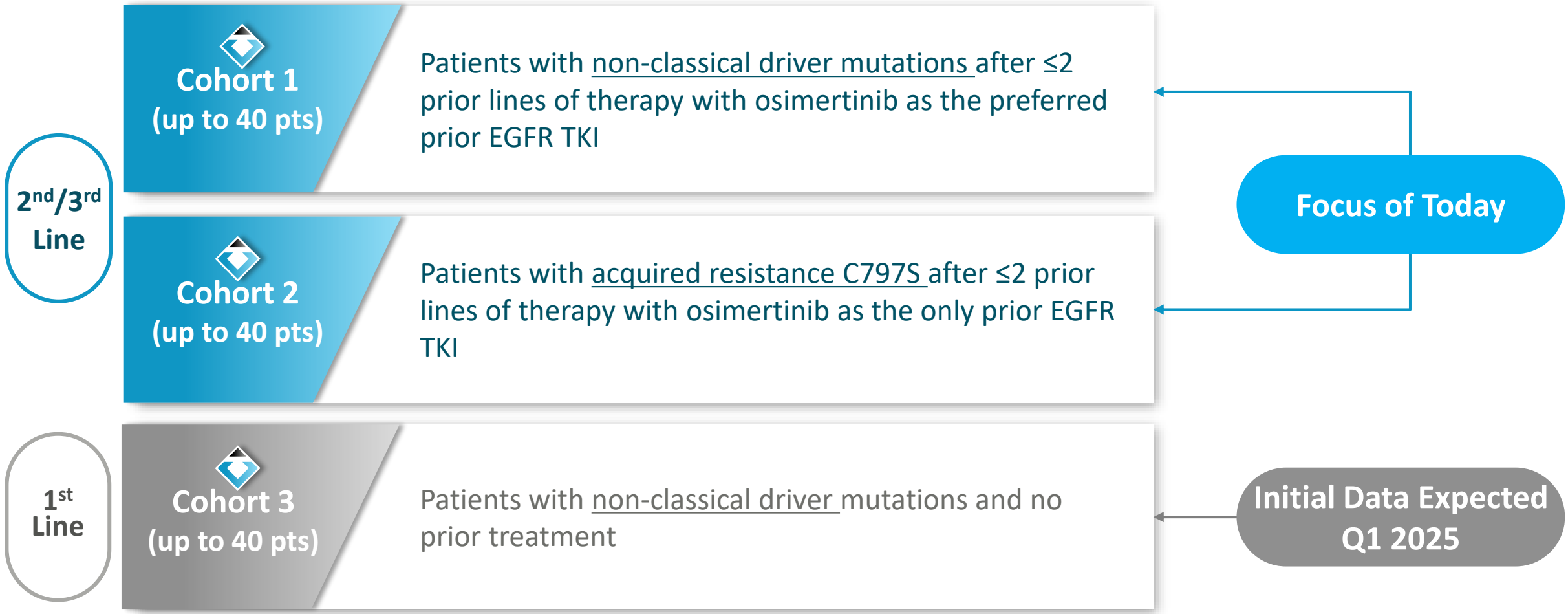
BDTX-1535 Preliminary Phase 2 Data in Recurrent Setting



Preliminary Phase 2 Data: Initial Safety Data Cut

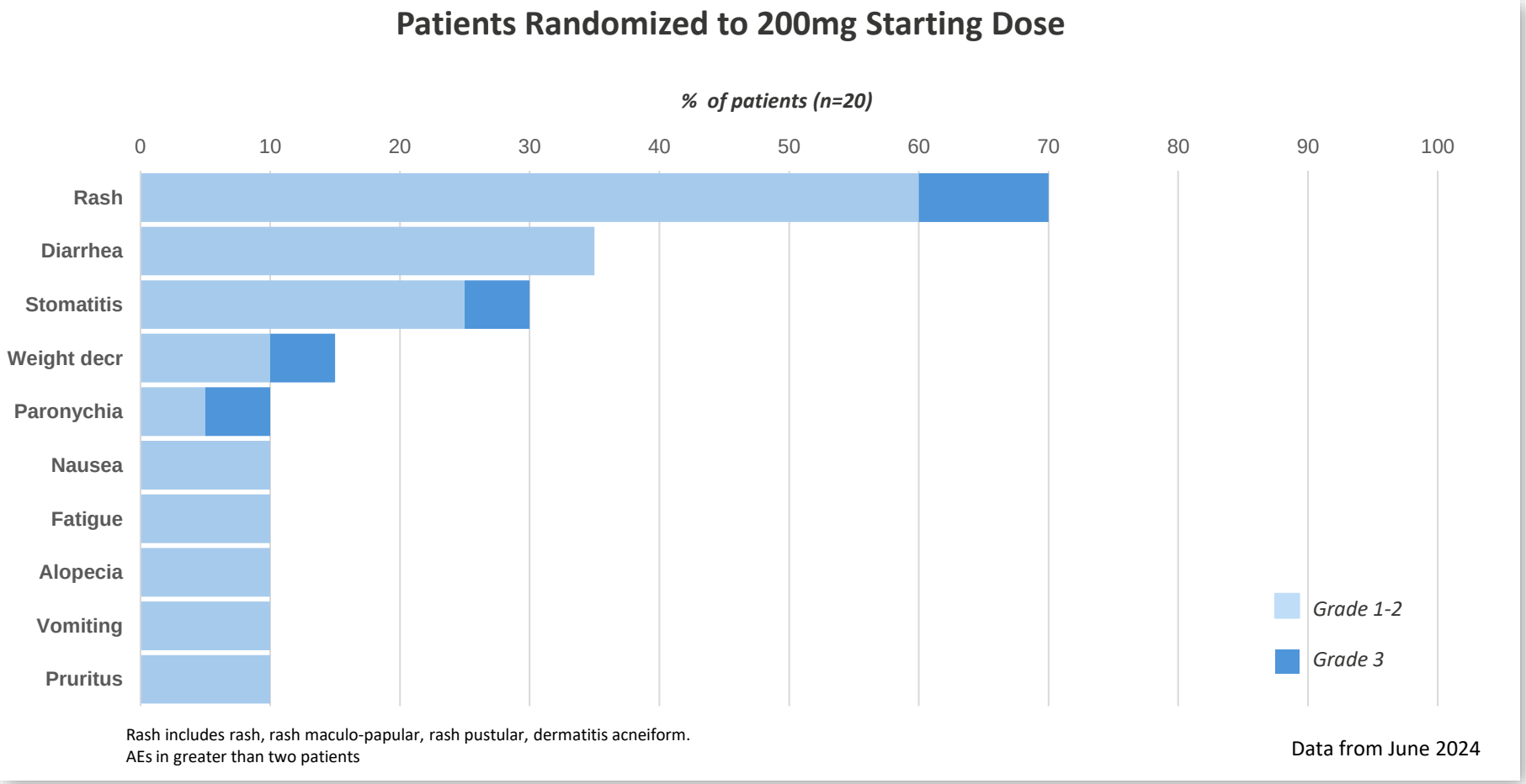
Safety/PK Assessment for Dose Selection

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

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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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

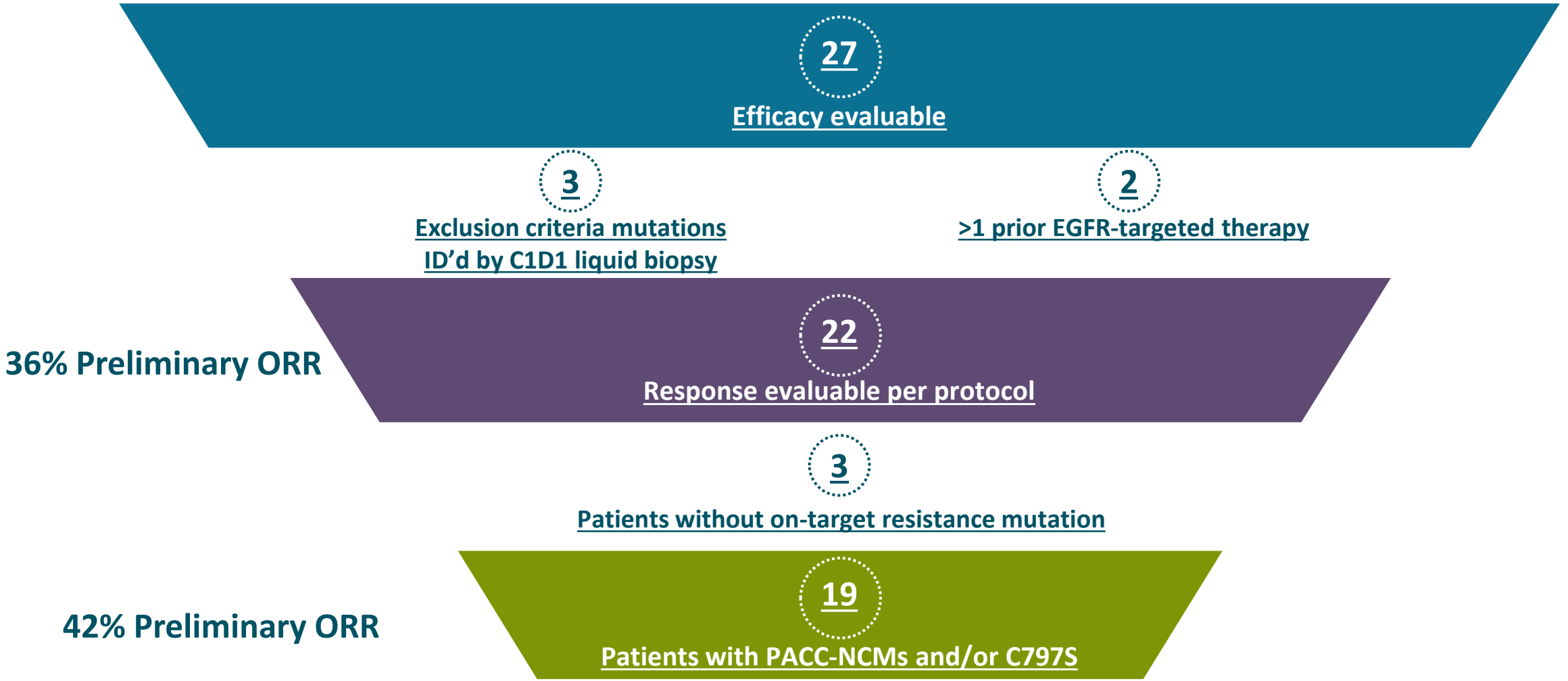
- Data cut on August 17, 2024
- 27 patients at 200 mg eligible for first post-baseline assessment

BDTX-1535: 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)

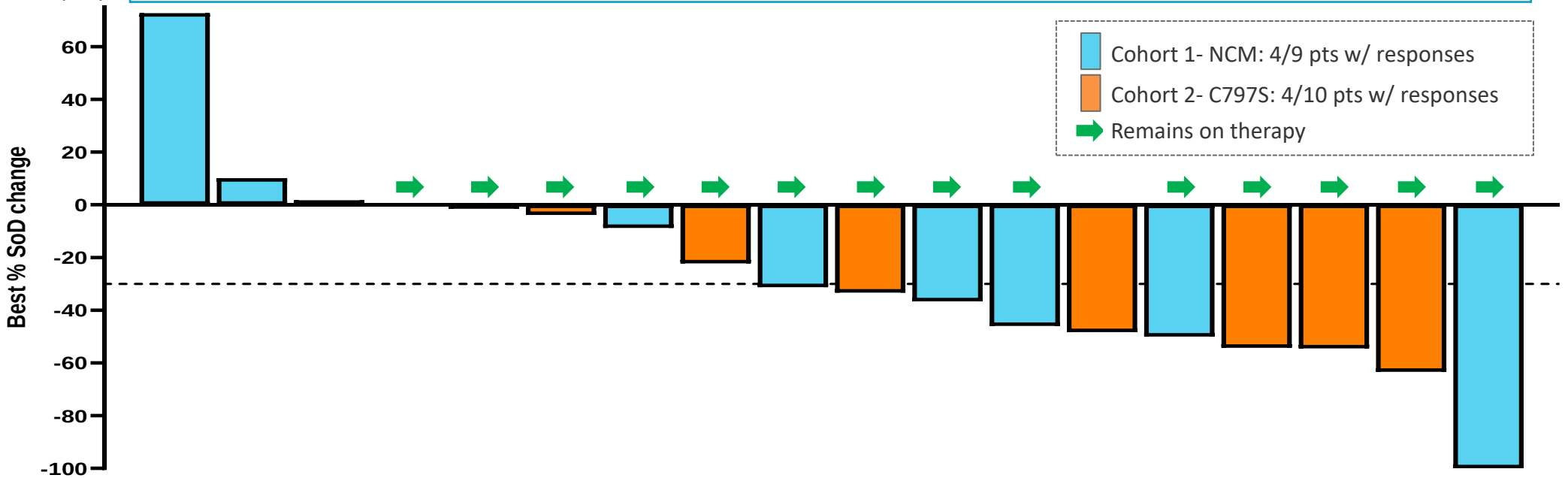
Phase 2: 200 mg patients from Aug. 17 data cut-off



BDTX-1535 Phase 2 Preliminary Waterfall Plot

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

Best response	PD	SD	SD	SD	SD	SD	SD	SD	uPR	cPR	SD	cPR	cPR	uPR	uPR	SD	cPR	uCR
Sum Target Lesion (mm)	22	89	48	46	46	51	159	24	77	75	71	63	29	40	46	55	41	33



	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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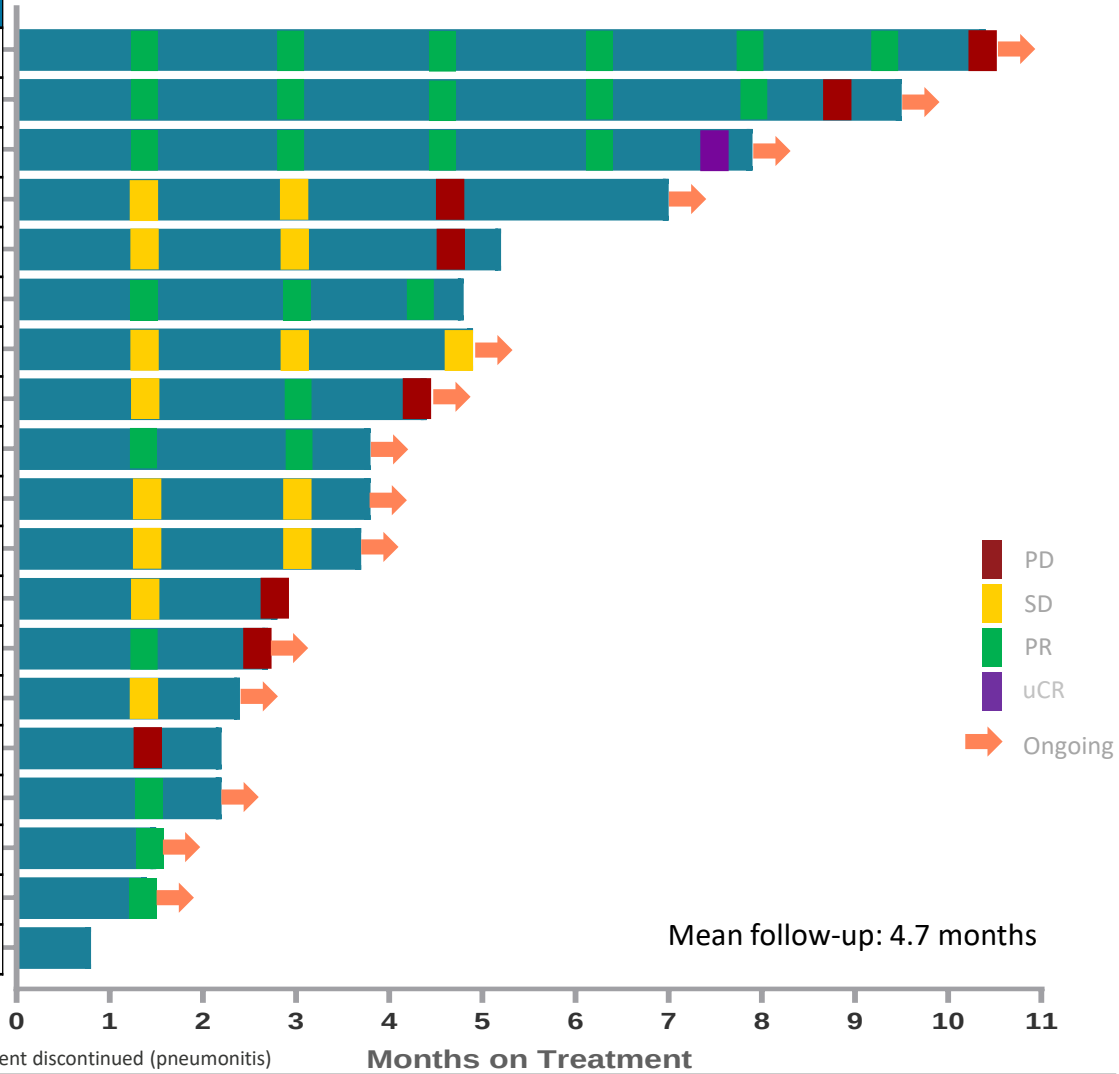
BDTX-1535 Phase 2 Preliminary Swimmer Plot

Encouraging durability with 14 out of 19 patients still on therapy

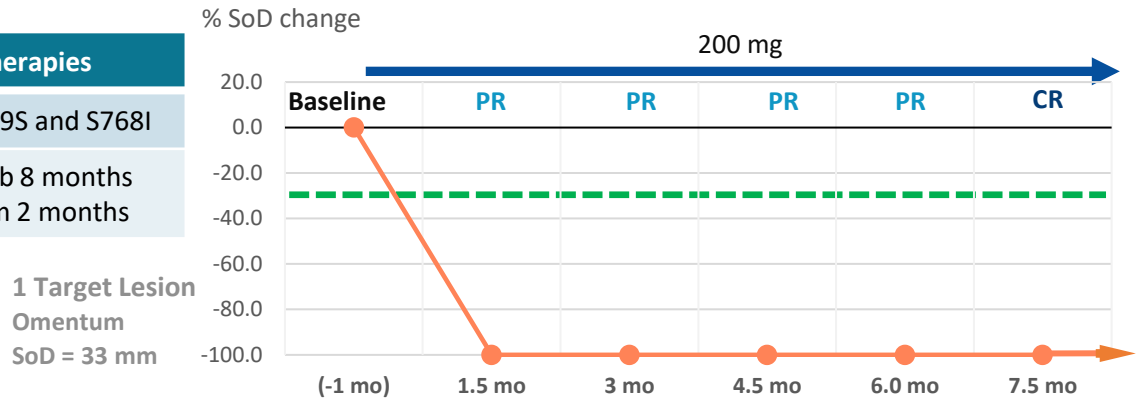
Pt ID	EGFR Mutation(s)			Prior Therapy		Best response
	Classical	Non-classical	C797S	1st	2nd	
2110	L858R	L833V	C797S	Osi	Osi+C+pem+bev	cPR
2115	L858R	L718V		Osi	HER3-DXd	cPR
2152		G719S; S768I		Osi	C+pac	uCR
2158		L747_A750delinsP	C797S	Osi		SD
2160	L858R	R108K	C797S	Osi		SD
2097	Exon 19del		C797S	Osi		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



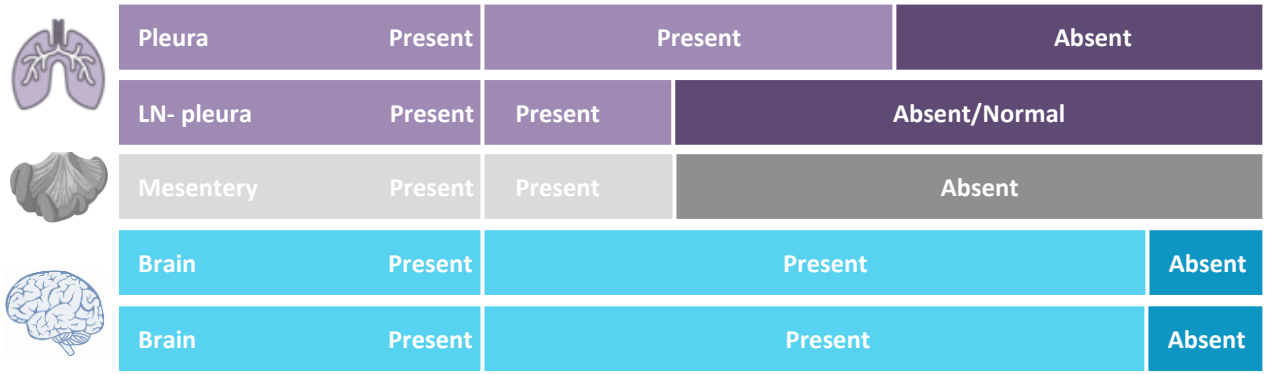
N=19 in swimmer plot, including Pt 2118 who withdrew consent (WC) prior to first scan *Patient discontinued (pneumonitis)

Patient 2152: Unconfirmed Complete Response and Remains on Therapy

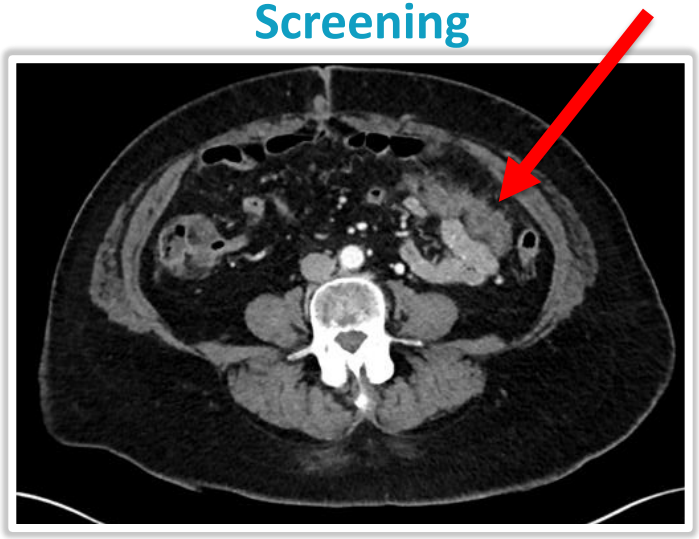
Mutations and Prior Therapies	
Mutations:	2 NCMs: G719S and S768I
Prior Therapies:	1L osimertinib 8 months 2L carbo/pem 2 months



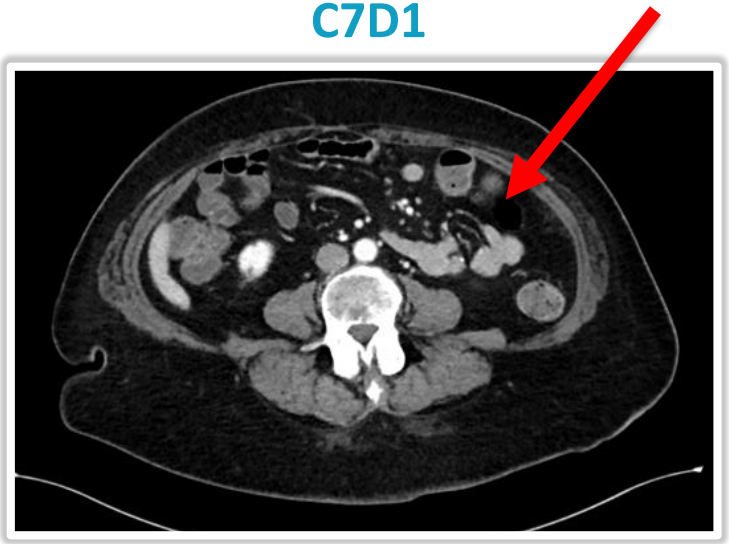
5 Non-Target lesions



Screening



C7D1

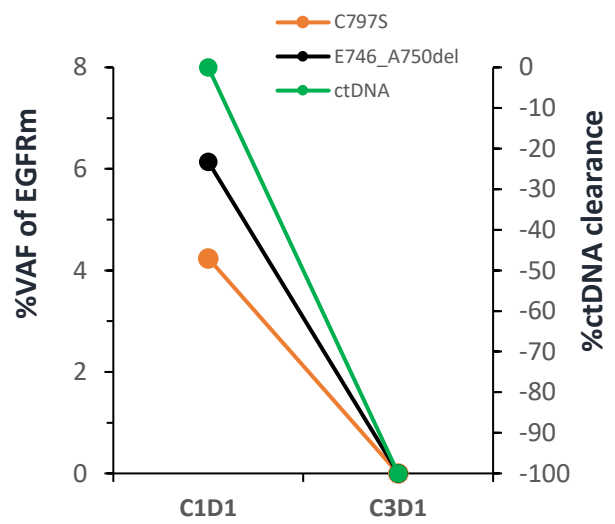


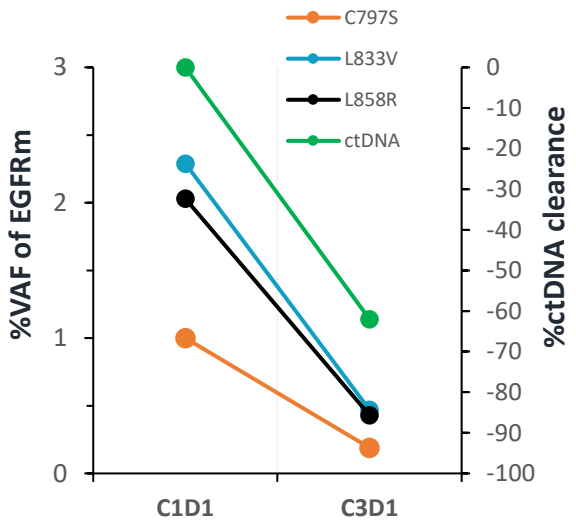
Source: Data on File as of Aug 17, 2024

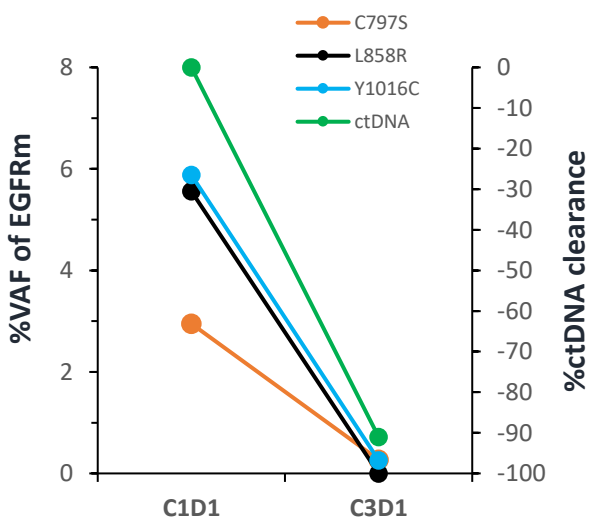
LN= lymph node, SoD = Sum of diameters per RECIST 1.1

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
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2207			L747_A755delinsSKD^	C797S
2118			L747_T751del^; V834L	C797S
2115	L858R	L718V		
2199	L858R	E709A		
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2124		E709_T710delinsD		
2197		K745_E746insIPVAIK	K745N	
2208		V774M; S768I		
2198		L718V	L747_P753delinsS^; G930R	
2203			L747P_P753delinS^	
2101			L861Q^	
2188			L861R^; L62R	

10 patients with C797S

9 patients with PACC-NCM

3 patients with other NCM

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

All mutations identified with common practice NGS

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*# 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

Safety/PK Assessment for Dose Selection

Data supporting 200 mg/daily

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

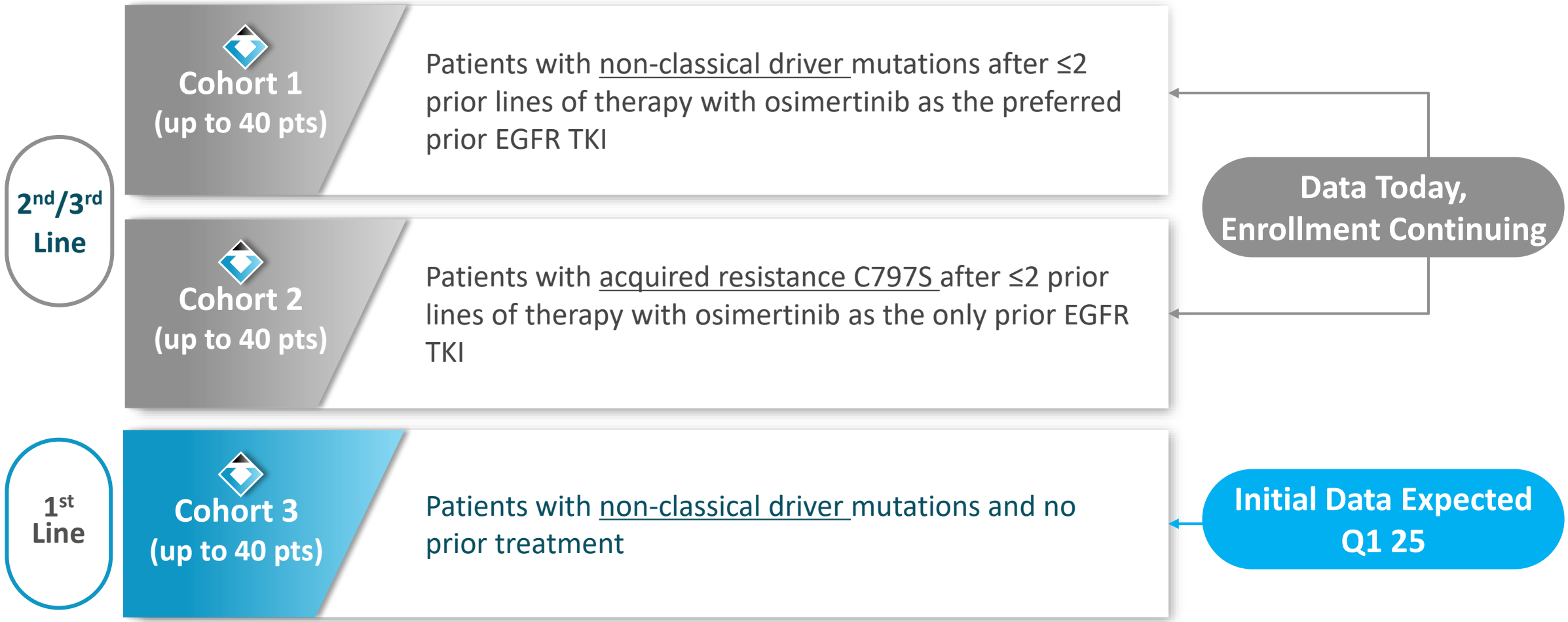
200 mg dose selected for pivotal development

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: anticipate regulatory feedback on registration paths and Phase 2 1L data

BDTX-1535 Preliminary Phase 2 Clinical Data in Recurrent Setting



Danny Nguyen, MD

Medical Oncologist and Assistant Clinical Professor, Department of Medical Oncology & Therapeutics Research

City of Hope

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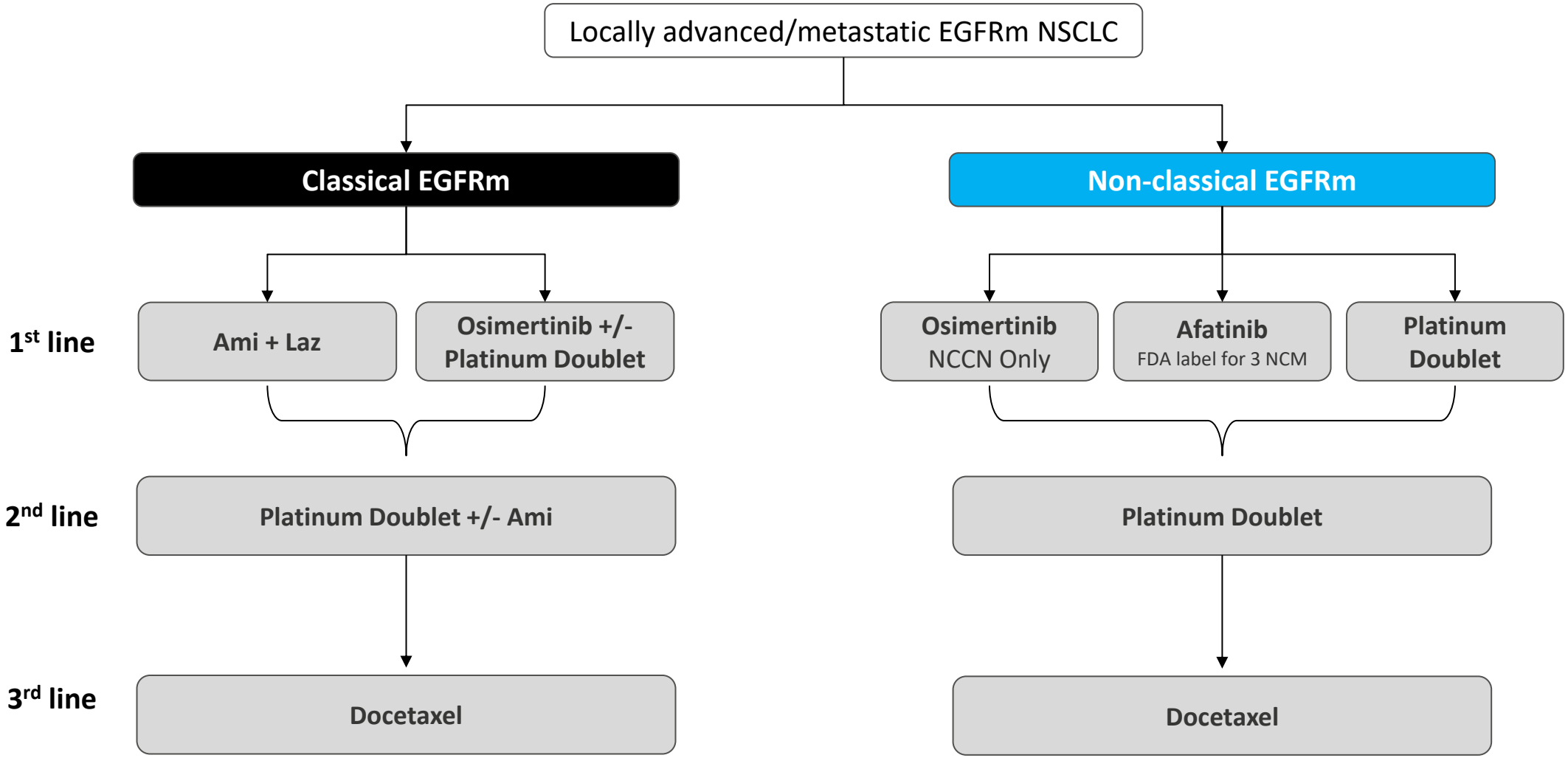
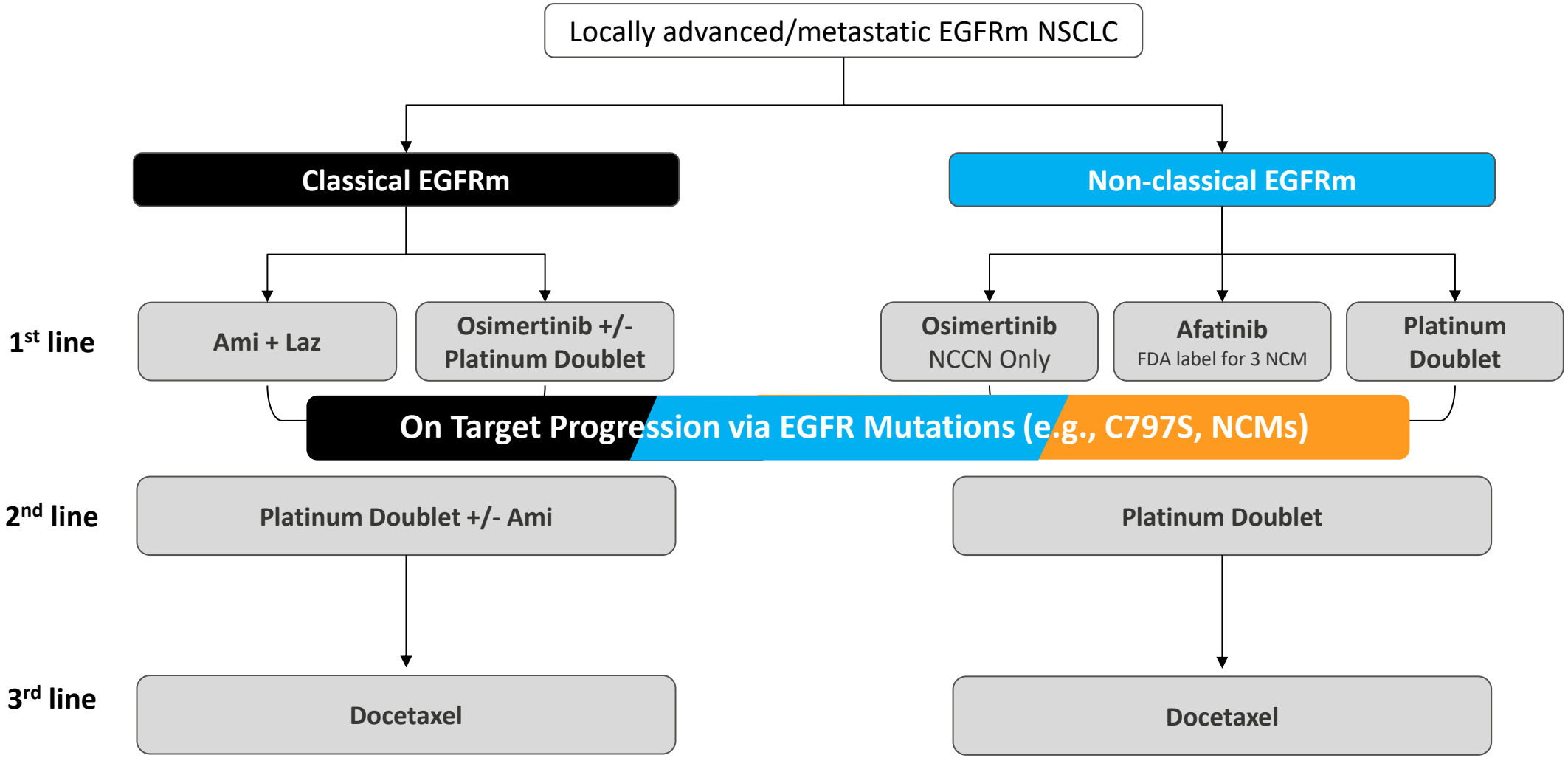
Current Treatment Landscape for EGFRm NSCLC



Ami: Amivantamab Laz: Lazertinib

Current Treatment Landscape for EGFRm NSCLC



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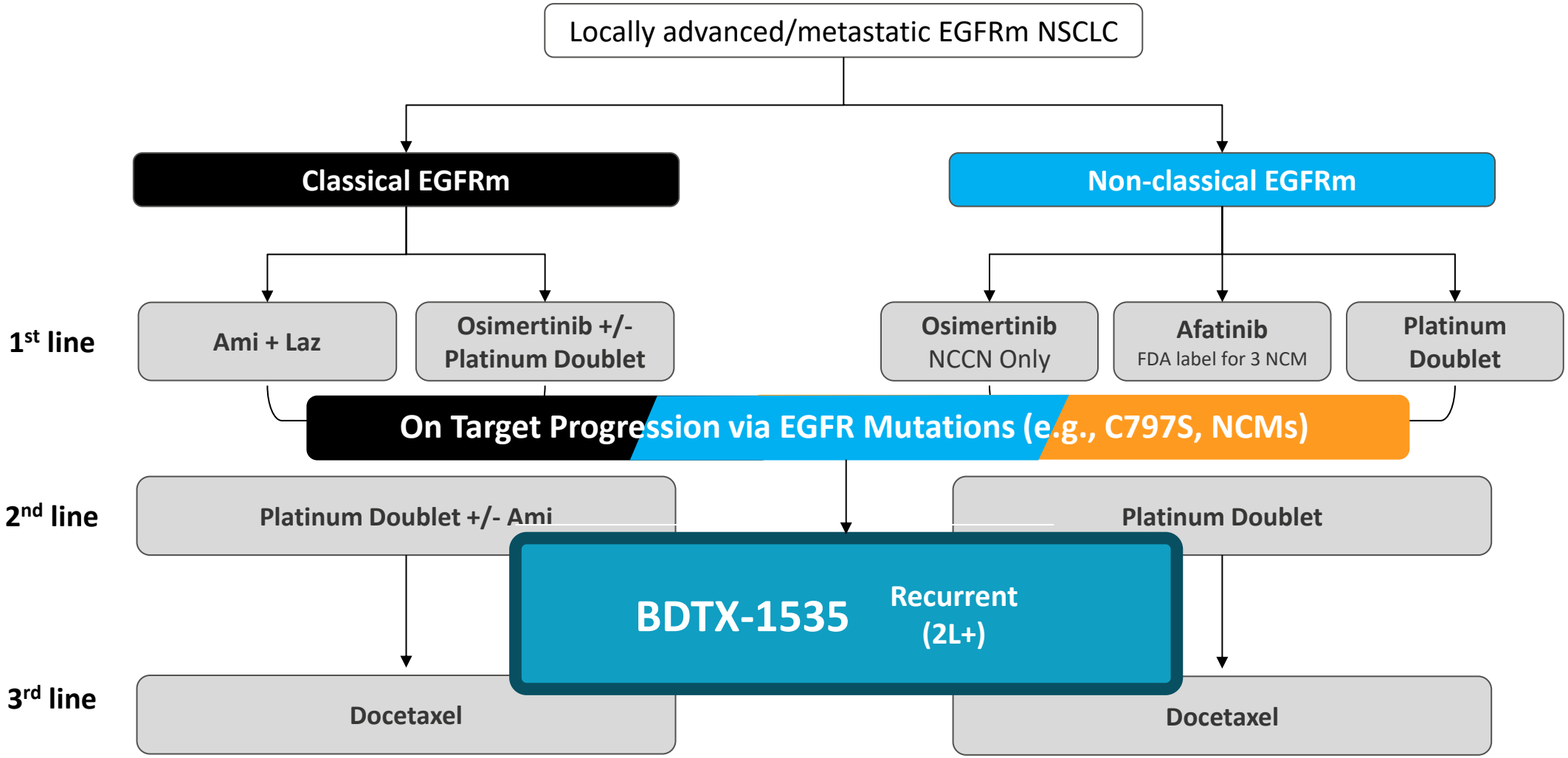
Current Treatment Landscape for EGFRm NSCLC



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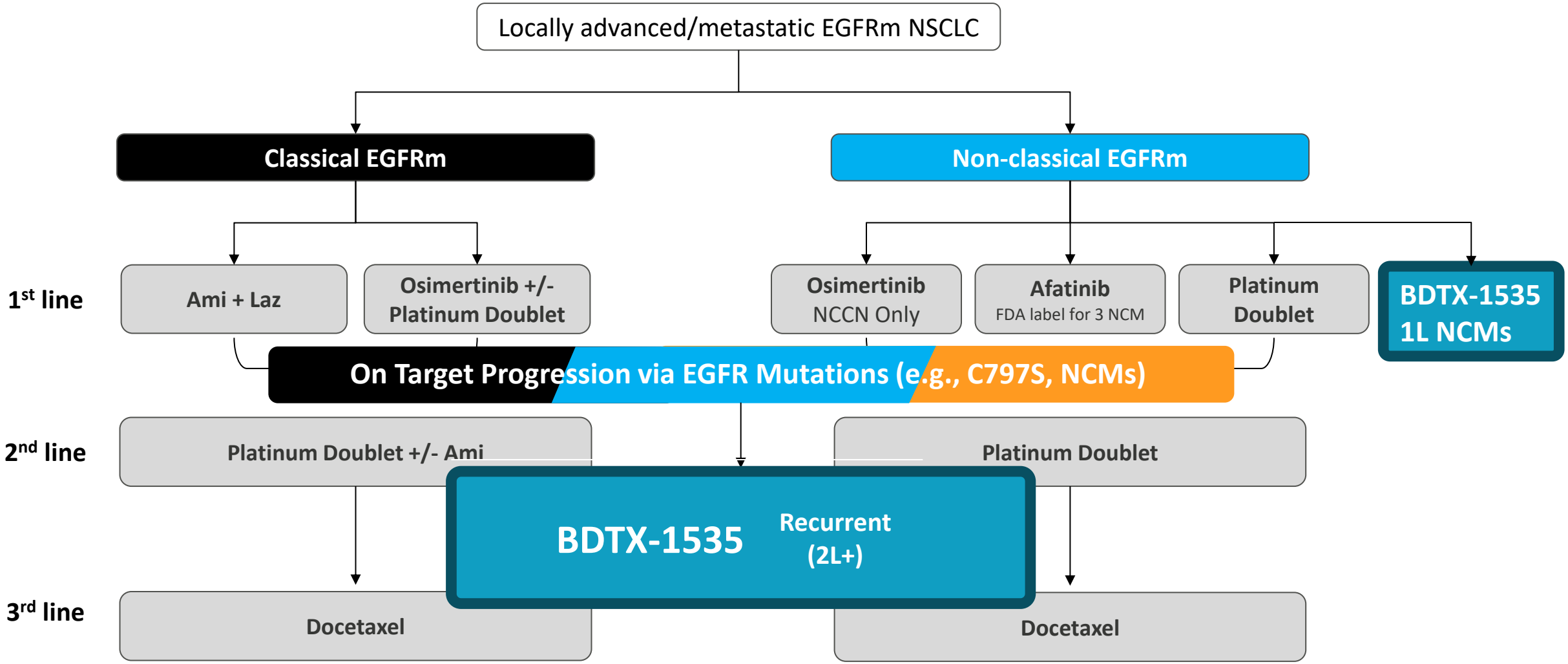
Current Treatment Landscape for EGFRm NSCLC



Ami: Amivantamab Laz: Lazertinib

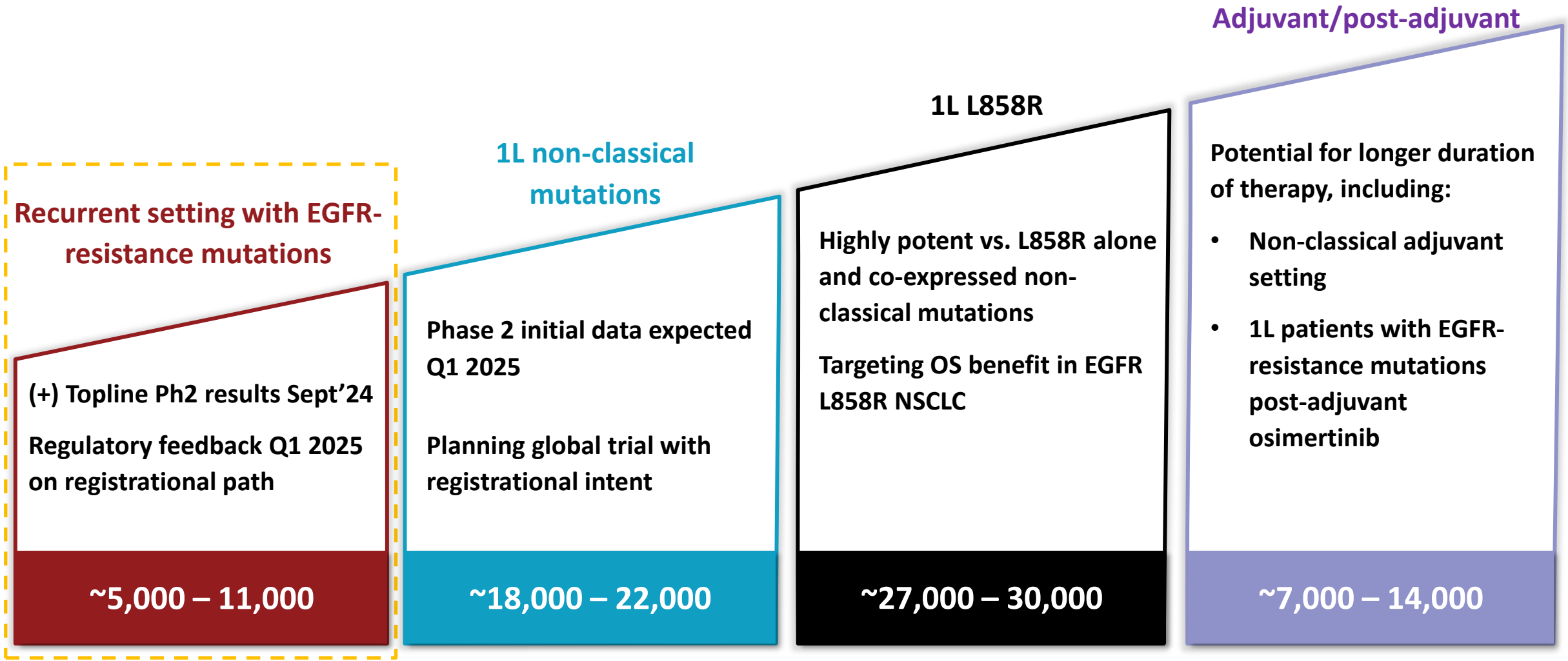
BDTX-1535: Well-Positioned Versus Chemo-Based Combination Regimens

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

Q&A

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