

Black Diamond Therapeutics, Inc.

Clinical Update on BDTX-1535 Potential First and Best-in-Class
4th Generation EGFR Inhibitor



June 27, 2023

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; our current and prospective product candidates, the timing and advancement of current and planned clinical trials, our ability to replicate results achieved in our preclinical studies or clinical trials; research and development costs; the competitive landscape and market for our product candidates; our ability to maintain our intellectual property portfolio; and the timing and success of our development and commercialization of our product candidates, including our ability to establish and maintain collaborations or strategic relationships. 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.

Agenda

CEO Introduction to BDTX-1535 Clinical Update



David M. Epstein, Ph.D.
President & CEO

Mutant EGFR NSCLC Landscape and BDTX-1535 Profile



Liz Buck, Ph.D.
Chief Scientific Officer

BDTX-1535 Phase 1 NSCLC Clinical Data



Sergey Yurasov, M.D., Ph.D.
Chief Medical Officer

KOL Perspective: Post-Osimertinib NSCLC



Melissa Johnson, M.D.
Director of Lung Cancer Research
Sarah Cannon

Key Milestones



Fang Ni, Pharm.D.
Chief Business and Financial Officer

BDTX-1535 Clinical Proof-of-Concept Achieved in Phase 1 Dose Escalation

EGFR Mutant Non-Small Cell Lung Cancer (NSCLC)



Clinical proof-of-concept achieved
Clinical presentation today

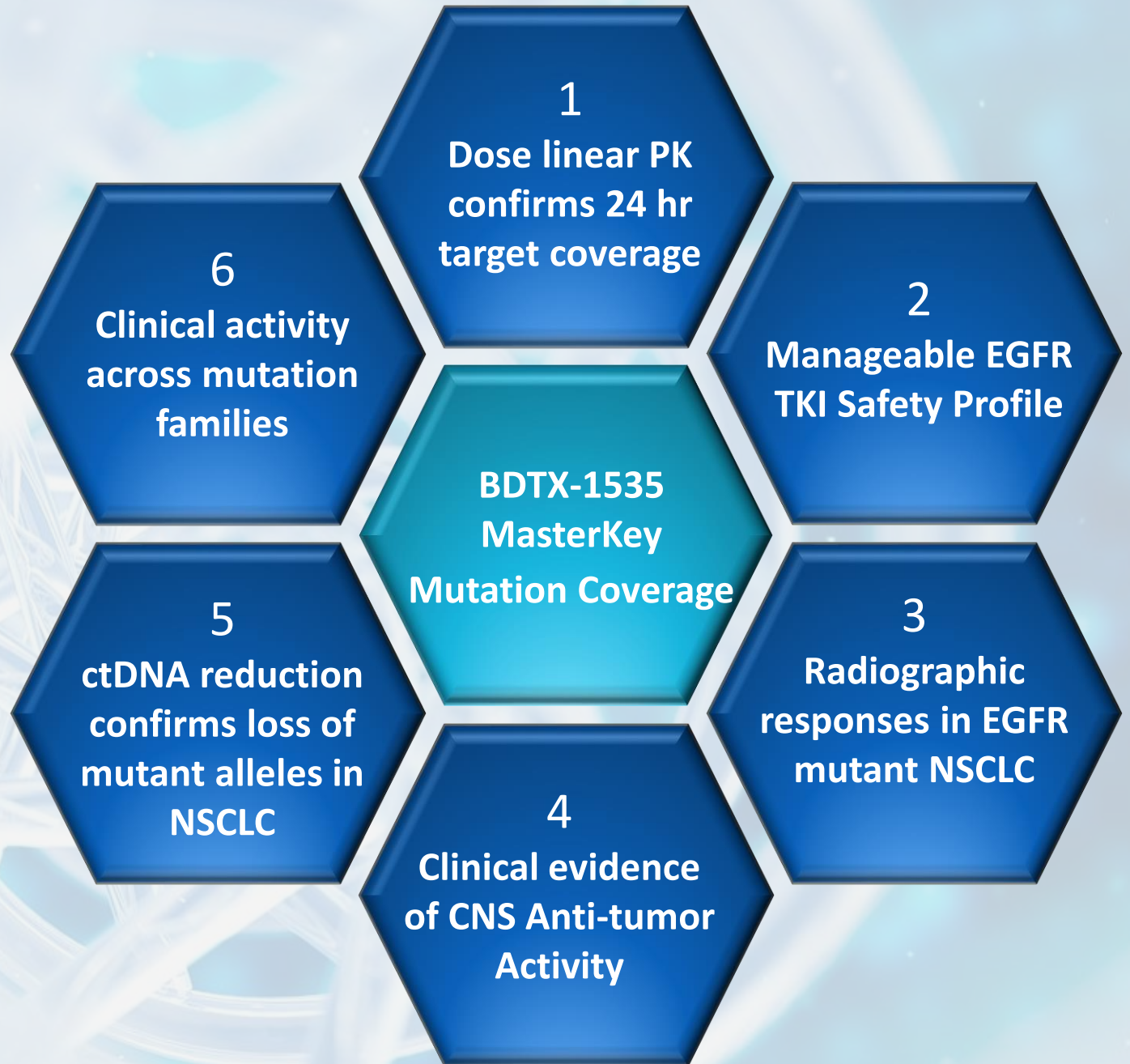
EGFR Altered Glioblastoma (GBM)



Update planned
Fourth Quarter of 2023

BDTX-1535 Phase 1 Highlights:

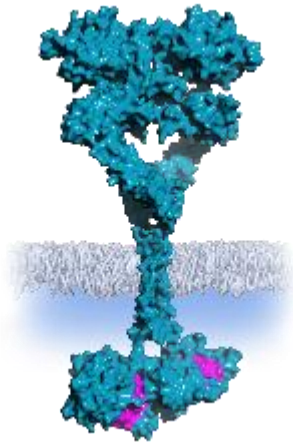
Clinical Proof-of-Activity in NSCLC



Black Diamond's MasterKey Approach Targets Oncogene Mutation Families

Classical/Current Approach:

Targeting single mutations
in individual tumor types



Limited addressable
patient population

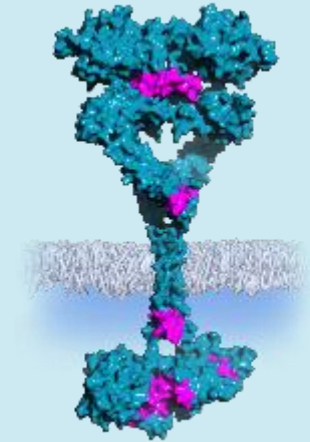


Genetic profiling of cancer patients
via Next Generation Sequencing
(NGS)

Less than 15% patients¹ with
metastatic cancer eligible for
approved precision
oncology medicines

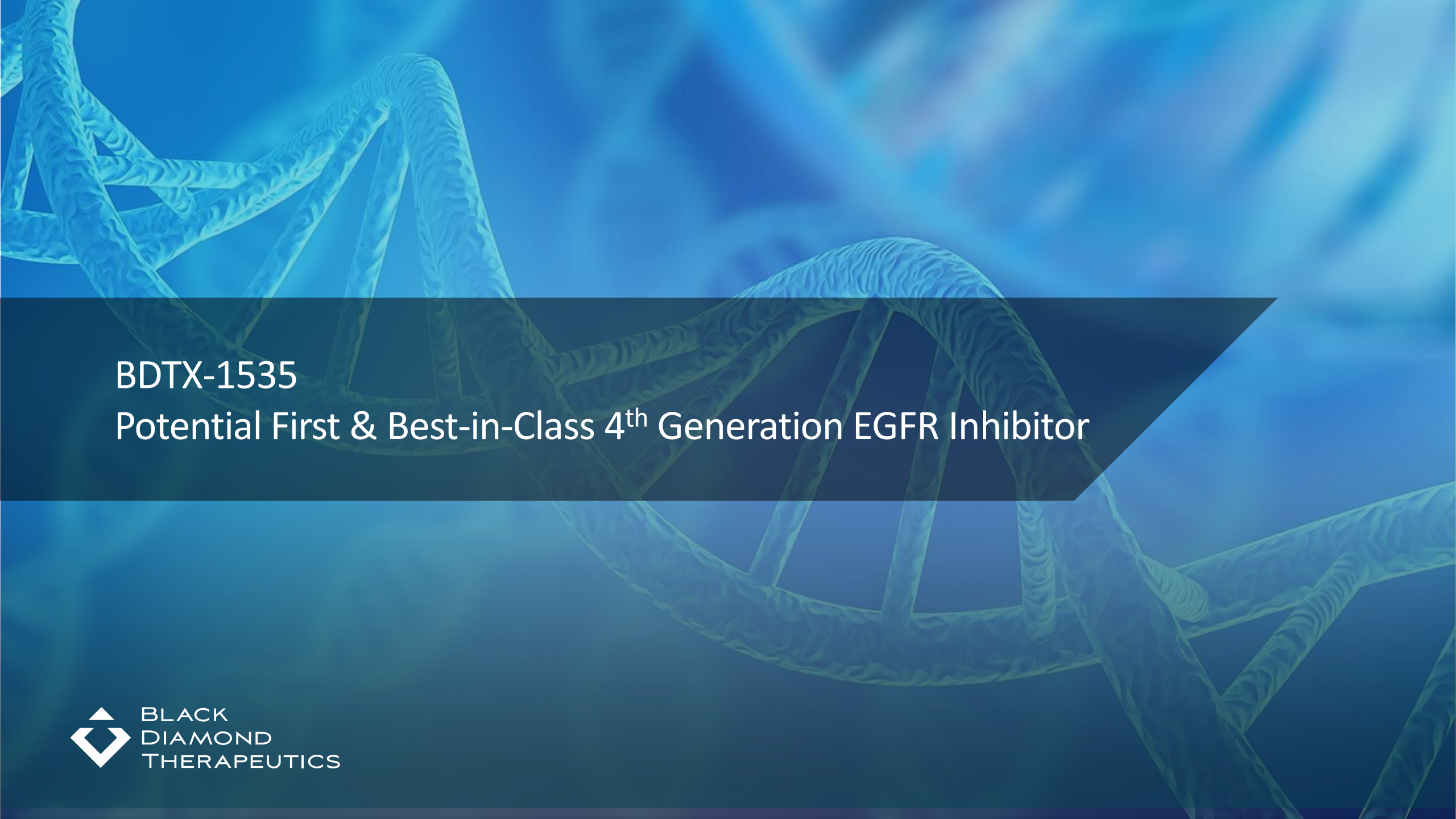
Black Diamond MasterKey:

Targeting family of oncogenic mutations



Expanded addressable
patient population





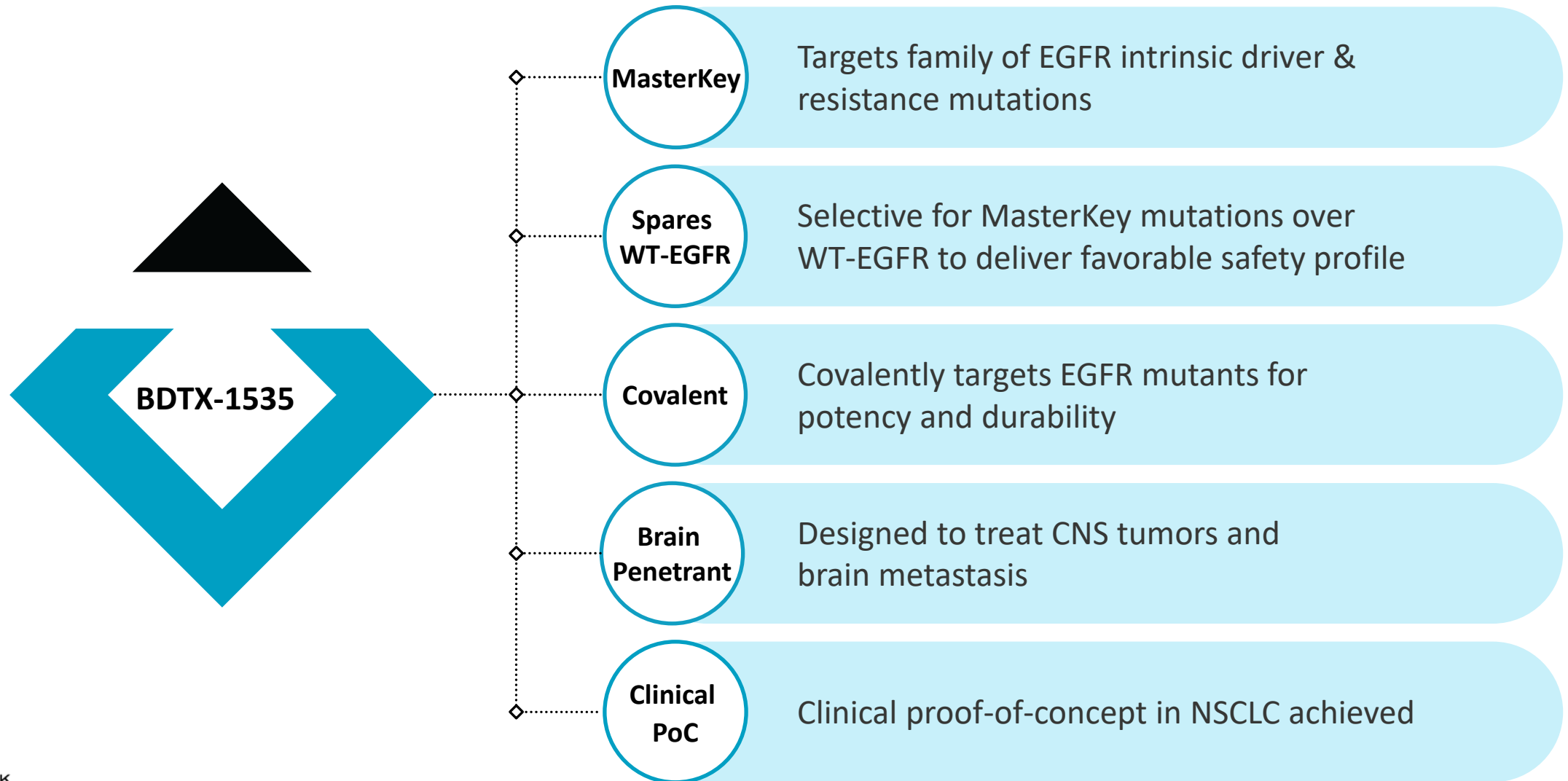
BDTX-1535

Potential First & Best-in-Class 4th Generation EGFR Inhibitor

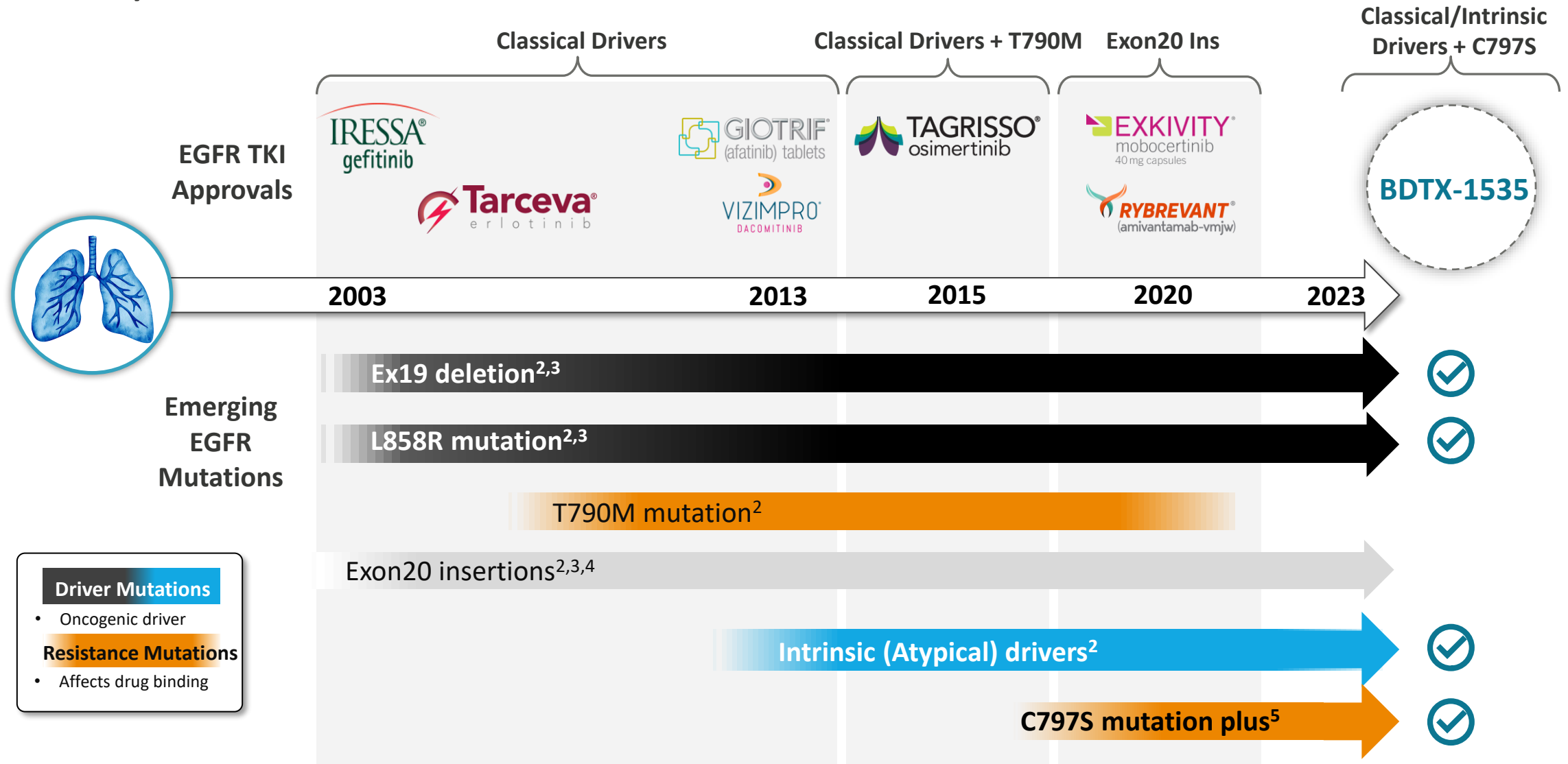


BLACK
DIAMOND
THERAPEUTICS

BDTX-1535: Selective EGFR MasterKey Inhibitor with Clinical Proof-of-Concept



Evolving EGFR Mutated NSCLC Market Predicted to Grow to Over \$6B Per Year¹ Globally



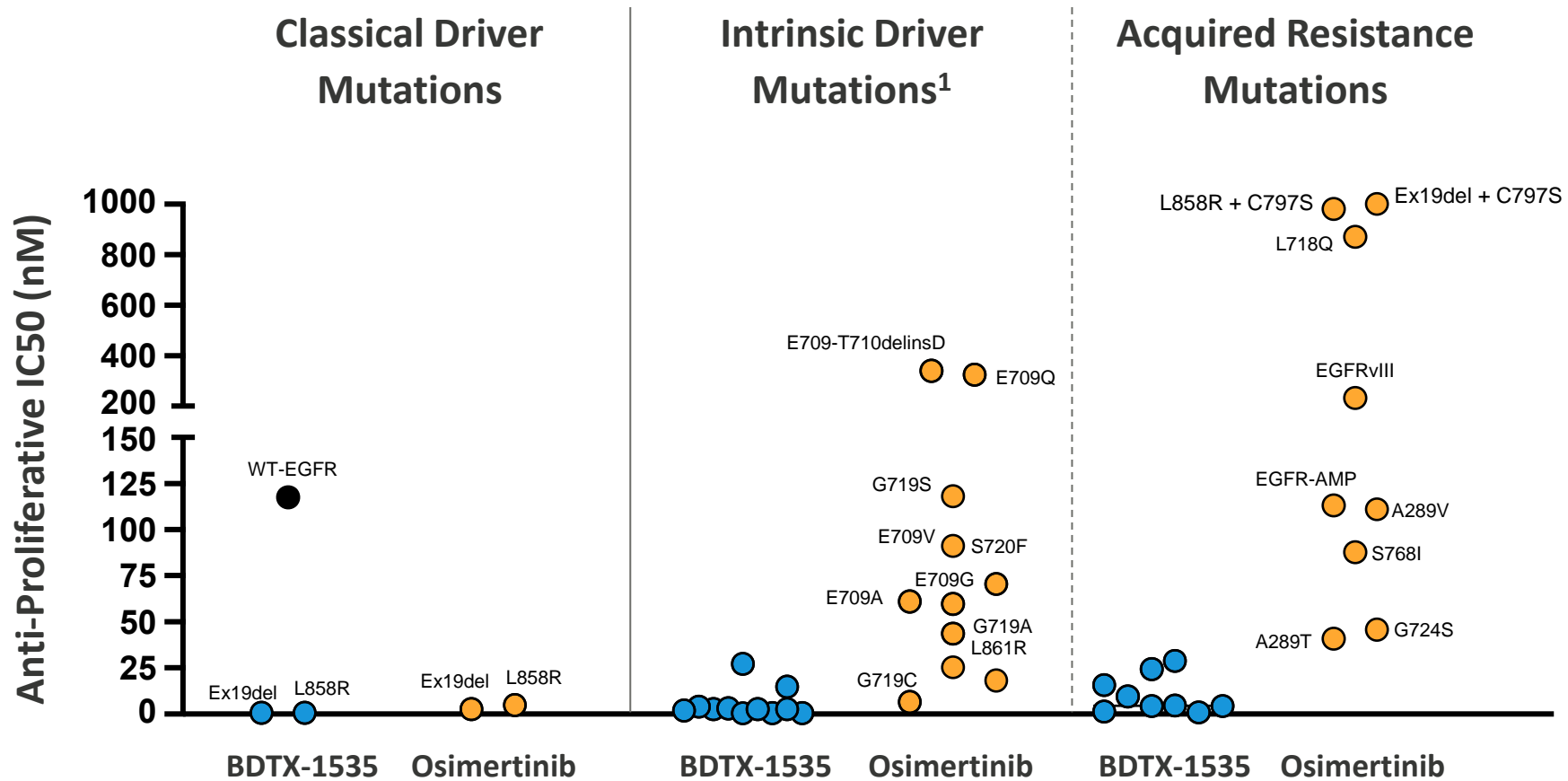
Note: Intrinsic drivers also called "Atypical", "PACC", "Uncommon"

1. EvaluatePharma 2. Bogdan Grigoriu, European Respiratory Journal Apr 2015; 3. Kosaka, T. Cancer Res., (2004); 4. Vyse, S., Sig Transduct Target Ther (2019); 5. Costa DB, Transl Lung Cancer Res. 2016

BDTX-1535 Demonstrated Potent Inhibition of EGFR Intrinsic Driver Mutations, C797S Resistance Mutation, and EGFR Amplification



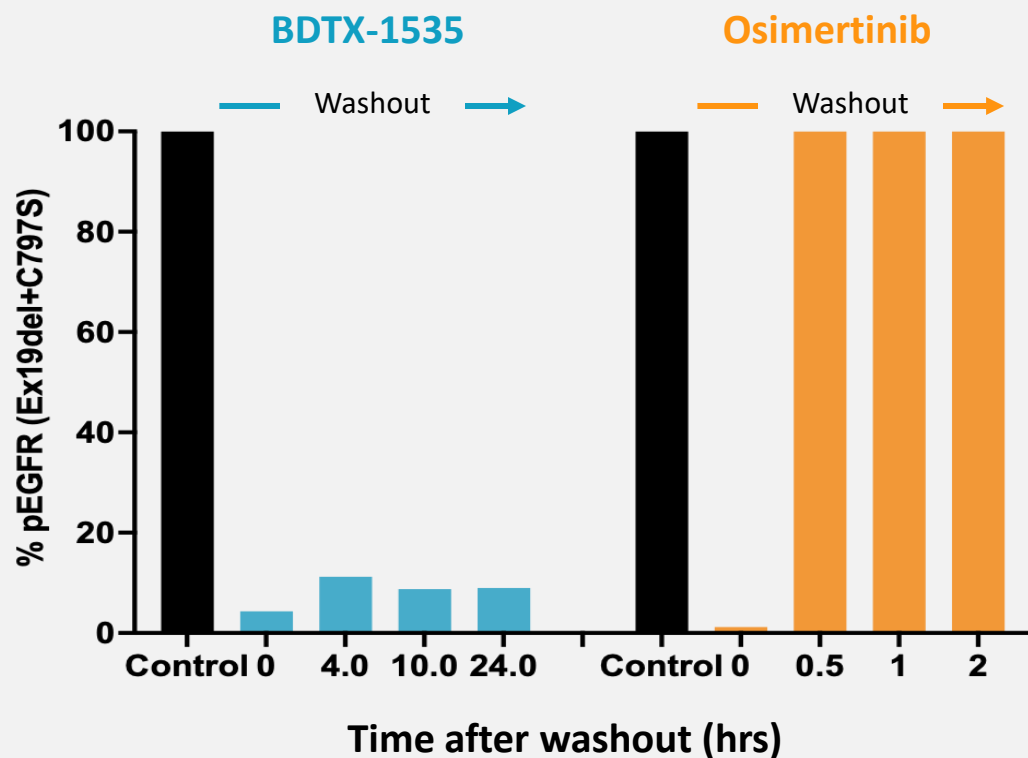
BDTX-1535 potently targets >50 EGFR MasterKey mutations



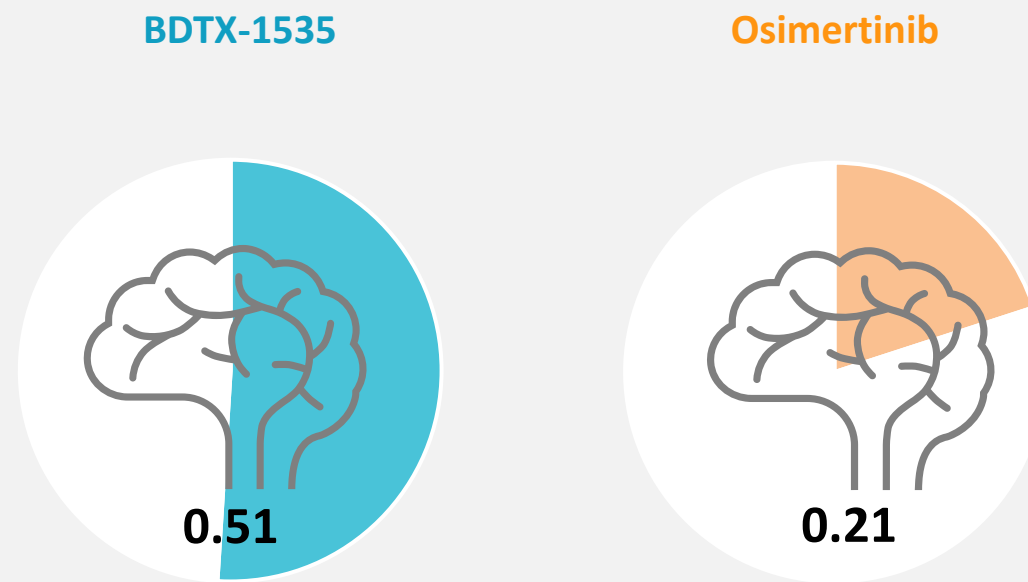
1. BDTX-1535 has demonstrated activity against greater than 50 intrinsic driver resistance mutations
 Source: AACR 2023 Poster

BDTX-1535: Designed as an Irreversible Brain Penetrant EGFR MasterKey Inhibitor

BDTX-1535 Exhibited Durable Irreversible Target Inhibition In Preclinical C797S mutant Study



BDTX-1535 Exhibited Superior Brain Exposure K_{puu} (rat)





BDTX-1535 – Potentially First and Best-in-Class 4th Gen EGFR TKI

Critical Features	BDTX-1535	BLU-945 ^{1,2}	BLU-701 ^{3,4} /525 ⁵	THE-349 ⁶	STX-241 ⁷
Classical Driver MasterKey Mutations	✓	✓	✓	✓	✓
C797S Acquired MasterKey Resistance	✓	✓	✓	✓	✓
Intrinsic Driver MasterKey Mutations	✓	?	?	?	?
Covalent Binding for potency/durability	✓	✗	✗	✗	?
CNS Penetration	✓	?	✓	✓	✓
Status	Phase 1 Monotherapy	Combination Study	Deprioritized / preclinical	Preclinical	Preclinical

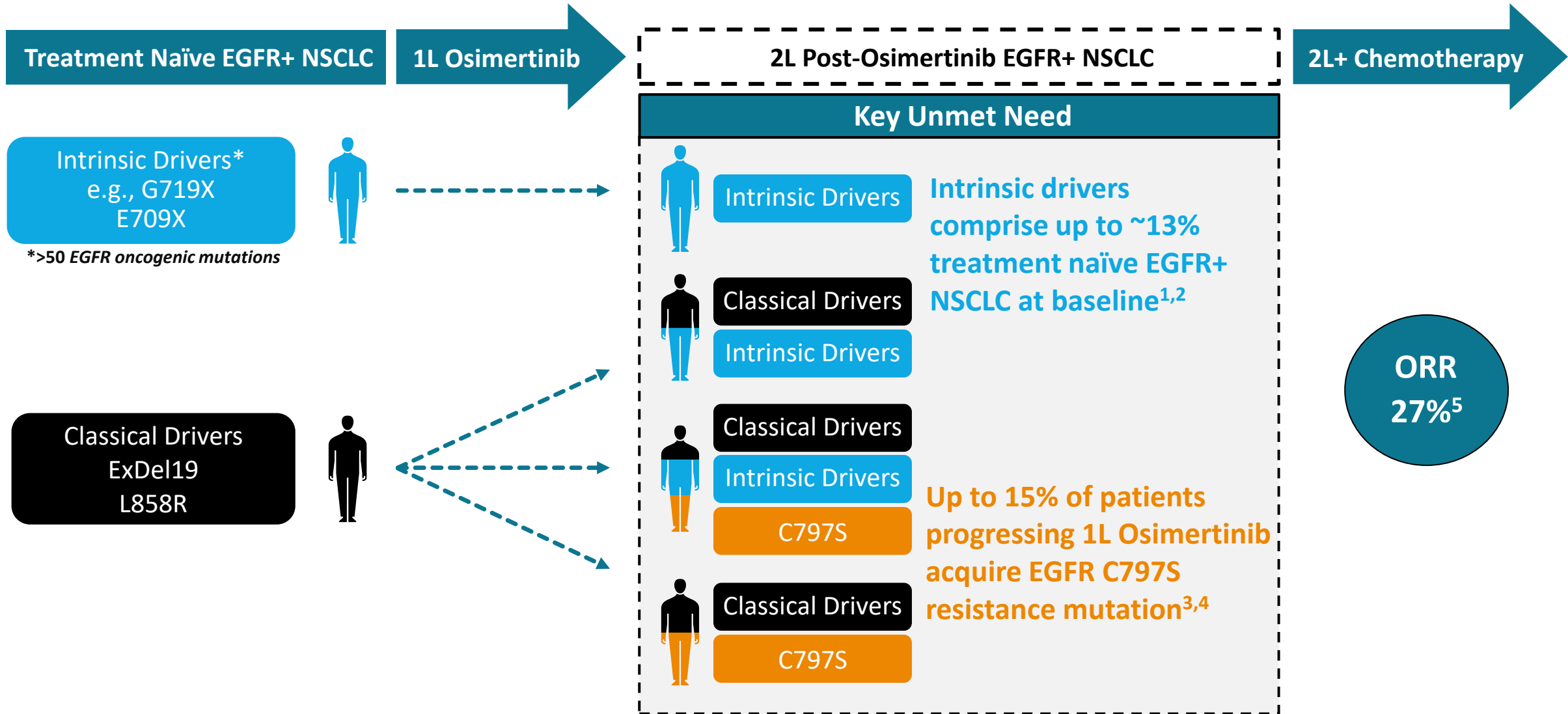
Note: Intrinsic drivers also called “Atypical”, “PACC”, and “Uncommon” mutations

1.) Eno, J Med Chem 2022; 2.) Elamin, ASCO 2023 Annual Meeting; 3.) Spira, ASCO 2022; 4.) Blueprint Medicines Investor Day, SEC 2022; 5.) Blueprint Medicines Corporate Presentation, June 2023; 6.) Zhang, EORTC-NCI-AACR 2022; 7.) Scorpion Therapeutics Press Release, April 2023



BDTX-1535 Designed to Address Current Pattern of EGFR Mutations

NSCLC EGFR Mutation Landscape Evolved with Early Line Use of Osimertinib

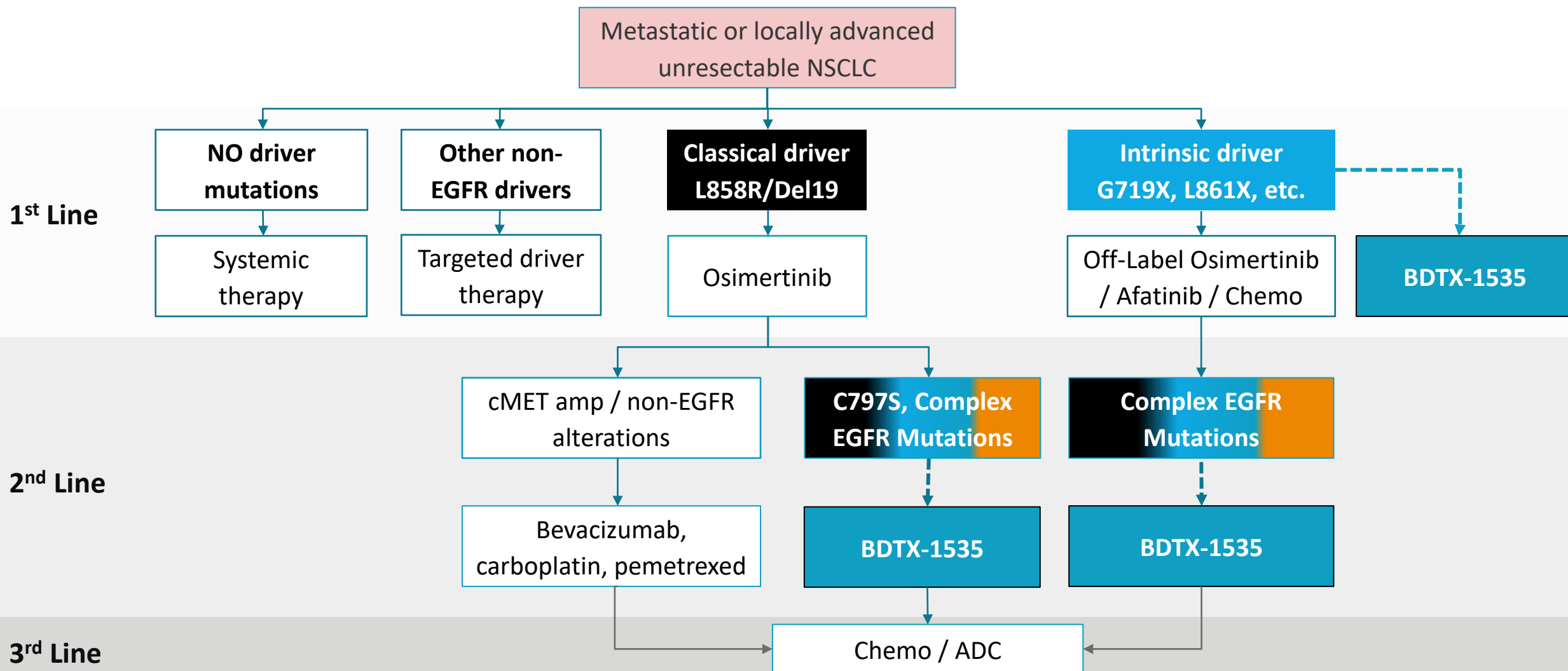


Note: Intrinsic drivers also called "Atypical", "PACC" and "Uncommon" mutations

1. John, Cancer Epidemiology, 2022; 2. Kuiper, BJC 2016; 3. Piotrowska Z, ESMO 2022, LBA53 ELIOS; 4. Ramalingam, WCLC 2022; 5. Keynote-789 ASCO 2023

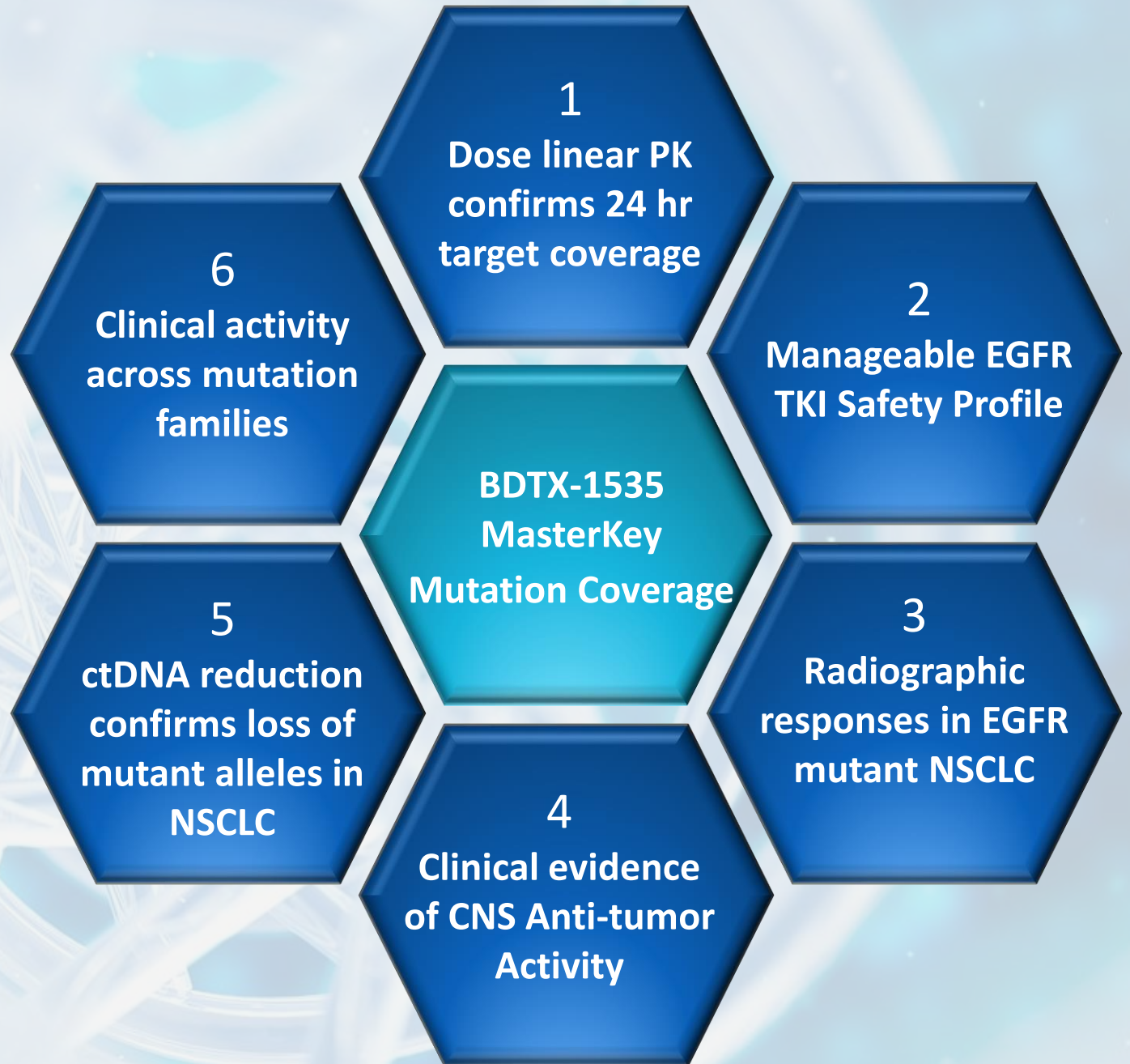
Current Treatment Paradigm for EGFR mutant NSCLC

BDTX-1535 Opportunity in Future 2L and 1L EGFR+ NSCLC Treatment Landscape



Note: Intrinsic drivers also called "Atypical", "PACC", and "Uncommon" mutations
 ADC = antibody drug conjugates
 Modified from KANTAR Health 2020

BDTX-1535 Phase 1 Dose Escalation Delivered Clinical Proof-of-Activity in NSCLC



BDTX-1535 Phase 1 Dose Escalation for NSCLC & GBM with Targeted EGFR Mutations

Mutation Matched Phase 1 Study



NSCLC Acquired & Intrinsic Cohorts:

- EGFR mutations at the time of progression:
 - **Intrinsic driver**, OR
 - **Acquired resistance**
- Progression on 1L 3rd Gen EGFR TKI
- Exclusion of EGFR T790M, Ex20ins, KRAS mutations, cMET amplification

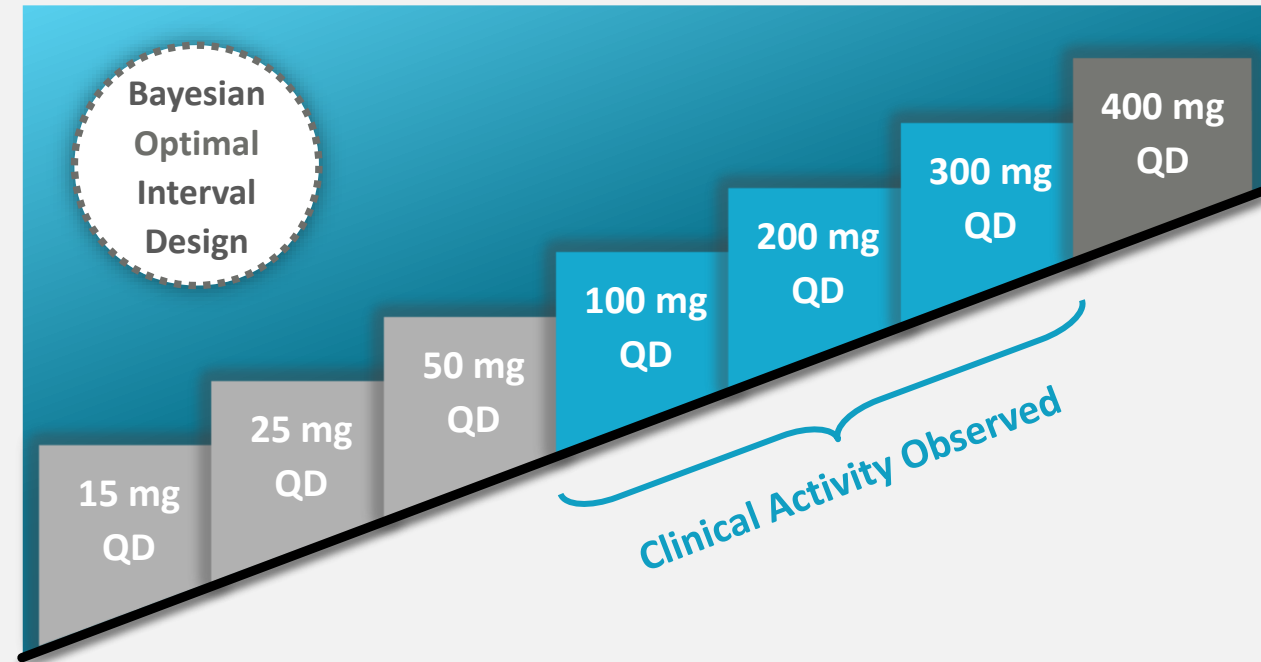


Recurrent GBM Cohort:

- EGFR alterations at the time of resection
- Wild-type isocitrate dehydrogenase (IDH)
- Recurrent disease

Dose Escalation

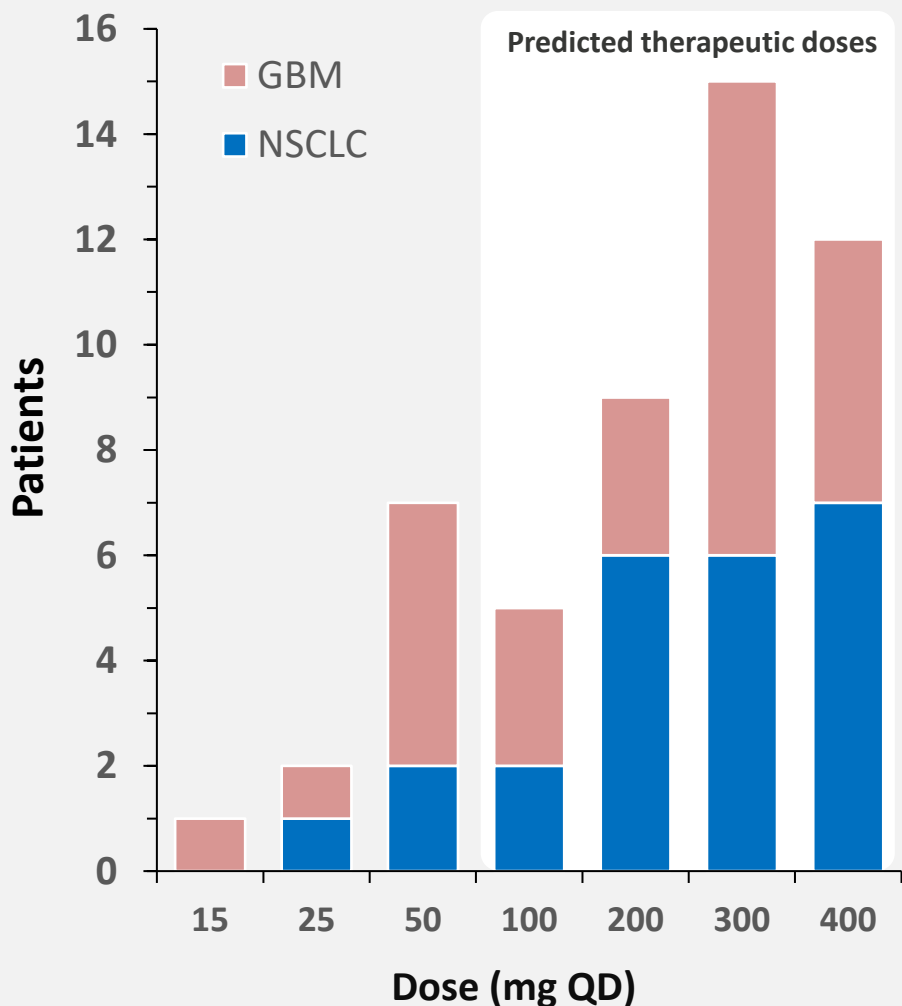
Patients: measurable and non-measurable disease
Primary objective: safety and PK



- N=51 for PK and safety analysis
- N=12 for NSCLC efficacy evaluable patients from 100mg, 200mg & 300 mg QD cohorts
- No DLTs at ≤ 200 mg QD



BDTX-1535-101 Phase 1 Dose Escalation Patient Characteristics



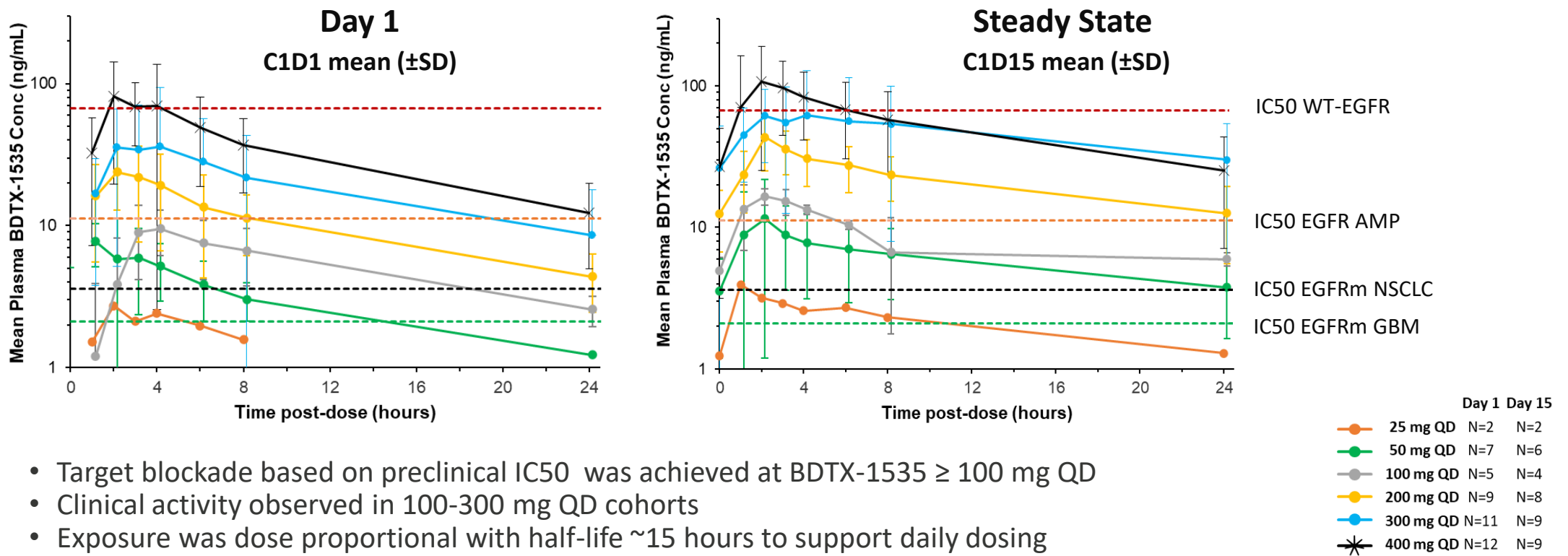
NSCLC	
Patient Characteristics and Treatment History	All Treated (N=24)
Age, median (range)	65 (47, 81)
Female	16 (67%)
ECOG PS	
0	7 (29%)
1	16 (71%)
Non-smoker	17 (71%)
Prior lines of therapies	
median (min, max)	2 (1, 9)
Prior anti-cancer agents	
EGFR TKI	24 (100%)
Chemo	16 (67%)
Anti-angiogenic or CPIs	10 (42%)
EGFR TKIs received	
Osimertinib	19 (79%)
1 st line treatment	16 (67%)
Erlotinib	4 (17%)
Afatinib	3 (13%)
Gefitinib	2 (8%)
Dacomitinib	1 (4%)
BLU-701	1 (4%)

GBM	
Patient Characteristics and Treatment History	All Treated (N=27)
Age, median (range)	58 (41, 85)
Female	10 (37%)
Karnofsky PS	
90	4 (17%)
80	12 (50%)
70	5 (21%)
60	3 (13%)
Prior lines of therapies	
median (min, max)	2 (1, 4)
Prior anti-cancer agents	
TMZ	27 (100%)
Anti-angiogenic or CPIs	11 (41%)
Chemo	7 (26%)

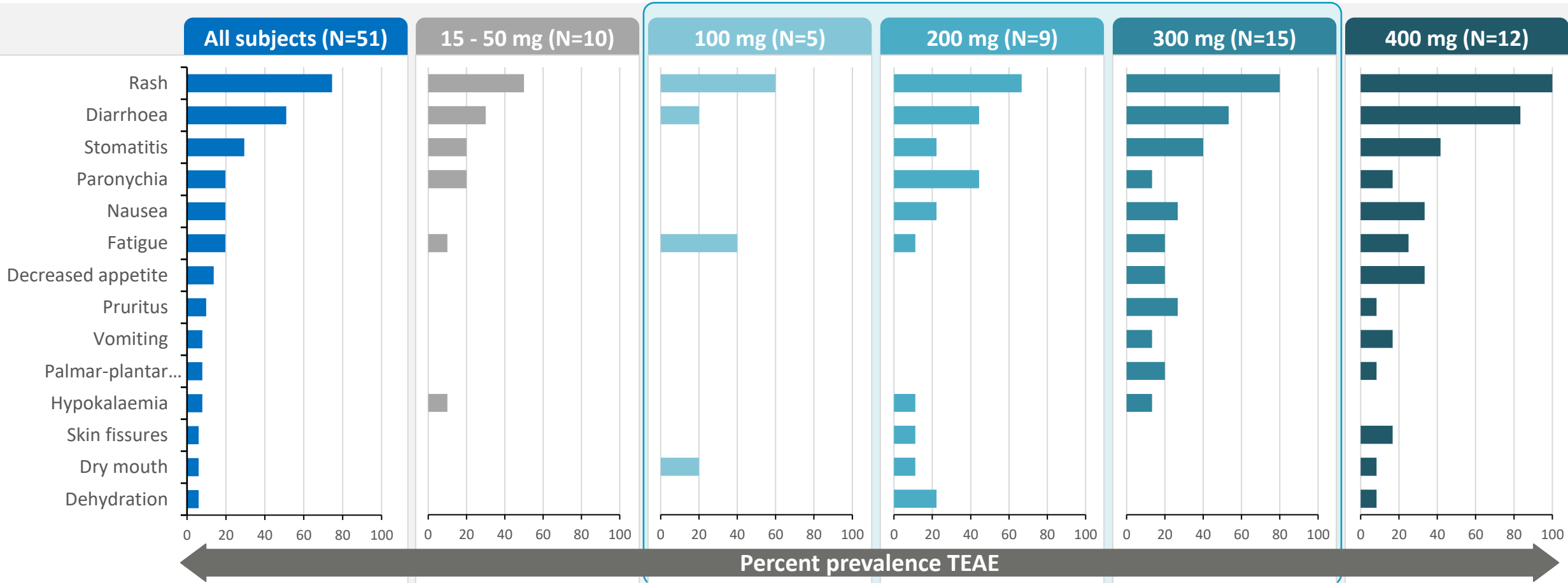
BDTX-1535 Linear Plasma PK Profile Supports Daily Dosing To Achieve 24 Hour Target Coverage in NSCLC and GBM Cohorts



Mean plasma concentration-time profile of BDTX-1535



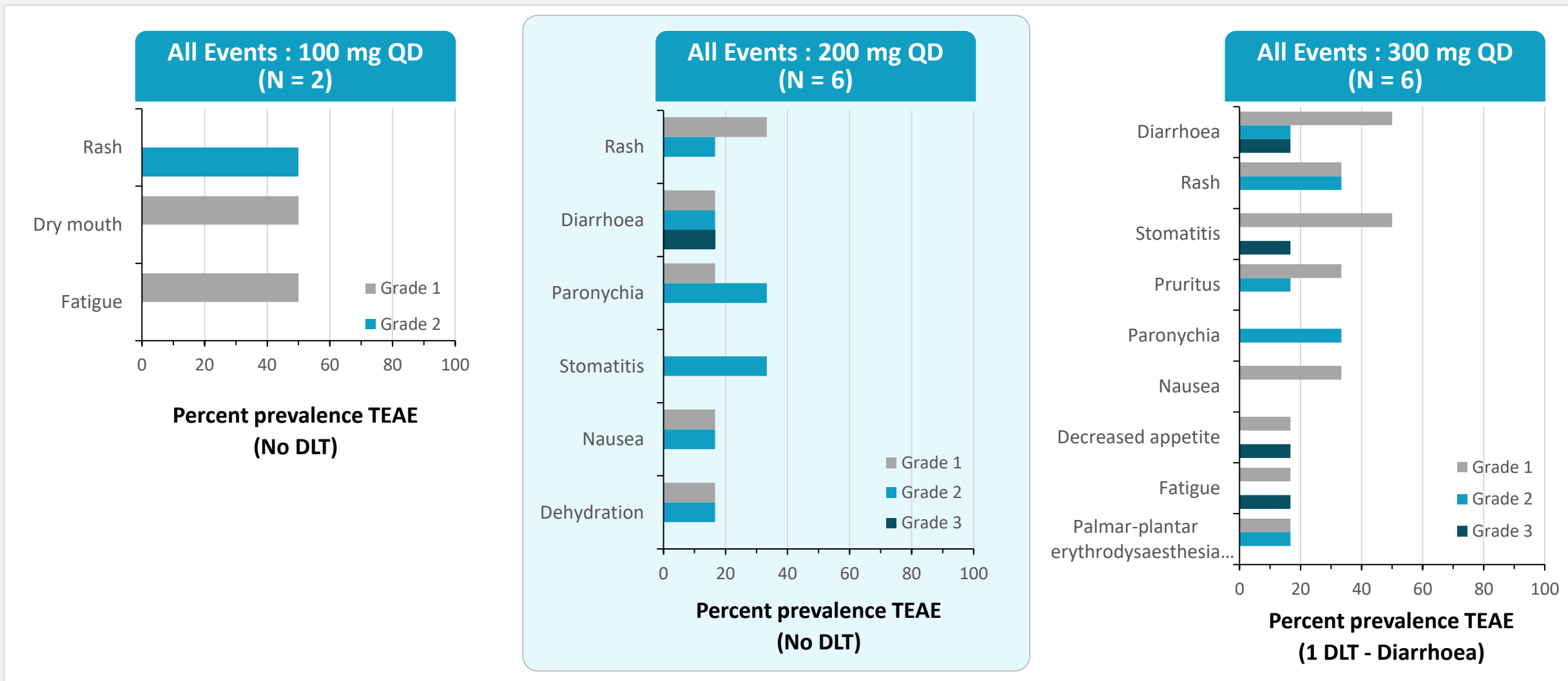
Dose Escalation Treatment Emergent Adverse Events Related to BDTX-1535



- TEAEs events occurring $\geq 6\%$
- Majority of adverse events were mild or moderate
- Rash, diarrhea, stomatitis and paronychia were consistent with WT EGFR effect
- No unexpected safety signal was identified

Comparison of BDTX-1535 Related Adverse Events in NSCLC Patients

BDTX-1535 200 mg QD was Observed to be a Well Tolerated Dose



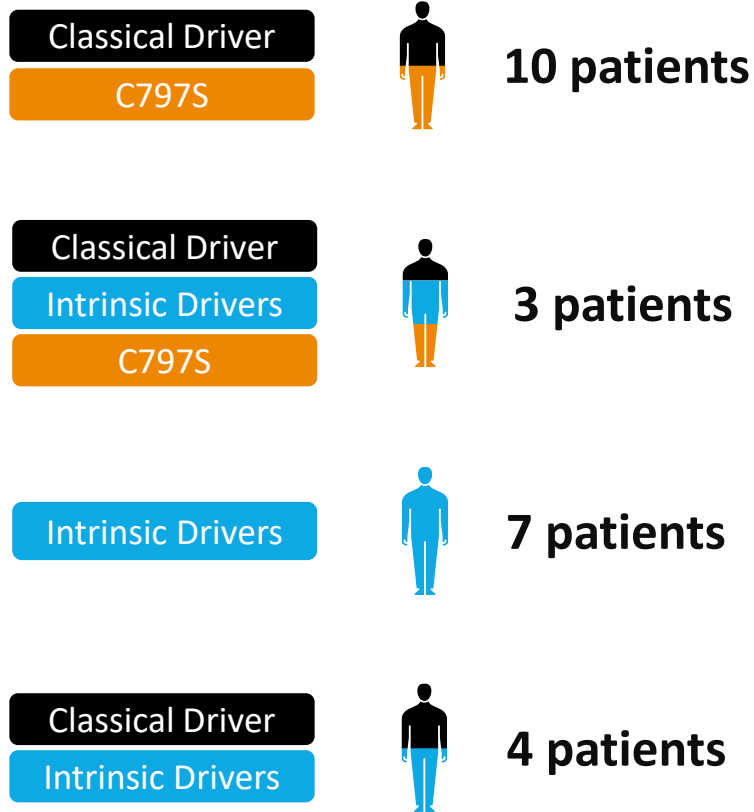
The image features a stylized illustration of human lungs in shades of blue, set against a background of a complex network of black dots and thin white lines. A semi-transparent dark grey banner is positioned across the middle of the image, containing the main title.

BDTX-1535 Summary of NSCLC Data

BDTX-1535 Dose Escalation NSCLC Patients Reflect Real World EGFR Mutation Landscape Post Osimertinib



n=24 patients enrolled in dose escalation; n=12 patients efficacy evaluable



Mutation Family	MasterKey Mutations
Acquired resistance mutation	C797S
	E709A/V
	L718Q
	G724S
	D1012V
Intrinsic driver mutation	L833V
	G719A
	L861Q
	L747P
	S768I
	T751K
	K754E
Classical mutation	L747_E759del
	E746_T751delinsA
	Exon 19del
	L858R

NSCLC Efficacy Evaluable Patient Population From BDTX-1535 Phase 1 Dose Escalation



Assigned Dose (QD) (n =24)	Reasons for Exclusion From Efficacy Evaluable Group	Efficacy Evaluable Group (n = 12)
25 mg (n =1) 50 mg (n = 2)	Sub-therapeutic doses (n=3)	25 mg (n = 0) 50 mg (n = 0)
100 mg (n = 2)	Physician decision to withdraw patient (n = 1)*	100 mg (n = 1)
200 mg (n = 6)	None	200 mg (n = 6)
300 mg (n = 6)	Protocol eligibility deviation (n = 2) Nine lines of therapy (n =1) Post-baseline tumor assessment is pending (n=1)	300 mg (n = 2)
400 mg (n = 7)	Non-measurable disease (n =1) Treatment discontinuation due to AE (n = 1)* Consent withdrawal by subject (n = 2)*	400 mg (n = 3)

RECIST1.1 Radiographical Responses in Efficacy Evaluable NSCLC Patients Treated with Therapeutic Doses of BDTX-1535

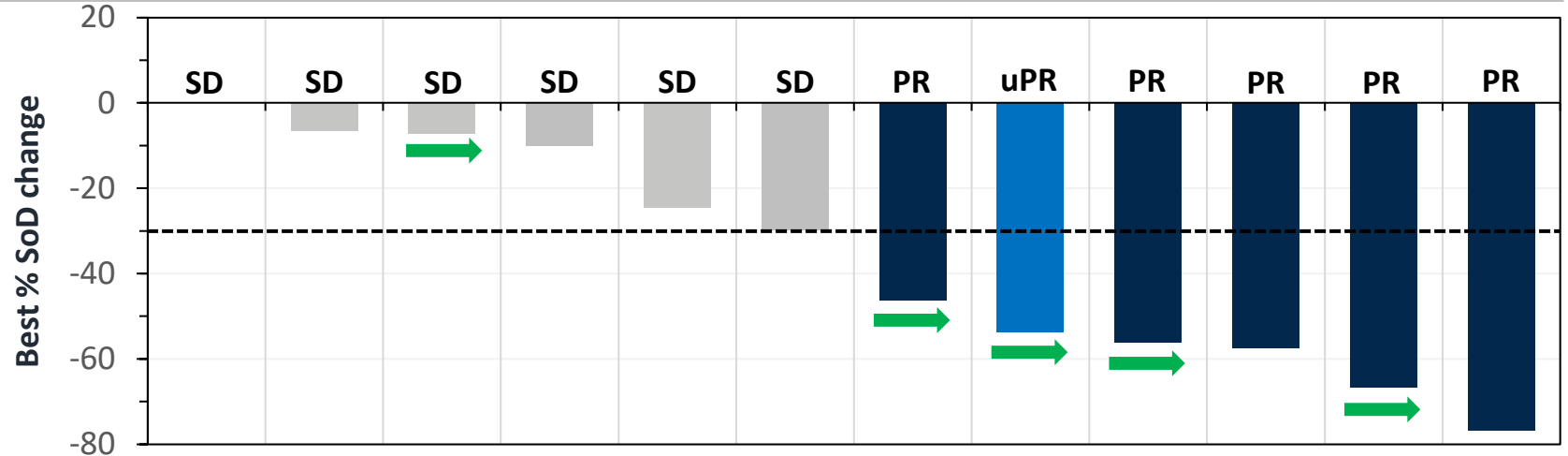


Efficacy Evaluable Patients
5 cPR, 1 uPR of 12 by RECIST

Post-Osimertinib Patients
5 cPR, 1 uPR of 10 by RECIST

➔ On study patient
Osi = osimertinib
C = chemotherapy
Afa = afatinib
Gef = gefinitib
Erlo = erlotinib
CPI = checkpoint inhibitor
NE = not evaluable
SoD = sum of diameters

Starting Dose	400 mg	200 mg	200 mg	200 mg	200 mg	400 mg	400 mg	200 mg	200 mg	300 mg	300 mg	100 mg
Dose at C3D1 (QD)	400 mg	200 mg	200 mg	200 mg	200 mg	300 mg	300 mg	200 mg	200 mg	300 mg	300 mg	100 mg



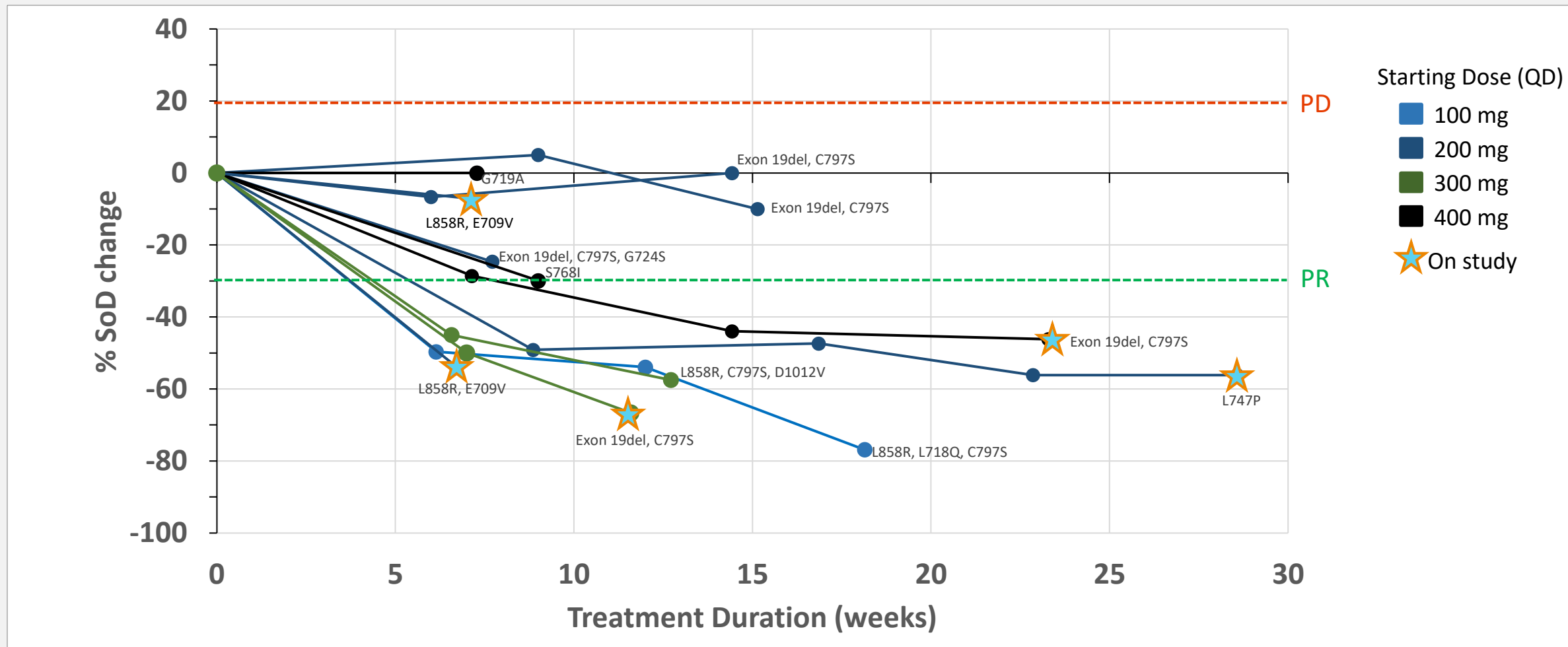
EGFR Mutation	Classical driver	Ex19del	L858R	Ex19del	Ex19del		Ex19del	L858R		L858R	Ex19del	L858R	
	Intrinsic driver	G719A		E709V		G724S	S768I		E709V	L747P	D1012V		L718Q
	Acquired resistance		C797S		C797S	C797S		C797S			C797S	C797S	C797S
ctDNA reduction, %	pending	-100%	pending	-100%	-95%	NE	-31%	pending	-100%	pending	pending	-74%	
Prior Lines of Treatment	Osi	Osi	Gef *	Osi	Osi	Erlo *	CPI, C **	Osi	Osi	C **	Osi	Osi	
	C		C	CPI, C		C	Osi	C	CPI, C	Osi	Osi + Gef		
	Afa								C		BLU-701		

Population to be Assessed for ORR in Expansion Cohorts

- Patients with measurable disease who have received 3rd gen EGFR TKI, no 1st or 2nd generation EGFR TKI
- No more than 2 prior lines of therapy
- Patients with no prior osimertinib excluded



BDTX-1535: Emerging Evidence of Durable Tumor Response in NSCLC



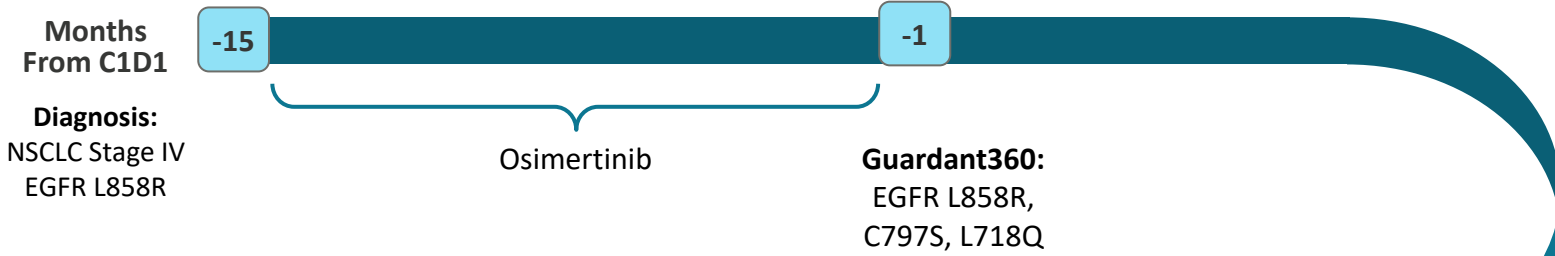
Confirmed PR by RECIST1.1 in NSCLC Patient with EGFR L858R + L718Q + C797S Complex Mutation

Classical Driver
L858R

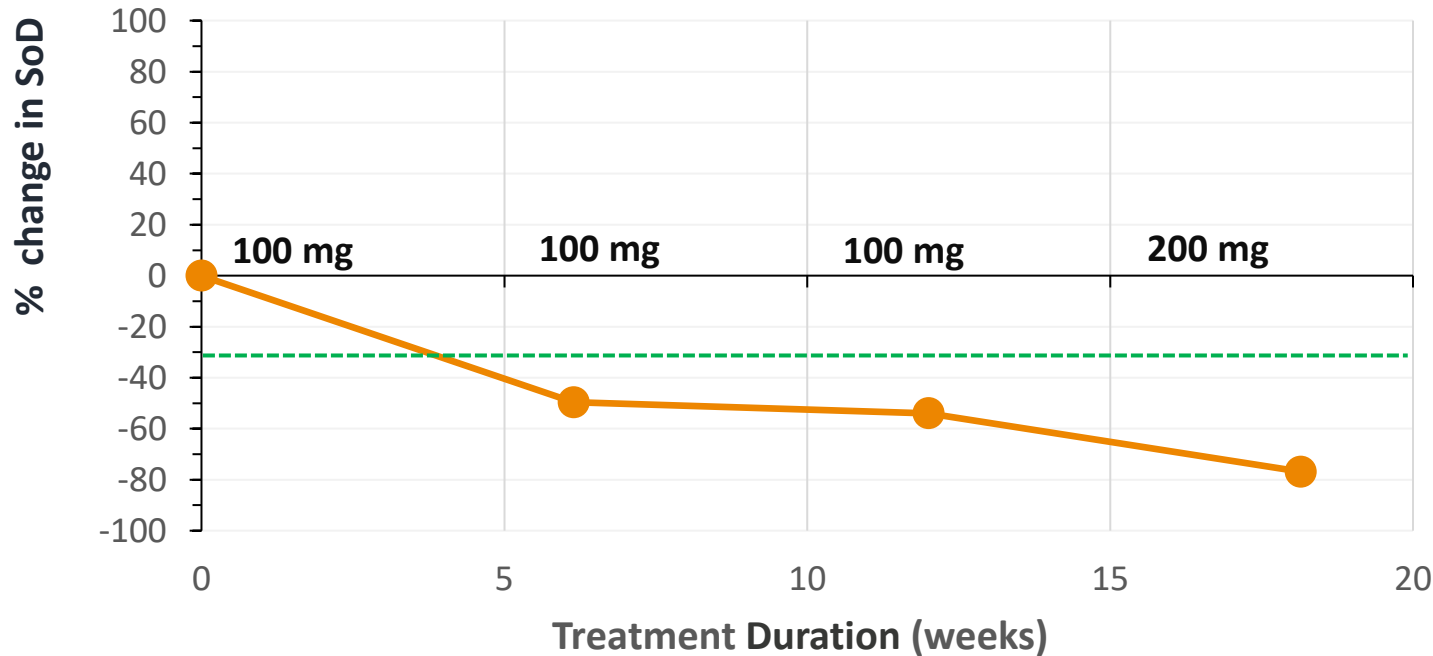
Intrinsic Driver

C797S

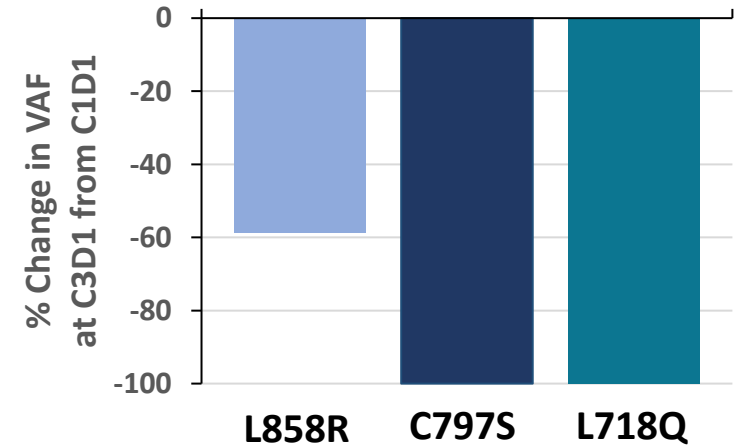
Disease History and Prior Therapies



BDTX-1535 Treatment



Changes in ctDNA VAF



Absence of EGFR C797S and L718Q mutant alleles with concomitant decrease in L858R VAF on C3D1

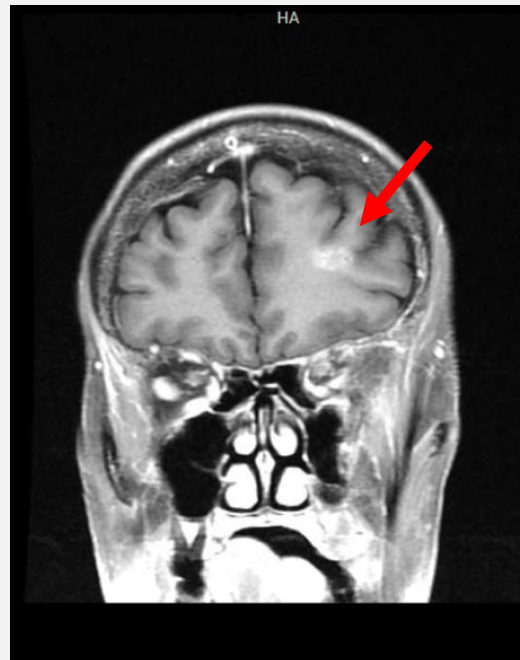
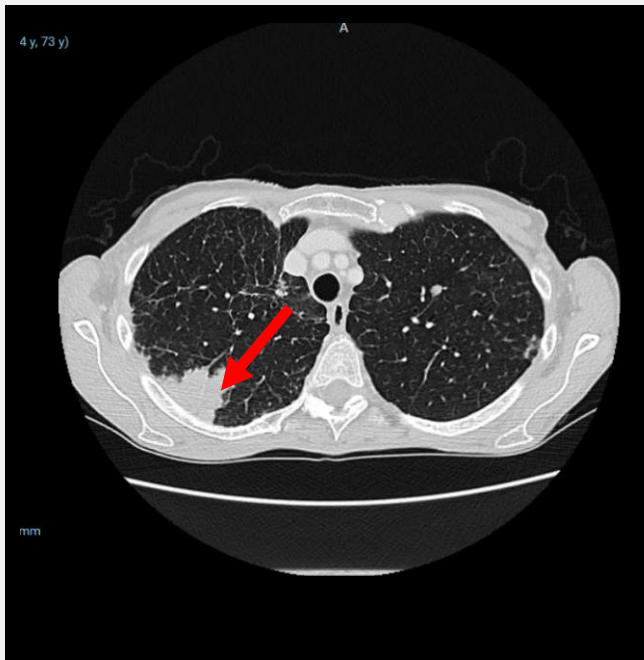
Confirmed PR by RECIST1.1 in NSCLC Patient with EGFR L858R + L718Q + C797S Complex Mutation

Classical Driver
L858R

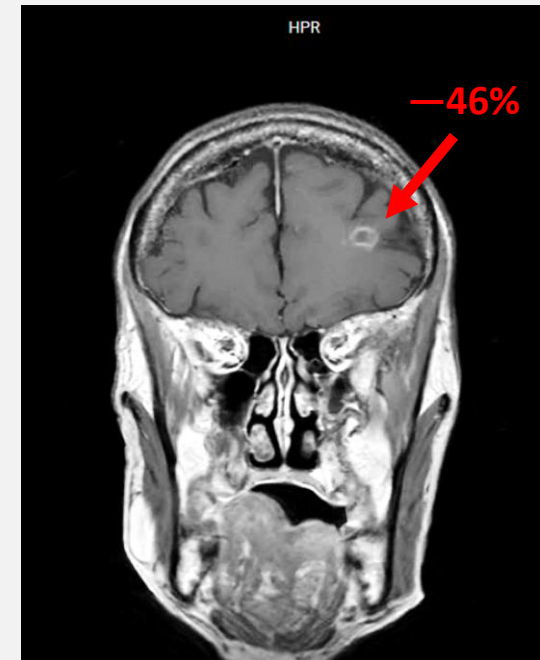
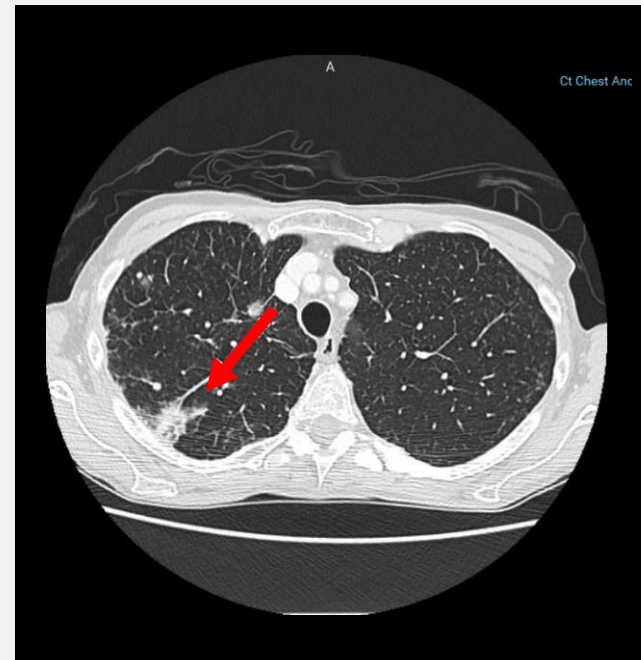
Intrinsic Driver

C797S

Baseline: SEP 2022



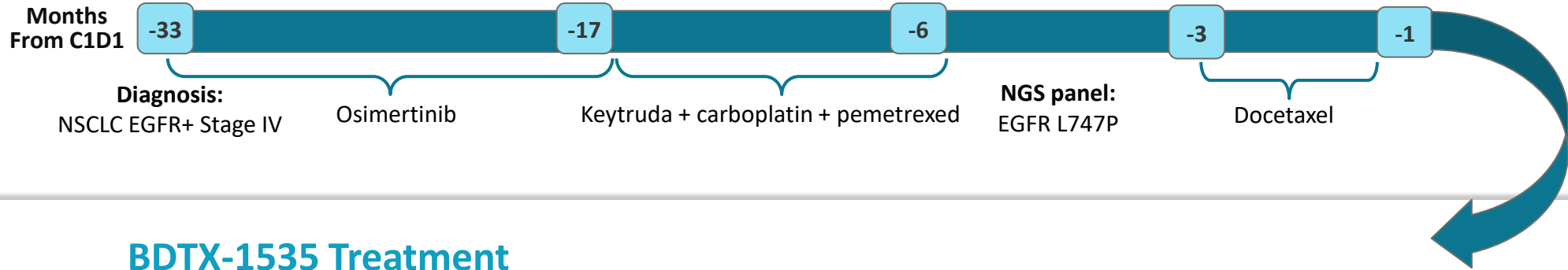
February 21, 2023



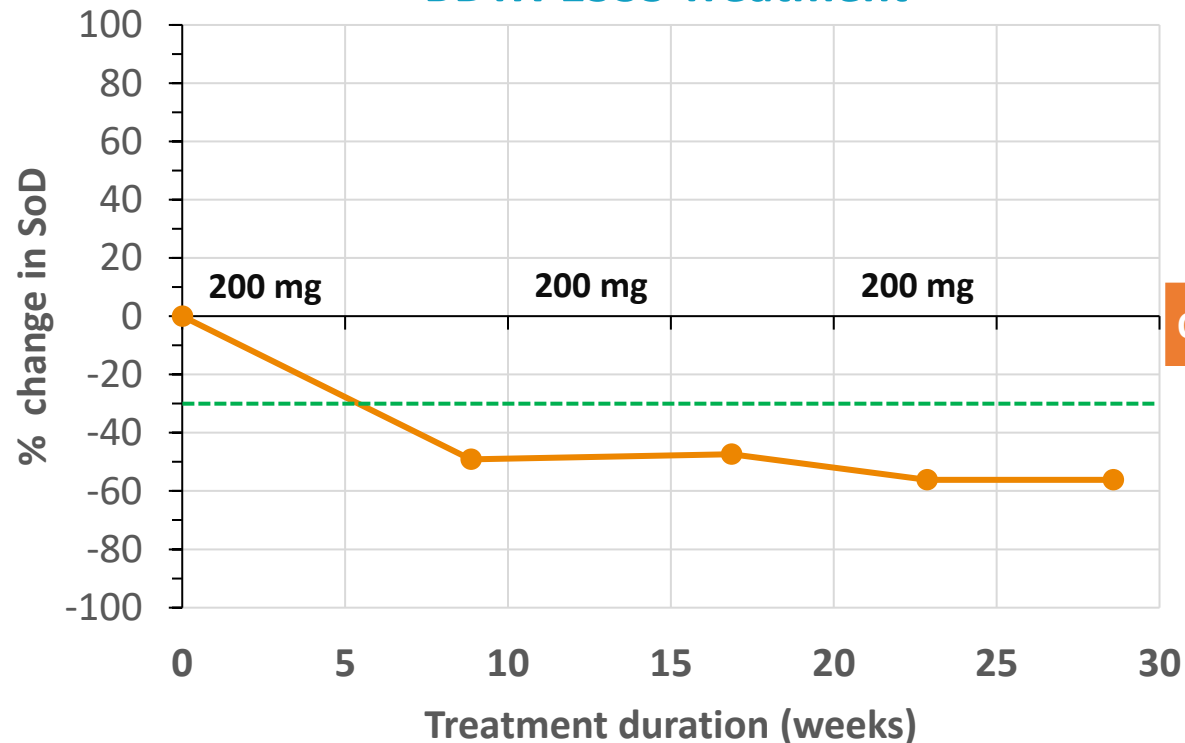
Confirmed PR by RECIST1.1 in NSCLC Patient with EGFR L747P Intrinsic Driver Mutation

Intrinsic Driver

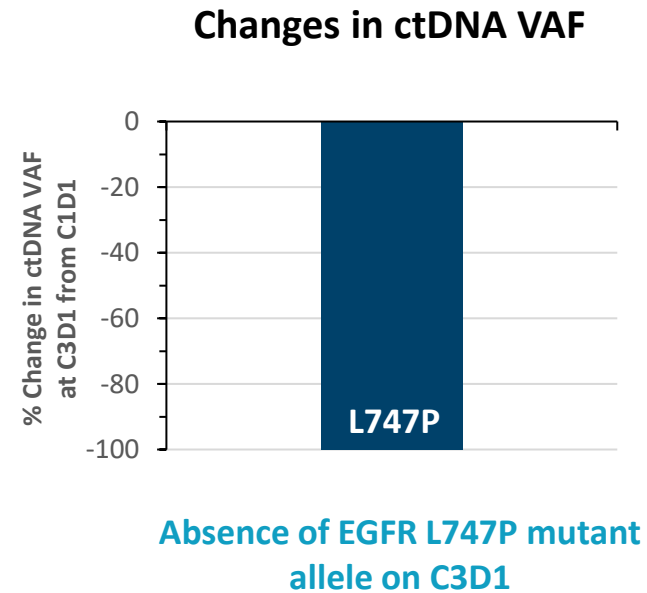
Disease History and Prior Therapies



BDTX-1535 Treatment



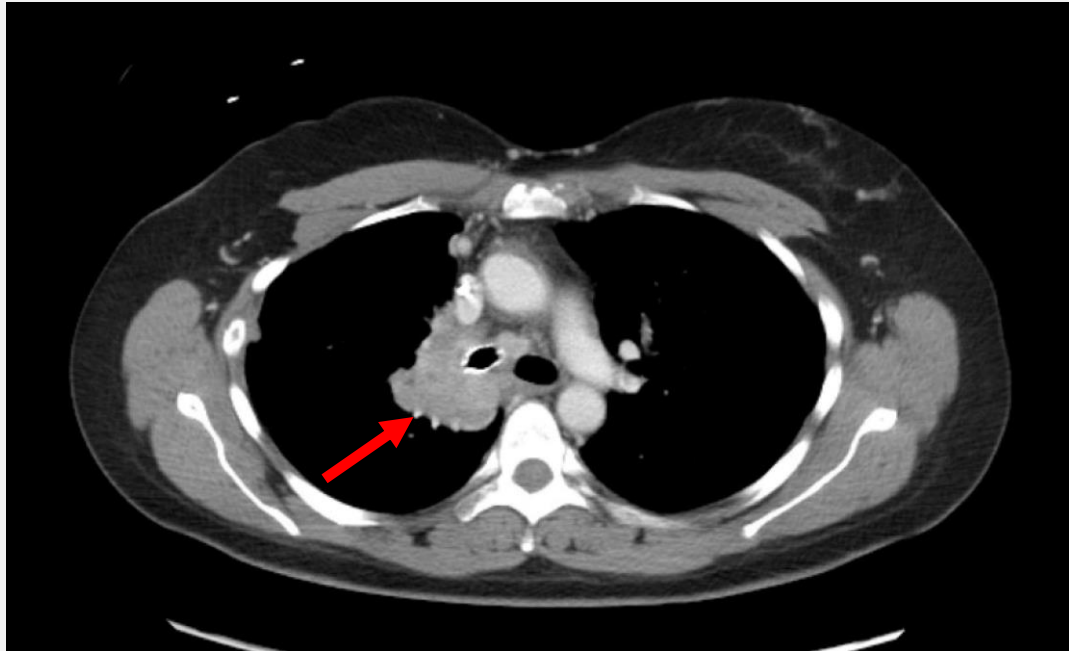
On therapy



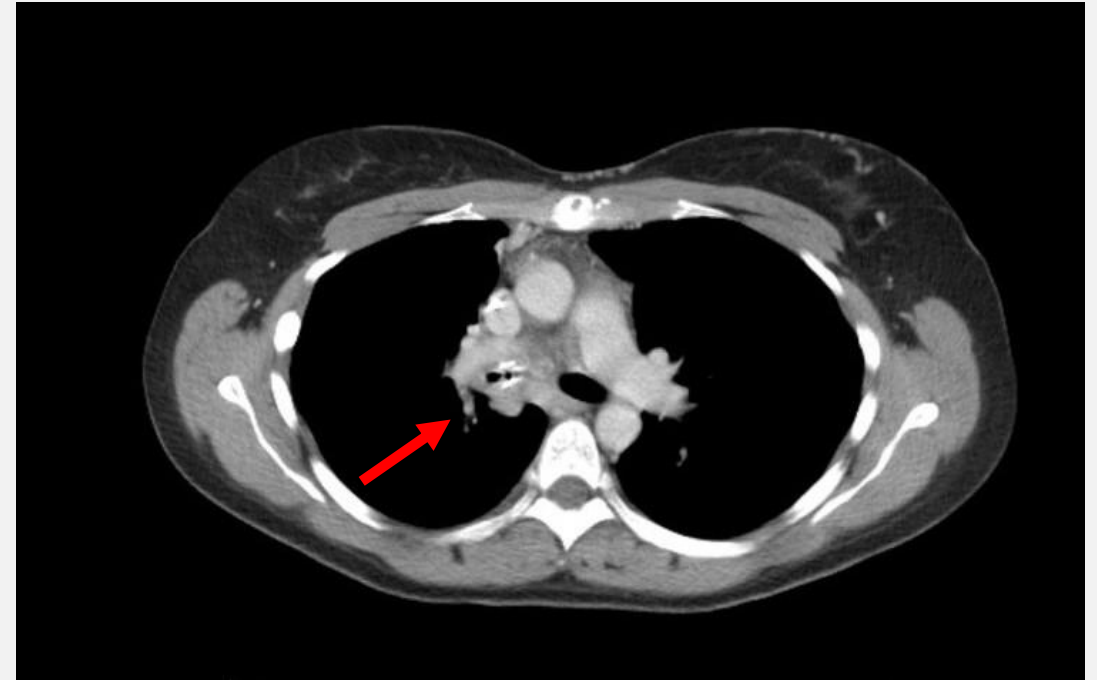
Confirmed PR by RECIST1.1 in NSCLC Patient with EGFR L747P Intrinsic Driver Mutation

Intrinsic Driver

Baseline: Oct 2022



May, 2023

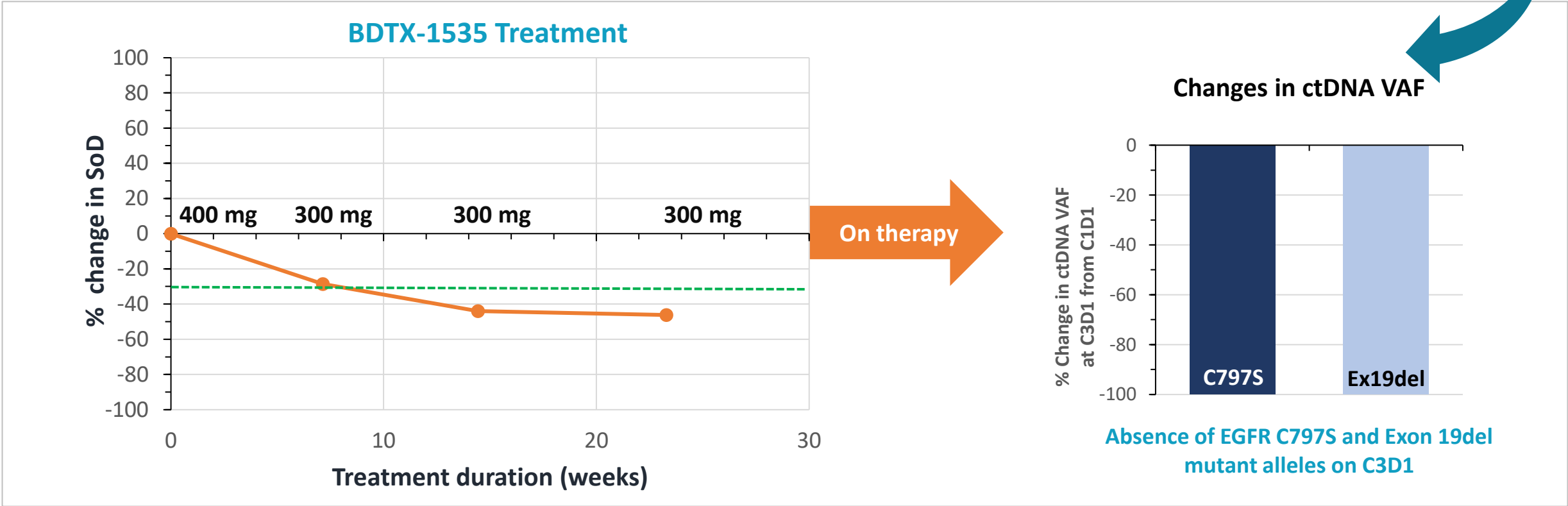
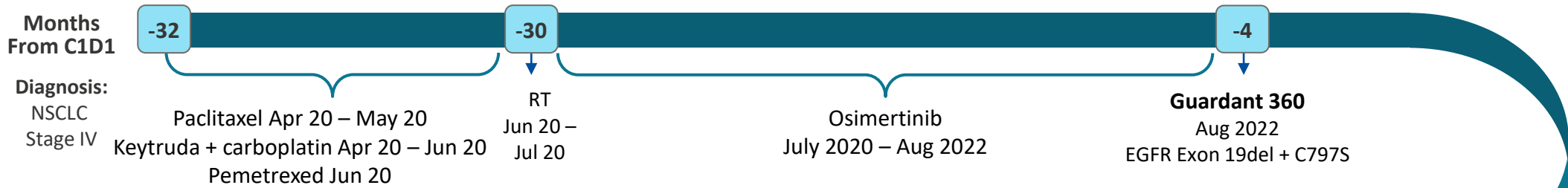


Confirmed PR by RECIST1.1 in NSCLC Patients With EGFR Exon 19del + C797S Acquired Resistance Mutation

Classical Driver
Del19

C797S

Disease History and Prior Therapies



Confirmed PR by RECIST1.1 in NSCLC Patient With EGFR Exon 19del + C797S Acquired Resistance Mutation

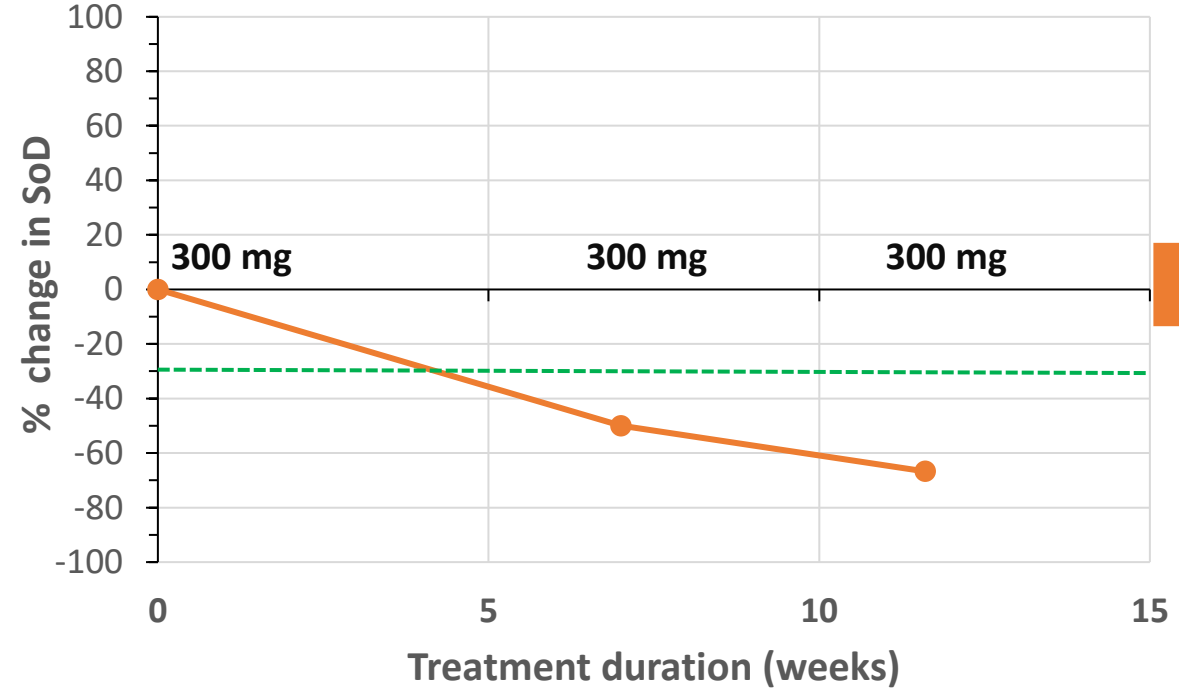
Classical Driver
Del19

C797S

Disease History and Prior Therapies



BDTX-1535 Treatment



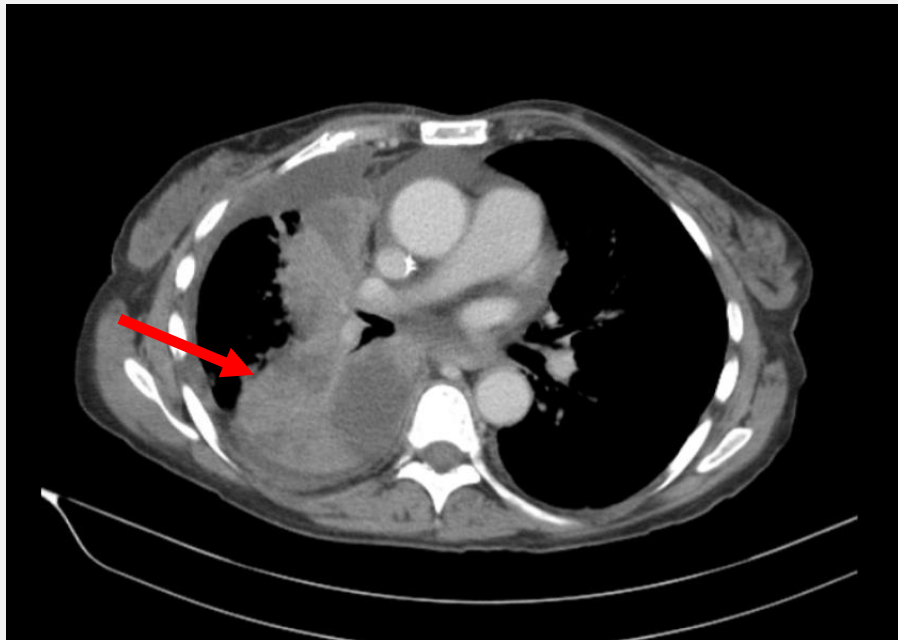
Pending ctDNA VAF analysis

Confirmed PR by RECIST1.1 in NSCLC Patient With EGFR Exon 19del + C797S Acquired Resistance Mutation

Classical Driver
Del19

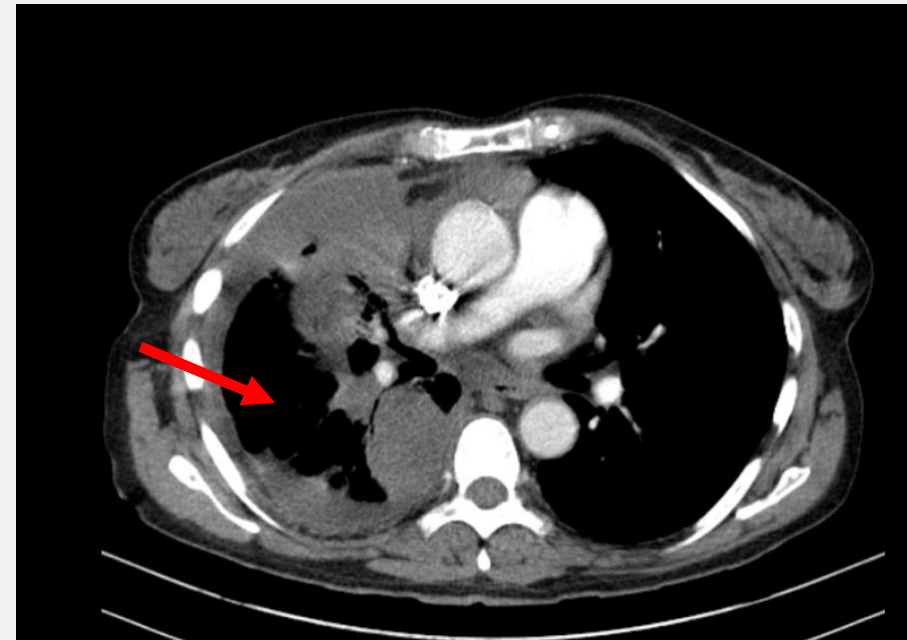
C797S

Baseline: Feb 20, 2023



On oxygen

APR 10, 2023



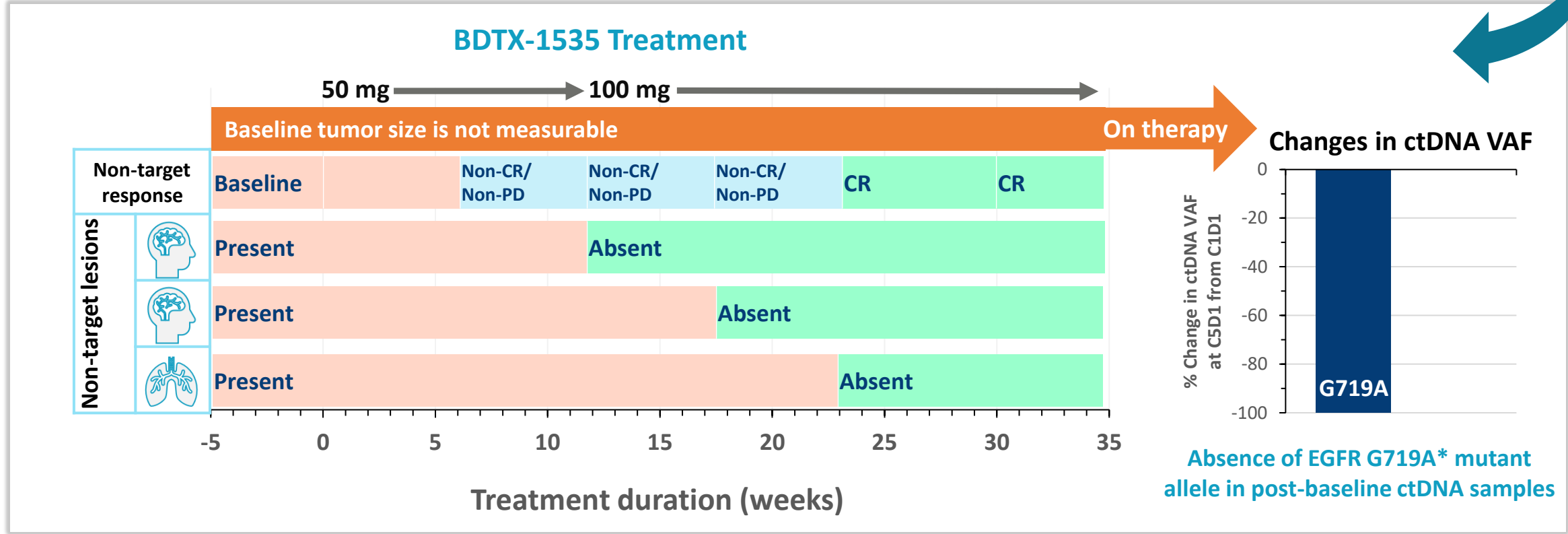
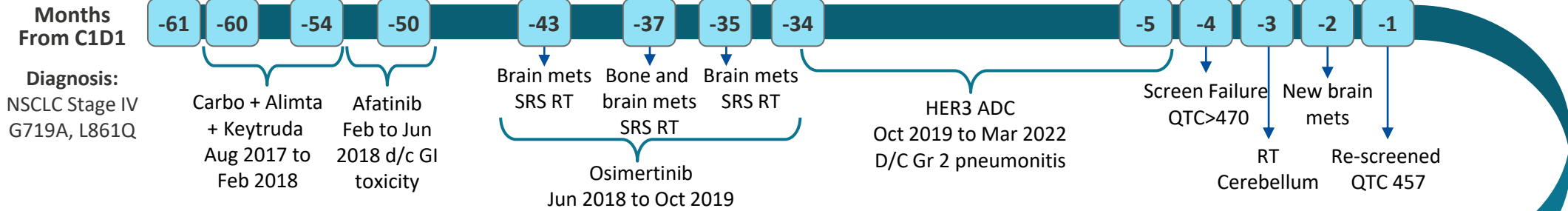
Off oxygen and able to travel to France

Clinical Benefit in NSCLC Patient With Non-Measurable Disease EGFR G719A + L861Q Complex Mutation

Intrinsic Driver

Intrinsic Driver

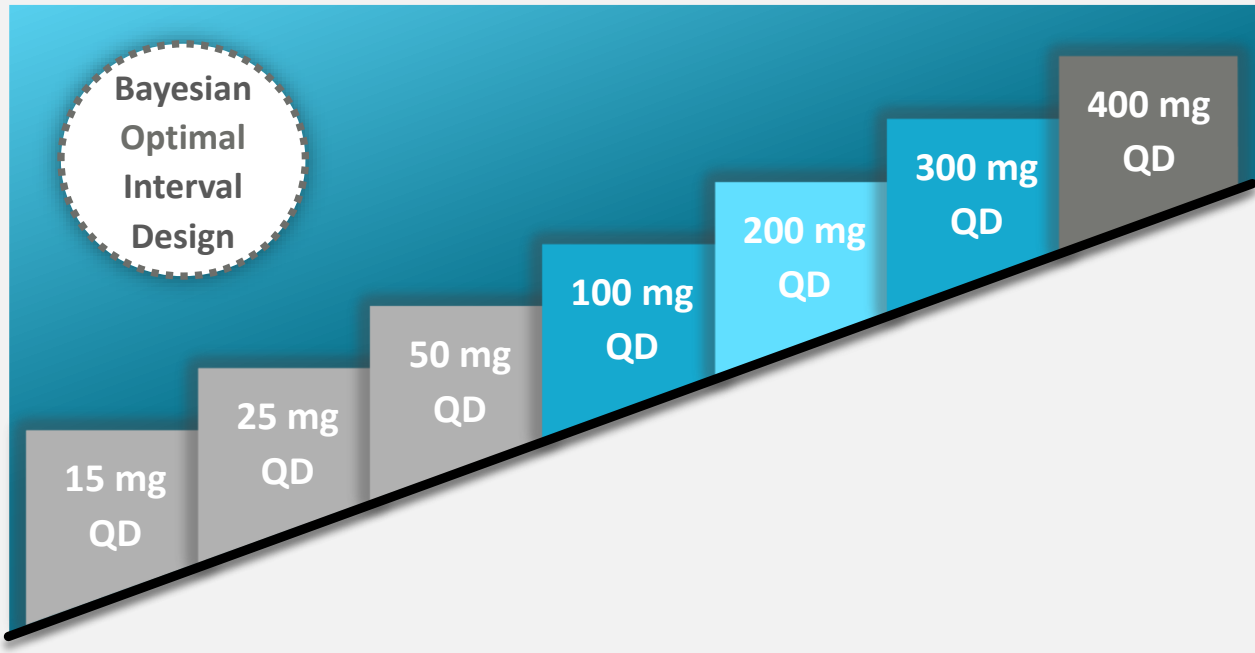
Disease History and Prior Therapies



BDTX-1535 200 mg QD Dose to be Evaluated for ORR in Expansion Cohorts To Support Path To Approval in NSCLC

Dose Escalation

Patients: measurable and non-measurable disease
Primary objective: safety and PK



Expansion Cohorts

NSCLC Patients: measurable disease only, ≤ 2 prior therapies
Primary objective: ORR by RECIST1.1

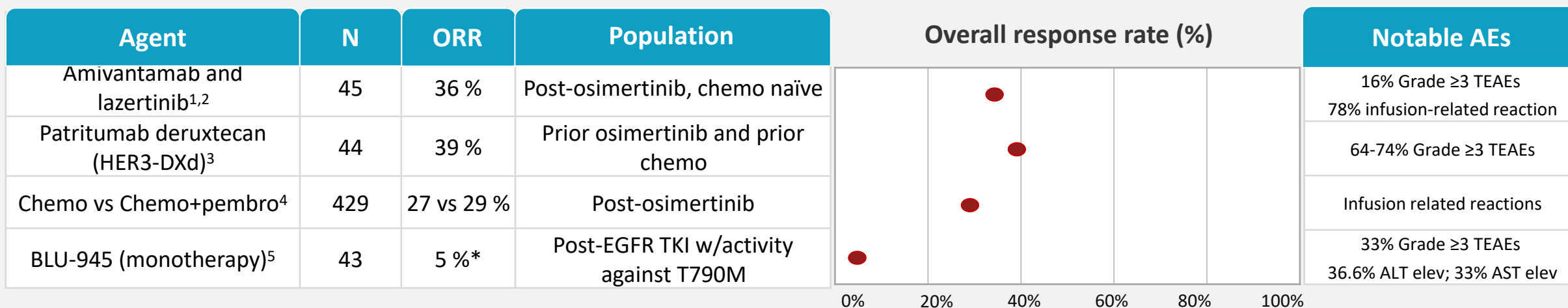
2L NSCLC with acquired EGFR resistance mutations +/- CNS metastasis

2L NSCLC with EGFR intrinsic driver mutations +/- CNS metastasis

1L NSCLC with EGFR intrinsic driver mutations +/- CNS metastasis
(after discussion with the FDA)

- The protocol allows for evaluation of additional doses in expansion cohorts
- Recommended phase 2 dose will be selected after data review with the FDA (FDA Project Optimus)
- Selection of dose(s) for expansion cohorts is based on optimal exposure response analysis of safety, ctDNA and target lesion reduction
- Primary endpoint of ORR by RECIST1.1 is an acceptable (FDA) efficacy surrogate endpoint in NSCLC

Competitor Data in Patients with Prior 3rd Generation EGFR TKI



Note: These data are derived from different clinical trials with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

*2 confirmed responses out of 42 patients from interim DE data presented

1. Bauml, ASCO 2021; 2. JNJ Press Release, 2021; 3. Janne, ASCO Cancer Discovery 2022; 4. Keynote-789, ASCO2023; 5. Elamin et. al., ASCO 2023

Key Anticipated BDTX-1535 Milestones

NSCLC

- Initiate BDTX-1535 dose expansion in 2L NSCLC with ORR as primary endpoint, 2H 2023
 - Initiation of dose expansion cohort in newly diagnosed patients with intrinsic driver mutations
- Alignment with FDA on dosing strategy for pivotal study (EOP1 meeting), Q4 2023
- Present BDTX-1535 dose escalation data in NSCLC at a medical conference, Q4 2023
- Update on clinical dose expansion cohorts, 2024

GBM

- Clinical update on BDTX-1535 Phase 1 dose escalation in RR GBM, Q4 2023

CMC

- Complete capsule to tablet transition (potential commercial formulation), Q3 2023



Thank You

Partnership: partnership@bdtx.com

Investors: investors@bdtx.com

Media: media@bdtx.com



BLACK
DIAMOND
THERAPEUTICS