Black Diamond Therapeutics, Inc.

Pioneering the Development of MasterKey Therapies

BLACK DIAMOND THERAPEUTICS

November 2022

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Black Diamond Therapeutics Overview

Black Diamond Therapeutics

Expanding the Reach of Precision Medicine Through the Development of MasterKey Therapies

MasterKey therapies address oncogene mutation families; providing precision oncology medicines to greater numbers of patients with genetically defined tumors

Clinical and late-preclinical pipeline of MasterKey inhibitors derived from our MAP drug discovery engine targeting oncogenic EGFR, RAF, FGFR2/3 and additional undisclosed targets

Our proprietary **MAP drug discovery engine** is designed to:

- Predict and validate novel oncogenic mutant families from population level tumor genomics
- Pioneer mutant family conformation-based MasterKey drug design
- Provide opportunities beyond oncology and small molecules

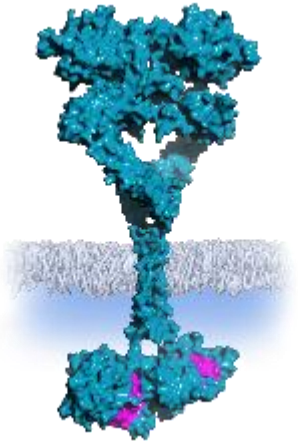
BDTX-1535: a brain-penetrant, mutant selective, irreversible EGFR MasterKey inhibitor, currently in Phase 1 development for treatment of patients with GBM and NSCLC driven by EGFR intrinsic & acquired resistance mutations

BDTX-4933: a brain-penetrant RAF MasterKey inhibitor targeting oncogenic BRAF Class I, II, III and RAS mutations, currently in IND-enabling studies

Black Diamond's MasterKey Approach Designed to Address Overlooked Mutation Families

Classic/Current Approach:

Targeting active site kinase domain mutations



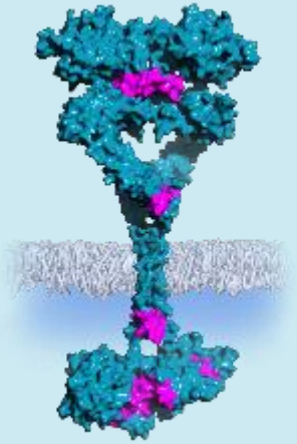
Targeting single mutations in individual tumor types

With expanding genetic profiling of cancer patients via Next Generation Sequencing (NGS)

Less than 15% patients[1] with metastatic cancer eligible for approved precision oncology medicines

Black Diamond Approach:

Targeting mutation families to expand the opportunity for precision oncology



Mutation families yield significant market opportunities for populations lacking suitable precision therapies

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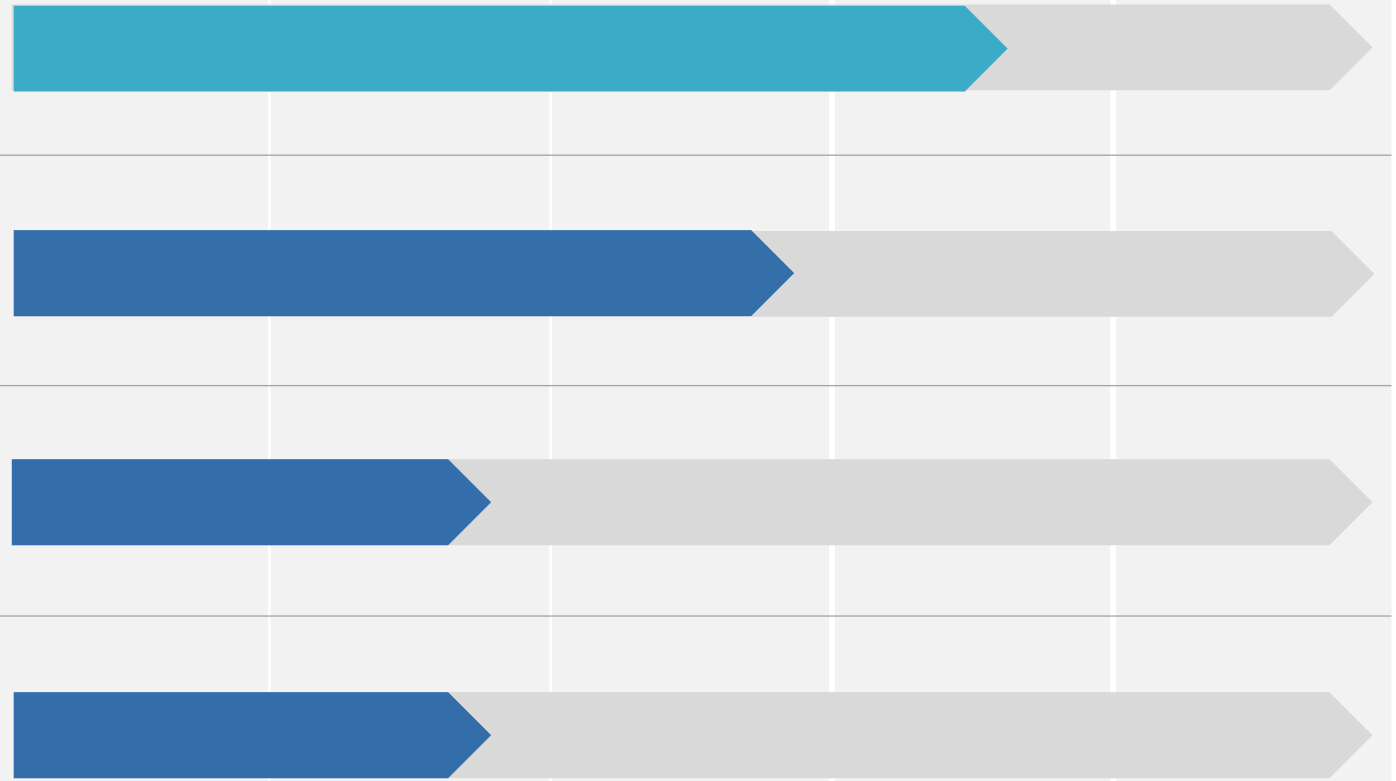
[1] Haslam, A., et al. Annals Oncology Vol 32, Issue 7, p926-932; July 2021

Wholly-Owned Novel MasterKey Precision Medicines

Target	Drug Candidate	Indication	Discovery	Optimization	IND-Enabling	Phase 1	Phase 2/3
EGFR	**BDTX-1535**	EGFR-driven GBM & NSCLC ± CNS mets					
BRAF	**BDTX-4933**	BRAF-driven solid tumors ± CNS mets					
FGFR	**Undisclosed**	FGFR3-driven solid tumors					
Un-disclosed	**Undisclosed**	Solid tumors					



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BDTX-1535

Brain-Penetrant Inhibitor of GBM and NSCLC MasterKey EGFR Mutations

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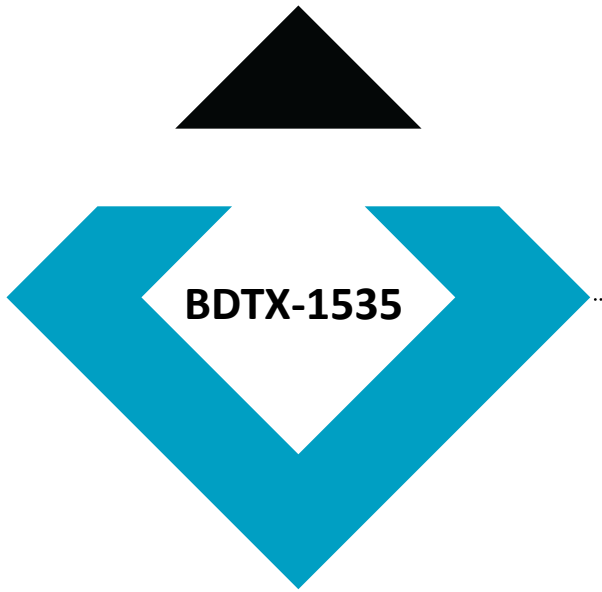
BDTX-1535: Oral, Brain Penetrant, Selective Inhibitor of Oncogenic EGFR MasterKey Mutations



Irreversible	**Designed to treat patients harboring EGFR oncogenic MasterKey mutations**
Brain Penetrant	**Designed to be brain penetrant to treat CNS tumors**
Selective	**Designed with selectivity versus WT-EGFR to deliver favorable safety profile**
Clinical Stage	**Phase 1 study in patients with either GBM or NSCLC, with and without CNS tumors**

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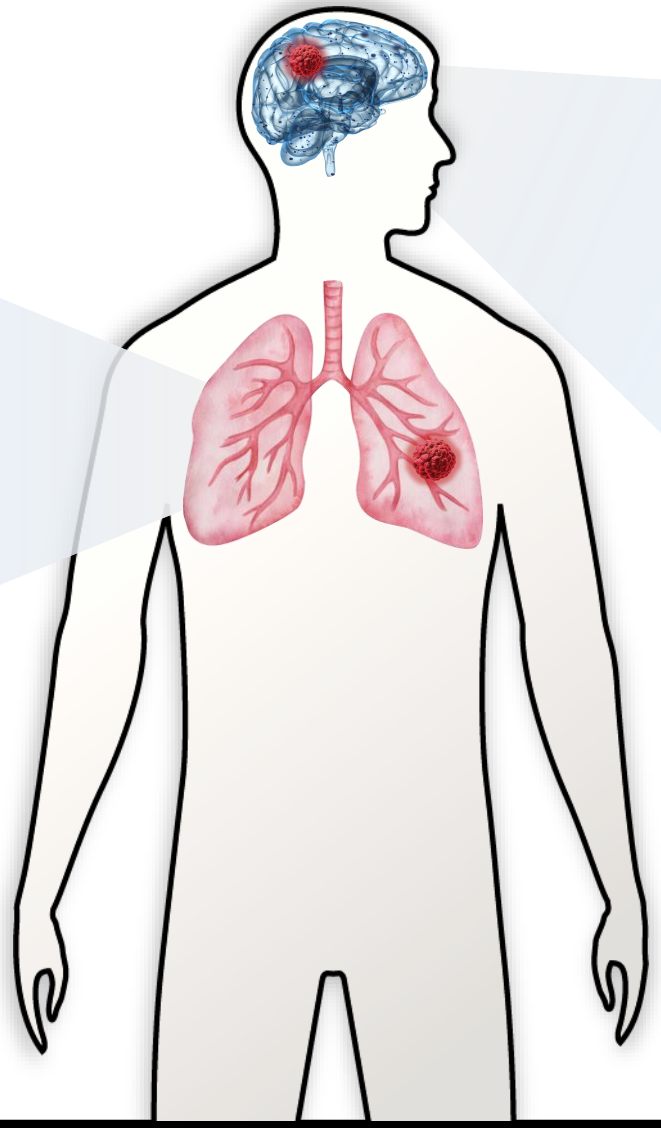
CNS=Central Nervous System; WT=Wild-Type; GBM=Glioblastoma Multiforme; NSCLC=Non-Small Cell Lung Cancer

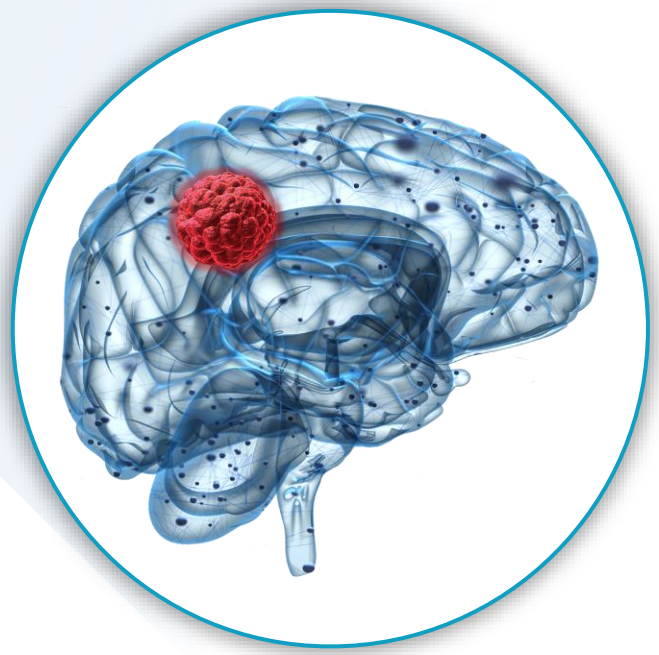
BDTX-1535 is a Novel 4th Generation EGFR MasterKey Inhibitor Positioned to Address Unmet Needs in NSCLC and GBM

EGFR Mutant Non-Small Cell Lung Cancer

- Potent across 3rd gen resistance mutations
- Covalent inhibition mechanism
- Wild type EGFR (WT-EGFR) sparing



EGFR Altered Glioblastoma



- Potent inhibition across GBM alterations
- Overcomes EGFR tumor heterogeneity
- Prevents paradoxical activation of EGFR
- Brain penetration by design

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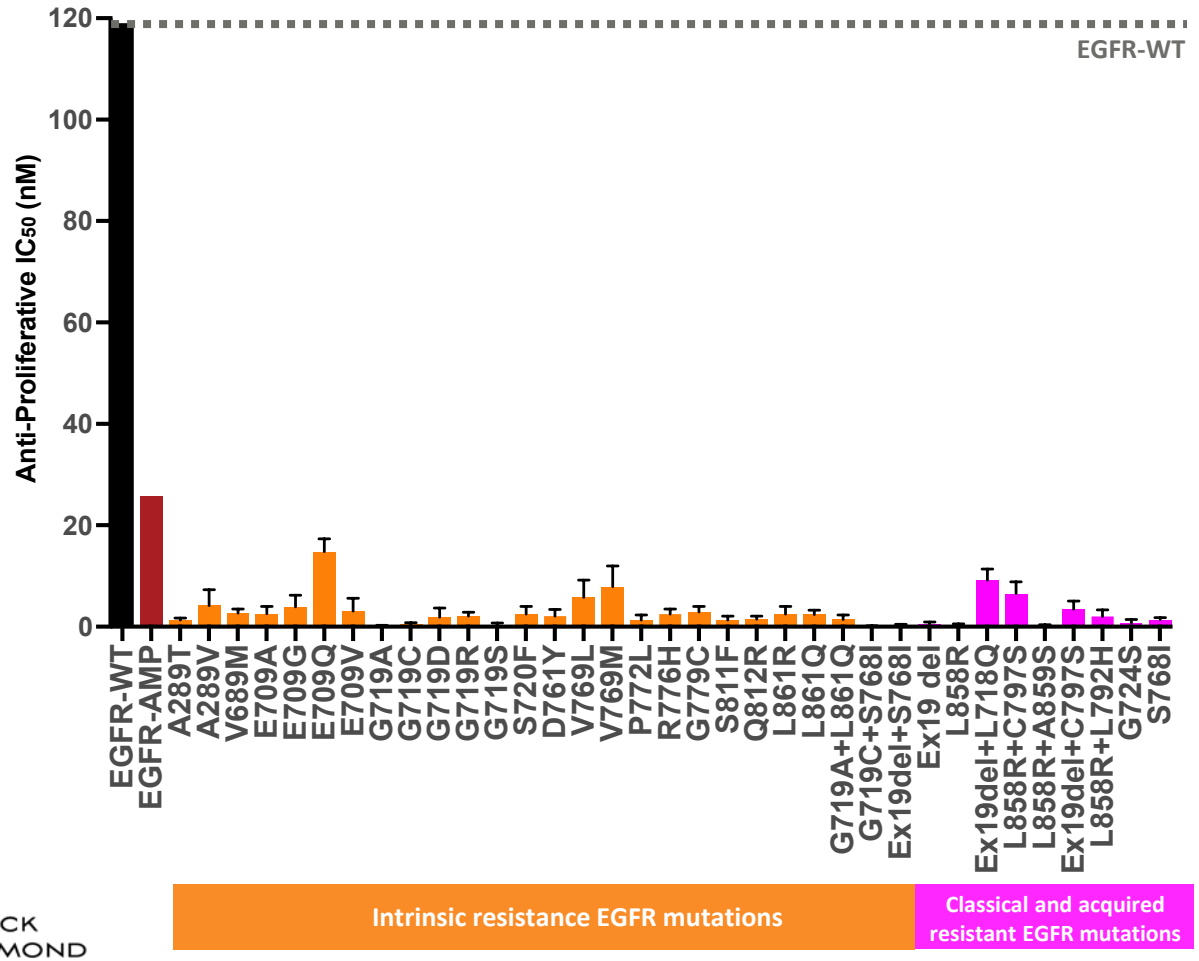
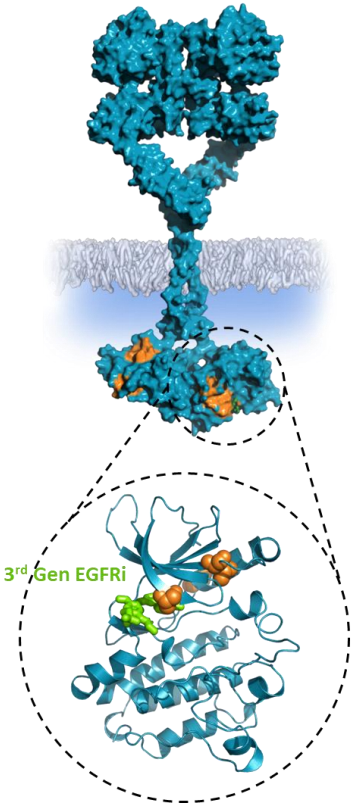
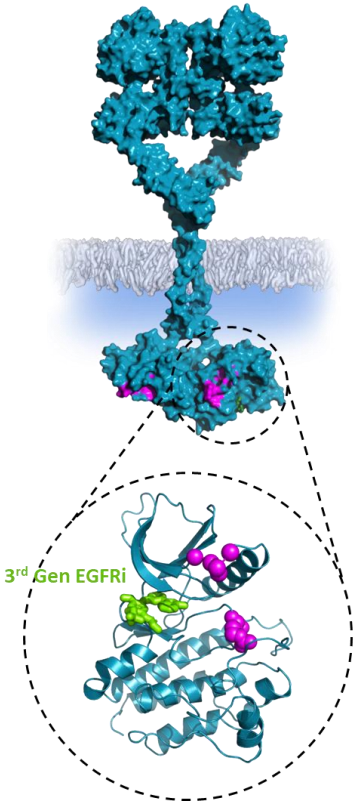
MasterKey Profile Potently Inhibits Broad Family of Oncogenic Mutations in NSCLC While Sparing Wild-Type EGFR (EGFR-WT)

Preclinically BDTX-1535 is highly potent against classical, intrinsic and acquired resistance EGFR mutations





Intrinsic Resistance EGFR Mutations



Classical & Acquired Resistance EGFR Mutations

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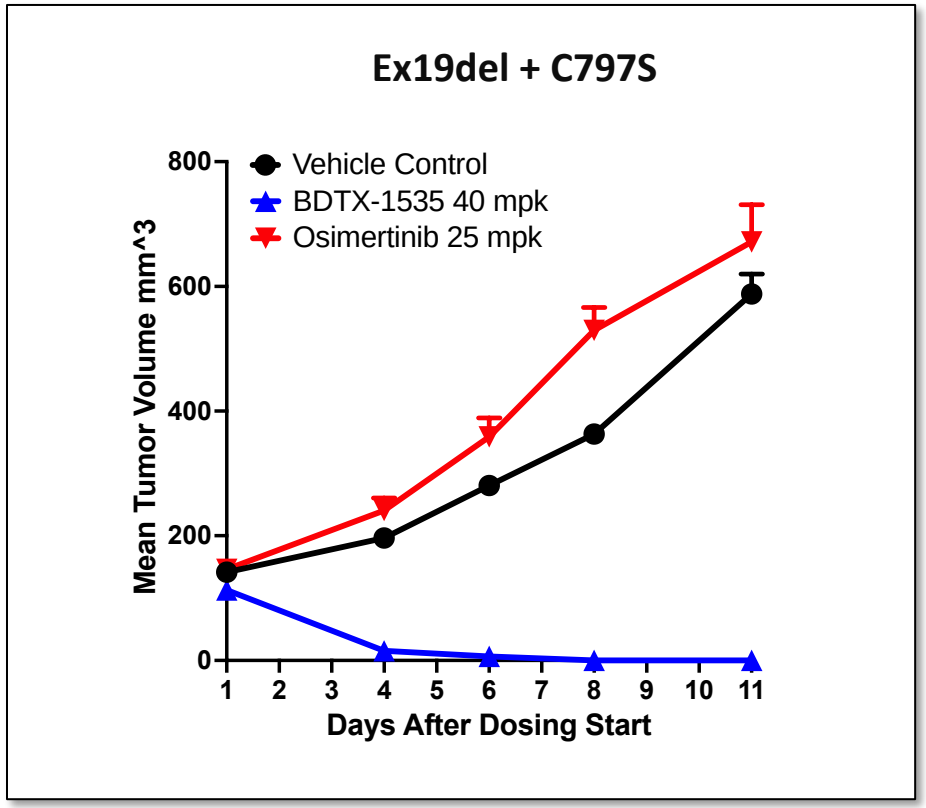
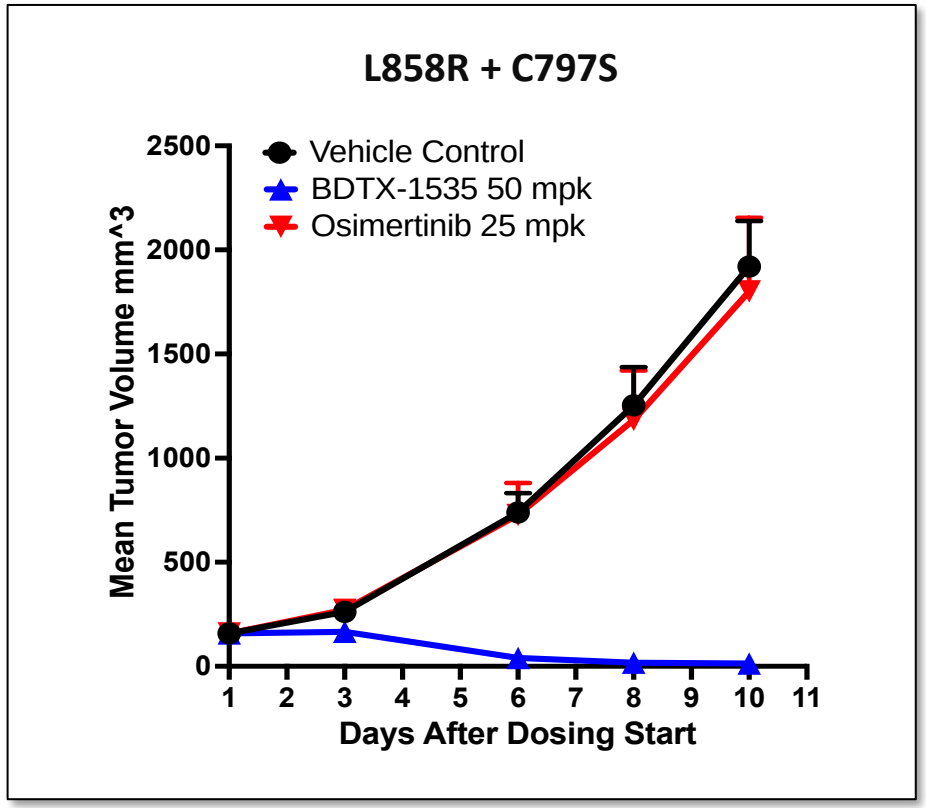
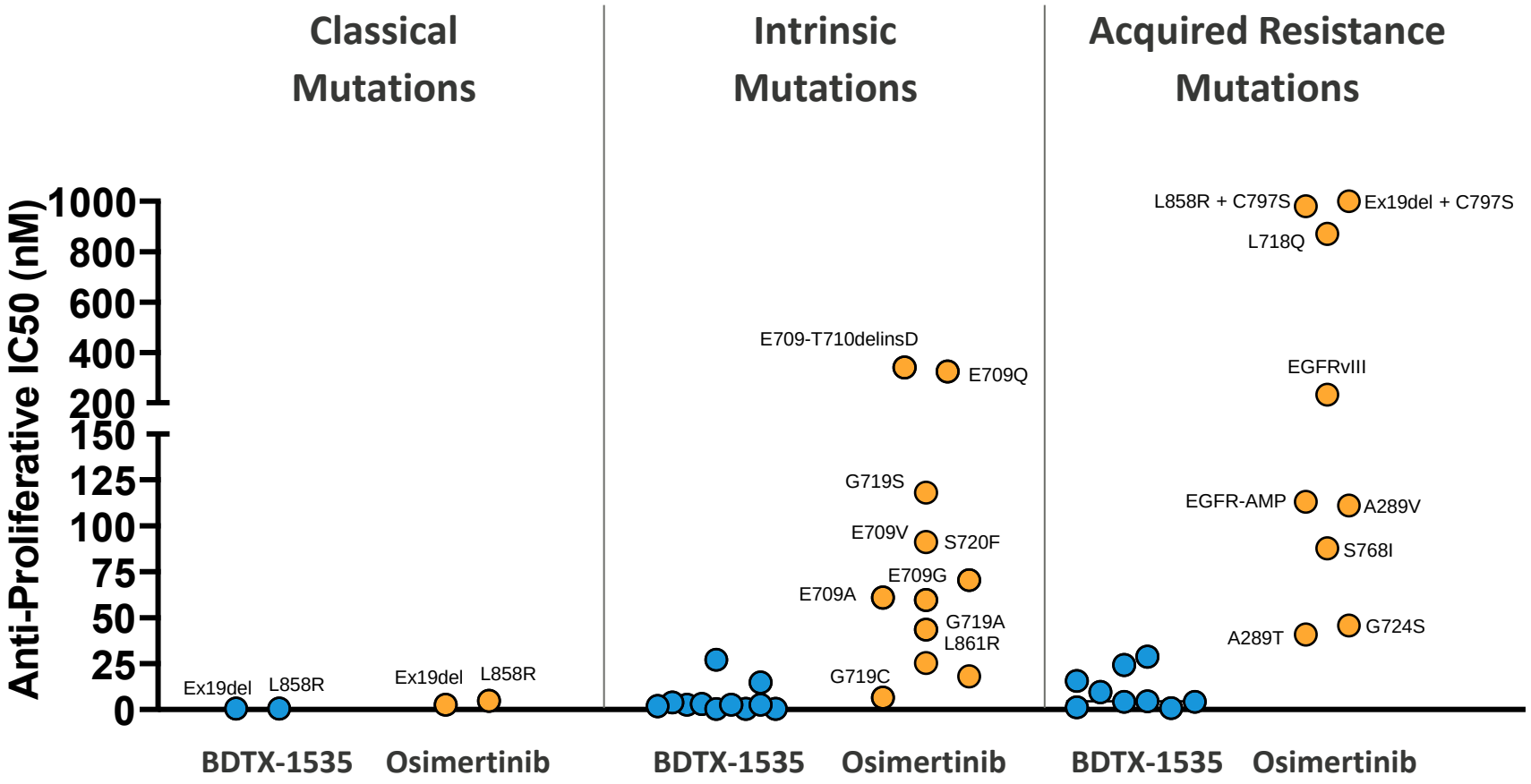
BDTX-1535 Achieves Tumor Regression in Osimertinib Resistant Models

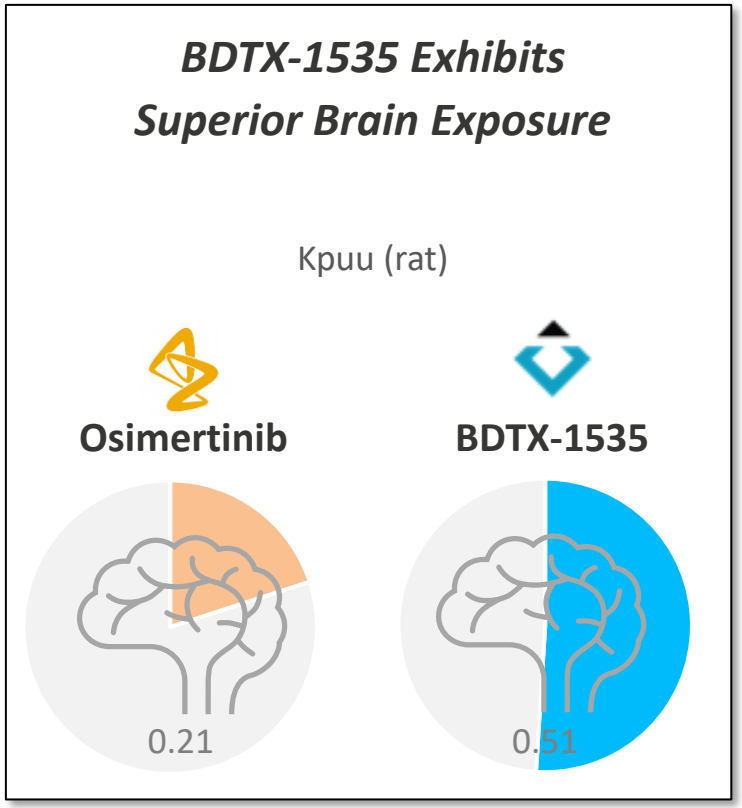
Potent, Irreversible Activity Across Exon19 deletion and L858R Primary and C797S Resistance Mutations





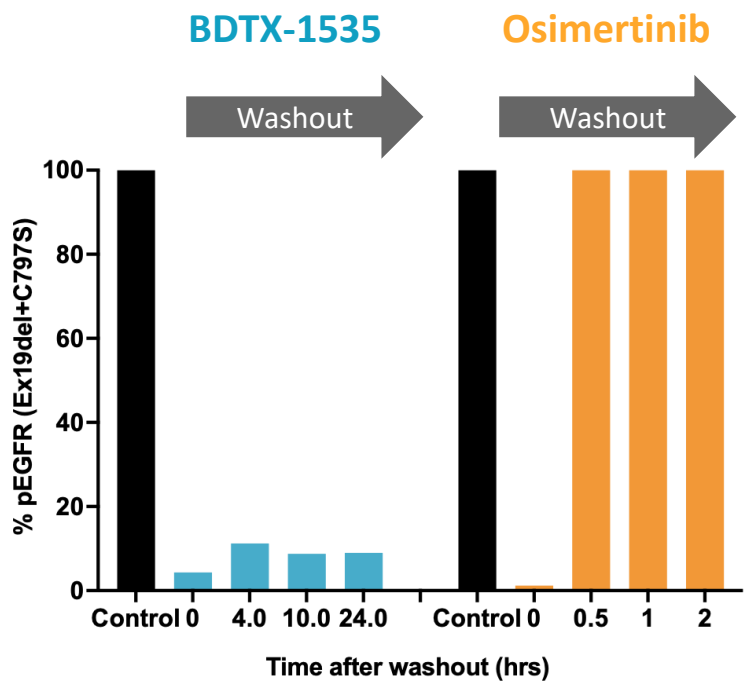
BDTX-1535 Potently Inhibits Classical and Resistance Mutations Preclinically Compared to Osimertinib



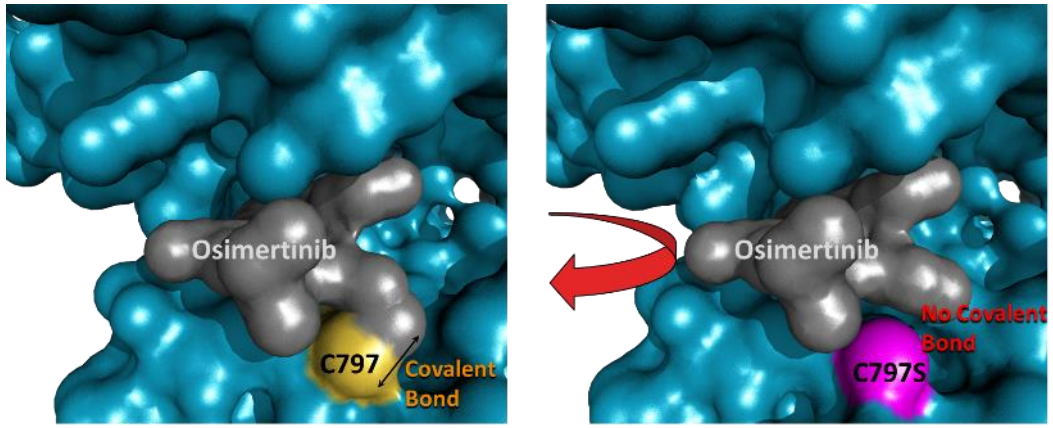


BDTX-1535 Is a Covalent Inhibitor of EGFR Resistance Mutations

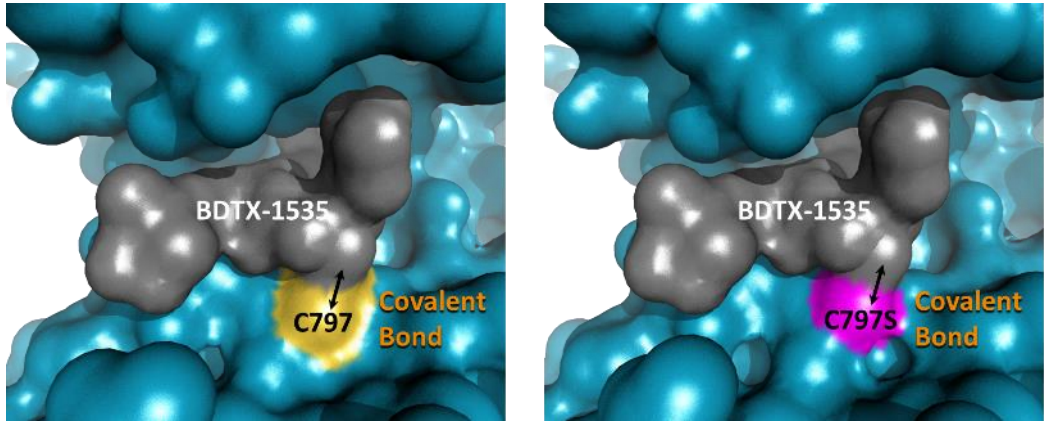
BDTX-1535 retains pEGFR shutdown after washout in preclinical C797S mutant study



Osimertinib Covalently Binds to C797 but not C797S



BDTX-1535 Covalently Binds to both C797 and C797S



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Next Generation In Wild Type Sparing, Irreversible EGFR TKIs
BDTX-1535 Is a Novel 4th-Generation Covalent EGFR MasterKey Inhibitor

Reversible

Tarceva® erlotinib

IRESSA® gefitinib

First Generation

Covalent

GILOTRIF® (afatinib) tablets

VIZIMPRO® DACOMITINIB

Second Generation

Covalent

TAGRISSO® osimertinib

Aumolertinib[1]

Furmonertinib[2]

Third Generation

Covalent

BDTX-1535

Fourth Generation (Investigational)

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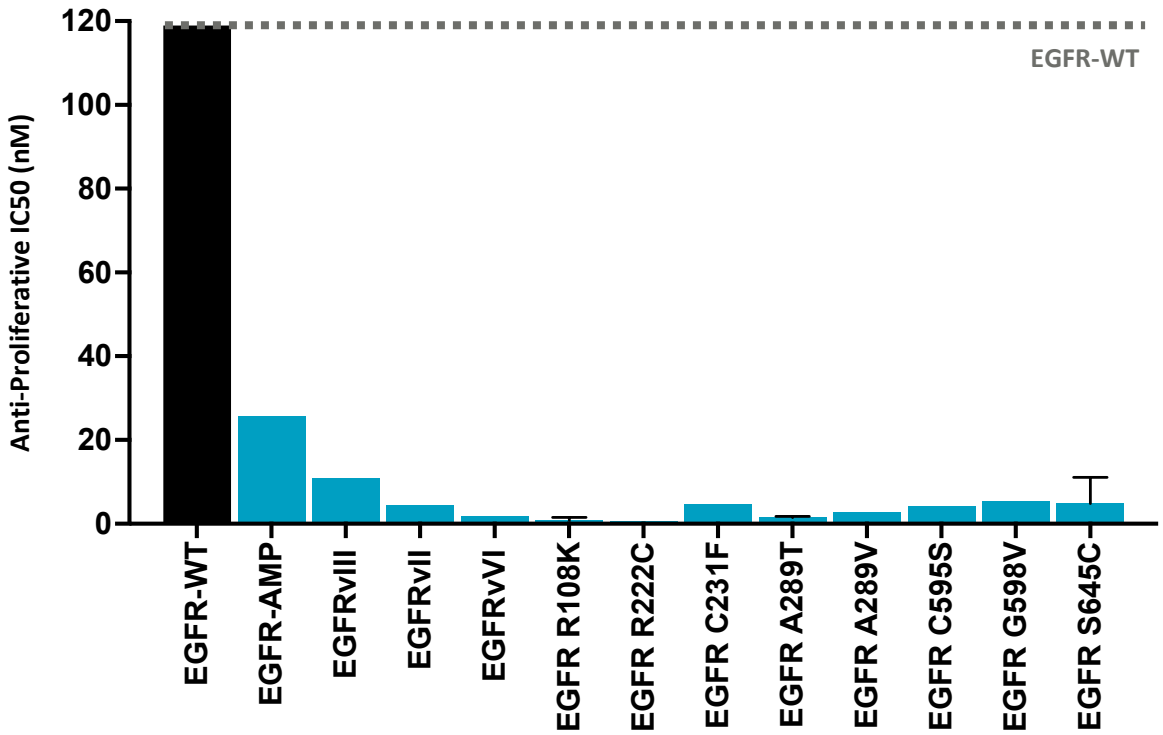
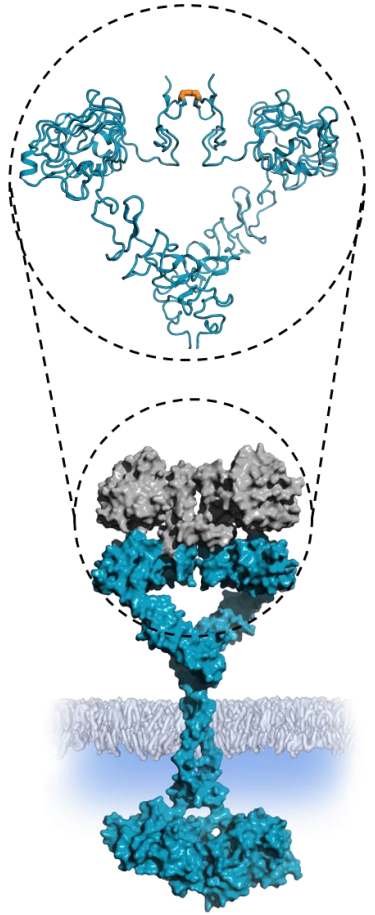
[1] Ameile® approved in People's Republic of China for 2L EGFRmut NSCLC with T790M mutation (formerly known as almonertinib)
[2] Ivesa® approved in People's Republic of China for 2L EGFRmut NSCLC with T790M mutation

MasterKey Profile Potently Inhibits Broad Family of Oncogenic Alterations in GBM While Sparing EGFR-WT

BDTX-1535 potently inhibits extra-cellular domain oncogenic EGFR alterations and amplification in preclinical studies



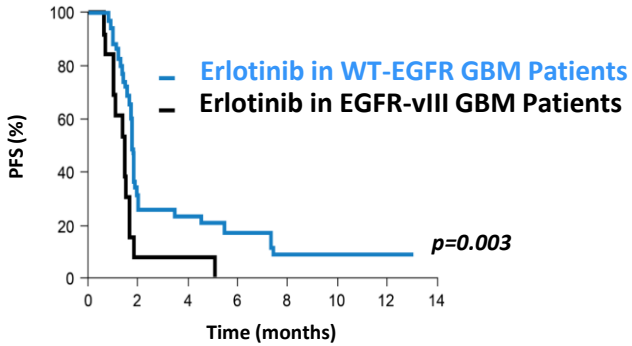
Extracellular Domain Mutations and Alterations in Glioblastoma

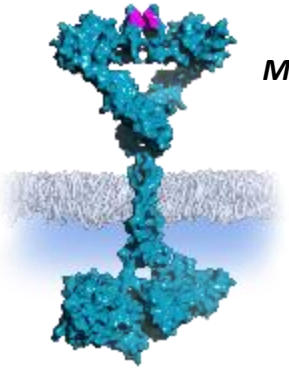


Reversible EGFR Inhibitors Show Potentially Detrimental Pharmacology in EGFR Driven GBM

Current EGFR TKIs Do Not Extend PFS in Patients with GBM Mutations

GBM Trial[1]

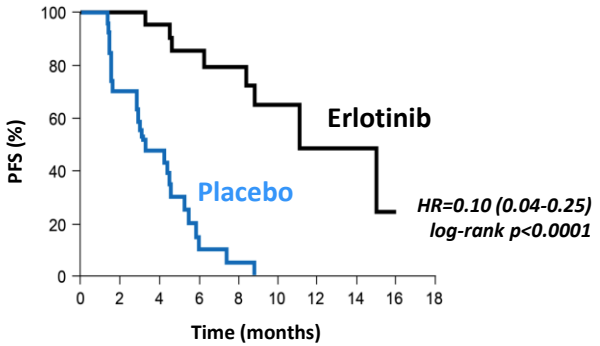


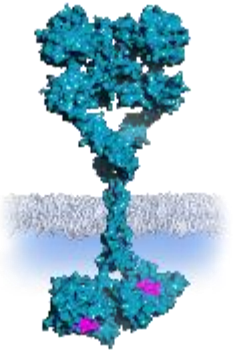


GBM Mutations

EGFR TKIs Extend PFS in Patients with Kinase Domain Mutations

NSCLC Trial[2]





Kinase Domain Mutations

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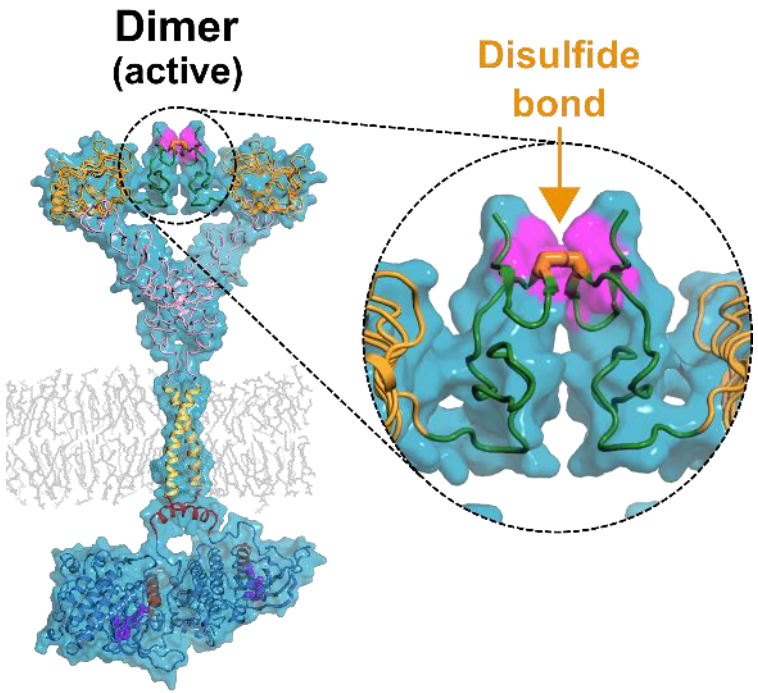
[1] Van den Bent et al JCO 2009
[2] Capuzzo et al Lancet 2010

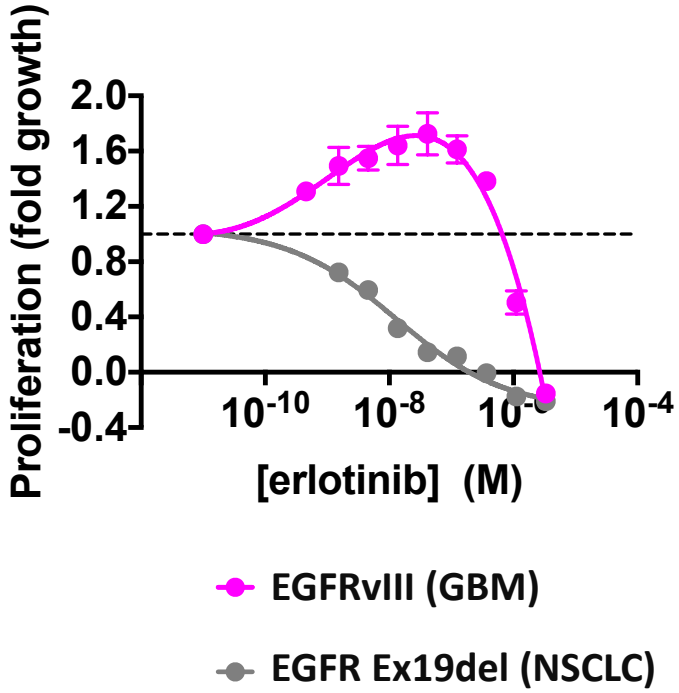
TKIs=Tyrosine Kinase Inhibitors.

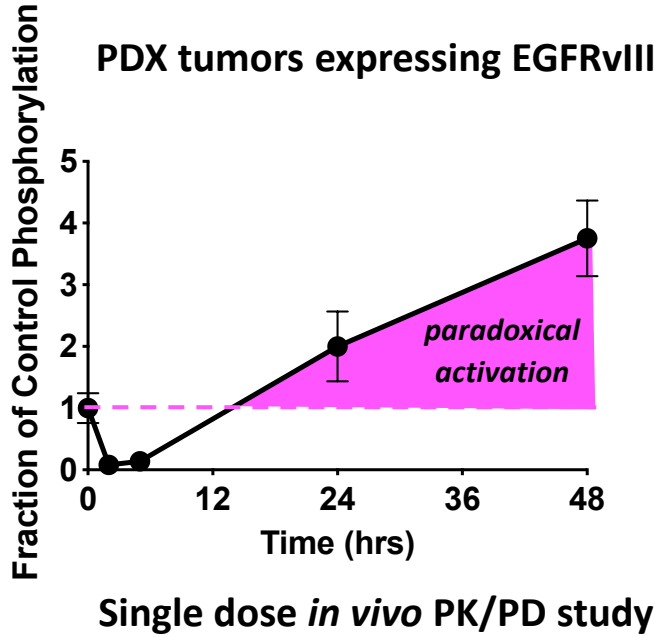
Black Diamond Revealed the Potential for Unwanted Paradoxical Activation of GBM Mutations by Reversible EGFR TKIs

The oncogenic conformation of mutant EGFR in GBM is a locked dimer



Reversible TKIs can stimulate the activity of mutant EGFR in GBM in preclinical models





Single dose *in vivo* PK/PD study

Inhibitors against EGFR mutants in GBM should be potent, selective & *irreversible* to avoid paradoxical activation

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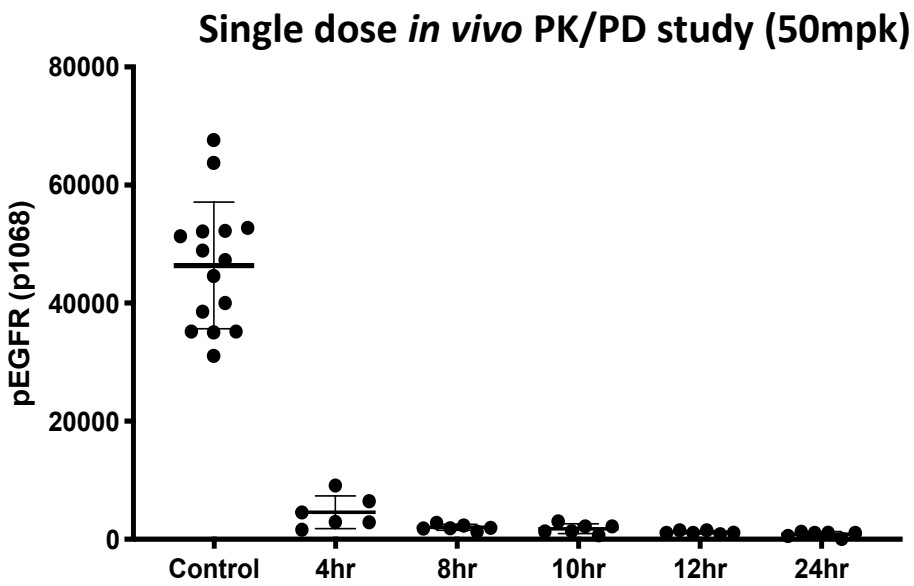
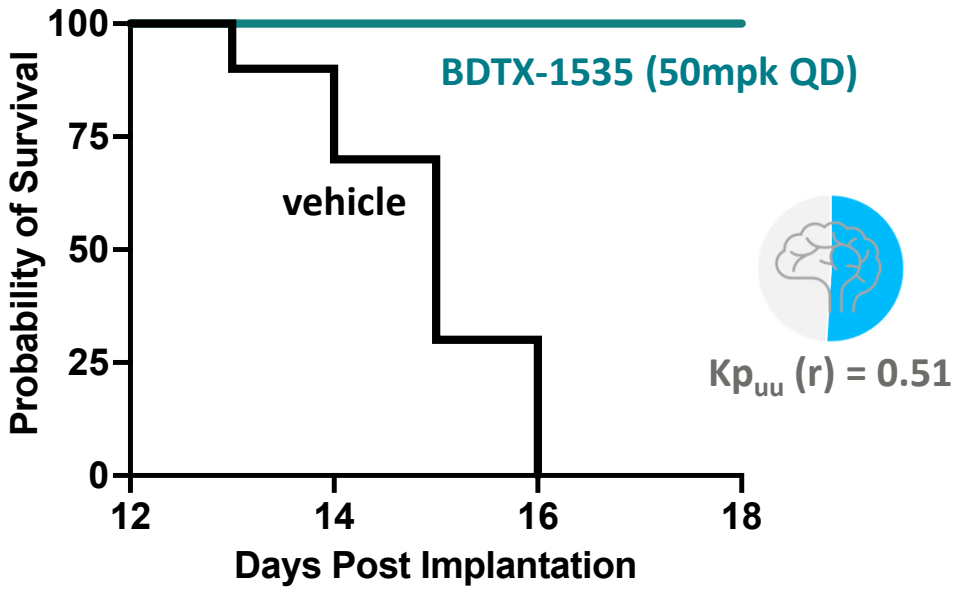
PK=Pharmacokinetics; PD=Pharmacodynamics; PDX=Patient-Derived Xenografts

BDTX-1535 Addresses Unique Pharmacology of EGFR Mutations in GBM to Achieve Sustained Inhibition and Activity in Preclinical Models

Complete & sustained inhibition of pEGFR/pERK

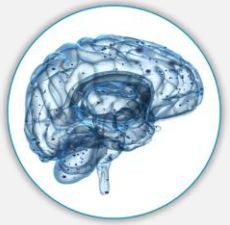


Increased survival of intracranial GBM PDX tumors



Kp_{uu} Partition Coefficient Calculation: $AUC_{brain:blood}$ x plasma Fu/brain Fu; QD=quaque die (once a day)

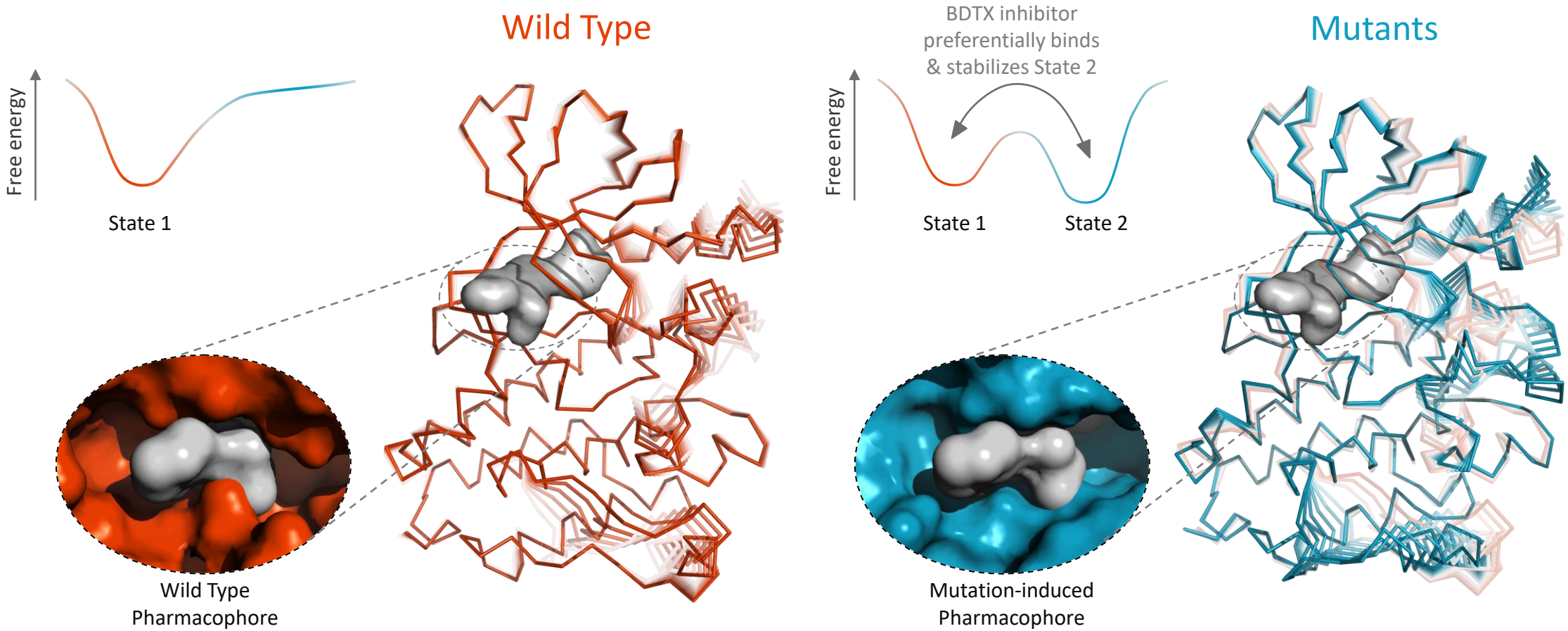
BDTX-1535 Can Potentially Fill A Critical Need For a Brain-Penetrant Inhibitor That Addresses The Limitations Of Other GBM Therapies



	Lessons From Past Failures	BDTX-1535
1	Heterogeneic expression of different EGFR oncogenic alterations within individual patients	Potent MasterKey inhibition of co-occurring EGFR alterations and amplification
2	Paradoxical activation of EGFR GBM oncogenes induced by reversible inhibitors	Overcomes paradoxical activation commonly found in GBM by reversible EGFR-TKIs
3	Poor tolerability driven by on target WT-EGFR activity	Spares WT-EGFR in normal cells while retaining potent activity against EGFR Alterations
4	Low brain exposure due to a lack of CNS penetrance	Designed to be brain penetrant to treat CNS tumors

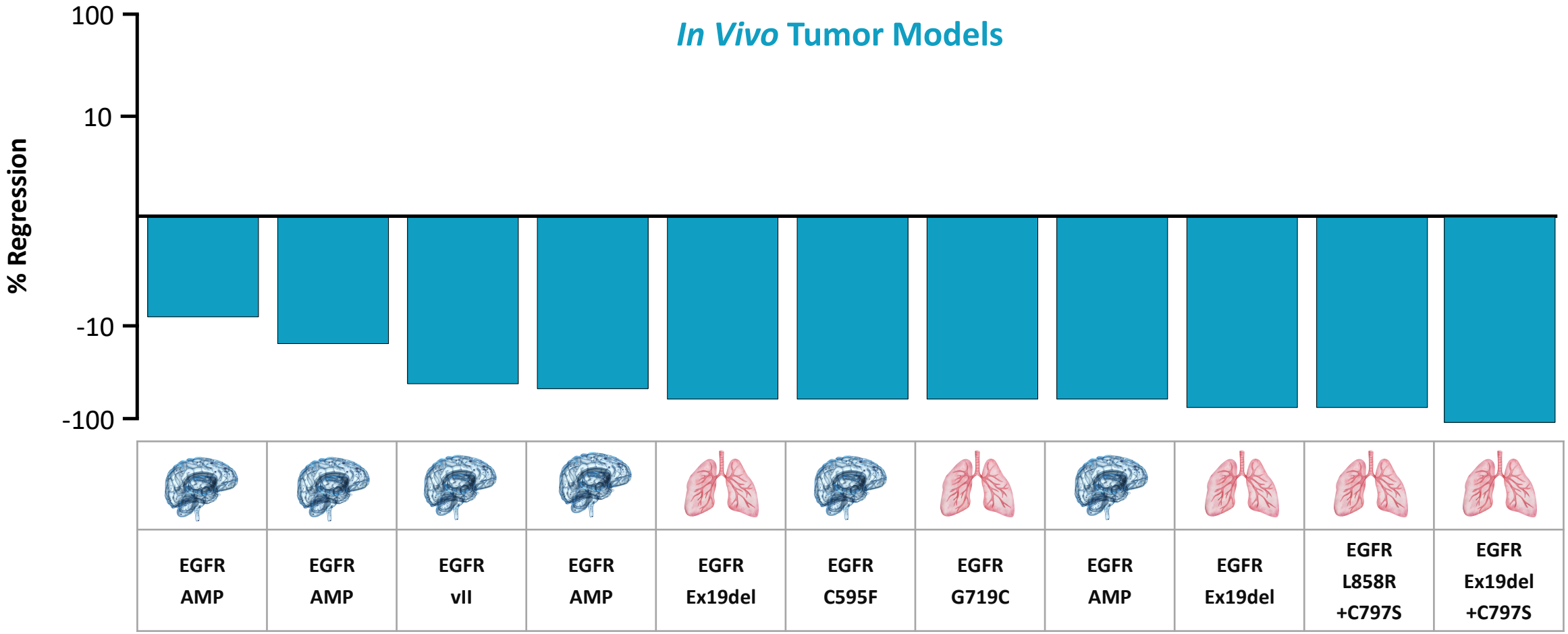
CNS=Central Nervous System; WT=Wild-Type; GBM=Glioblastoma Multiforme; NSCLC=Non-Small Cell Lung Cancer

MAP Discovery Engine Reveals Actionable Differences in Mutant Active Site Conformations



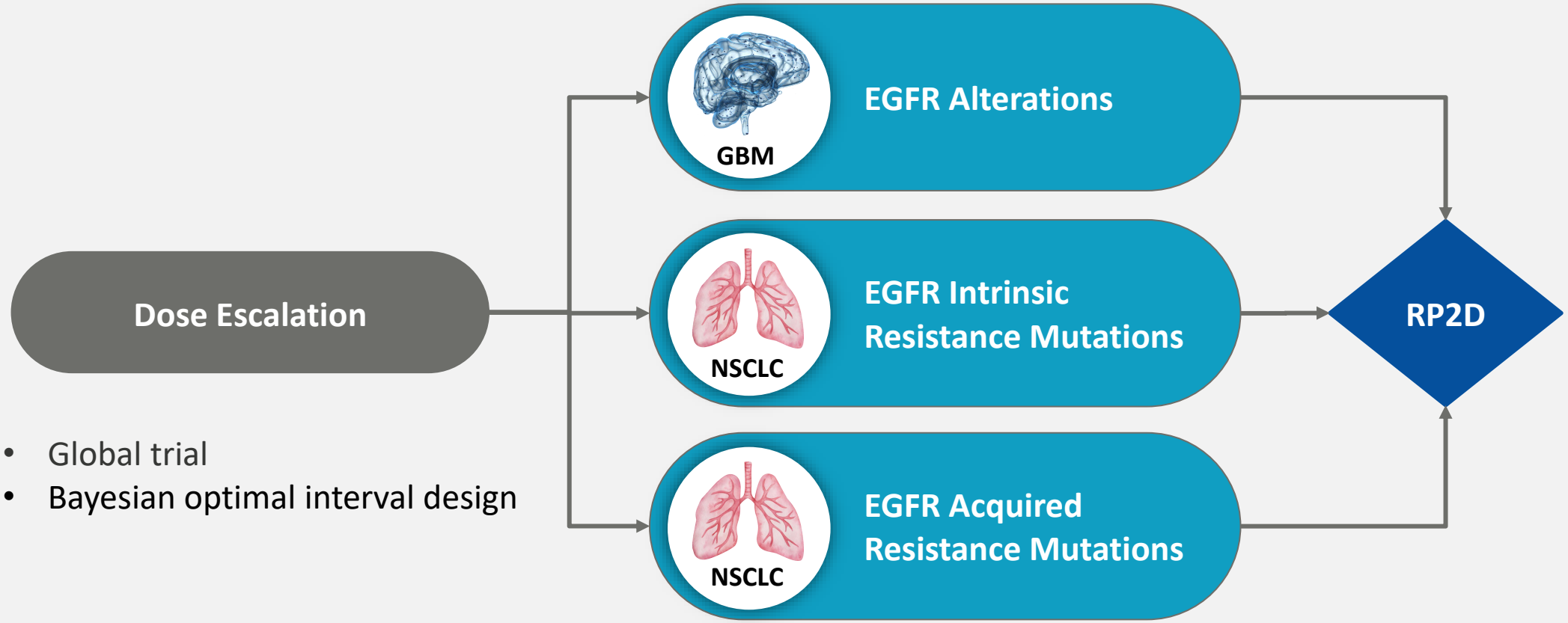
Clustered oncogenic variants with a common mutation-induced pharmacophore can be targeted by a BDTX inhibitor

BDTX-1535 Promotes Regression Across Range of Preclinical GBM & NSCLC Models Expressing MasterKey EGFR Mutations & EGFR Amplification



AMP=Amplification

BDTX-1535: Focused, Biomarker-Driven First-in-Human Phase 1 Study Design

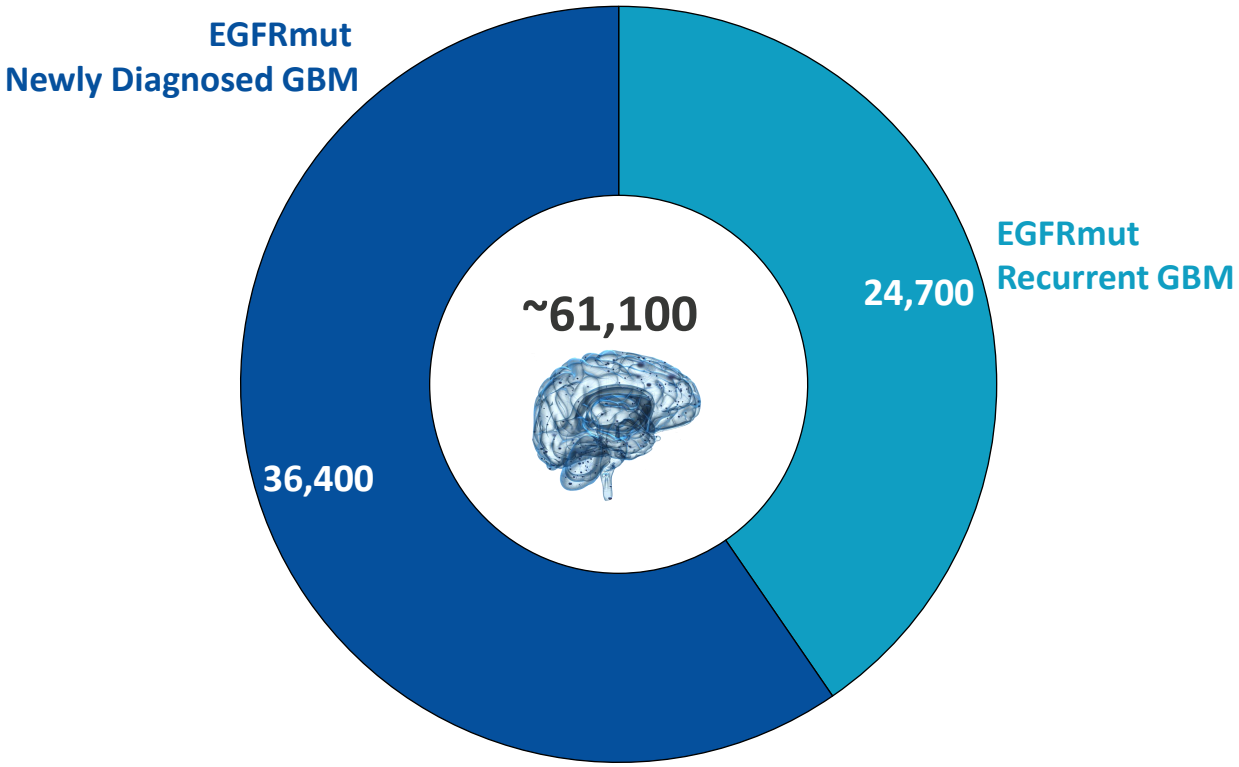


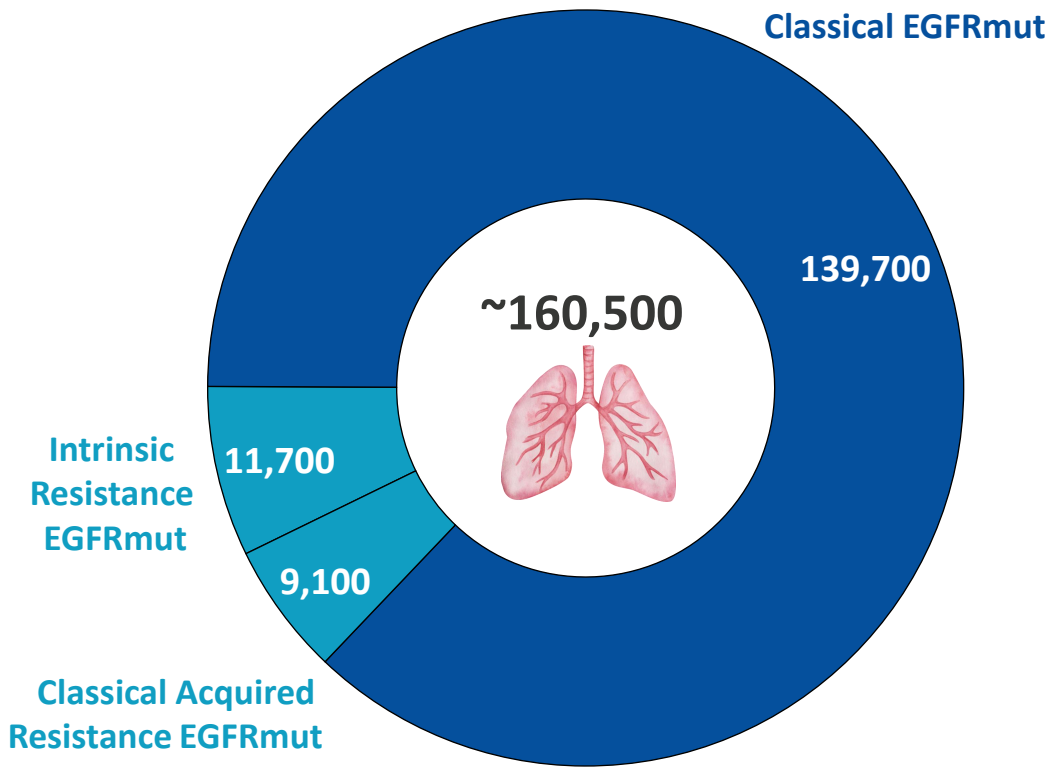
- Global trial
- Bayesian optimal interval design

RP2D=Recommended Phase 2 Dose

BDTX-1535: Large Addressable Patient Population Harboring MasterKey Mutations Across GBM and NSCLC

Addressable Patient Population (US / EU / Japan / China)





Sources: Epidemiology data from EvaluatePharma

BDTX-1535 is a Novel 4th Generation EGFR MasterKey Inhibitor Positioned to Address Unmet Needs in NSCLC and GBM

Potent & selective inhibition of EGFR mutations (Avg IC_{50} ~3nM) that drive intrinsic and acquired resistance to current generation TKIs

- Irreversible inhibition of family of resistance mutations to 3rd-gen EGFR inhibitors in NSCLC
- Irreversible inhibitor of EGFR mutation family to address heterogeneity & avoid paradoxical activation of EGFR in GBM
- Regression across panel of in vivo tumor models harboring EGFR mutations in NSCLC and GBM

Robust brain penetration to treat patients with EGFR mutations and CNS tumors

- Unbound brain fraction (Kp_{uu}) = 0.51 in rat; activity demonstrated in intracranial GBM model

Favorable drug like properties

- Prolonged blood stability
- Projected $t_{1/2}$ of 15 hours for QD dosing

$t_{1/2}$=half-life; IC_{50} =half maximal inhibitory concentration

BDTX-4933

Brain-Penetrant RAF MasterKey Inhibitor of Oncogenic BRAF Class I, II, & III and RAS Mutations

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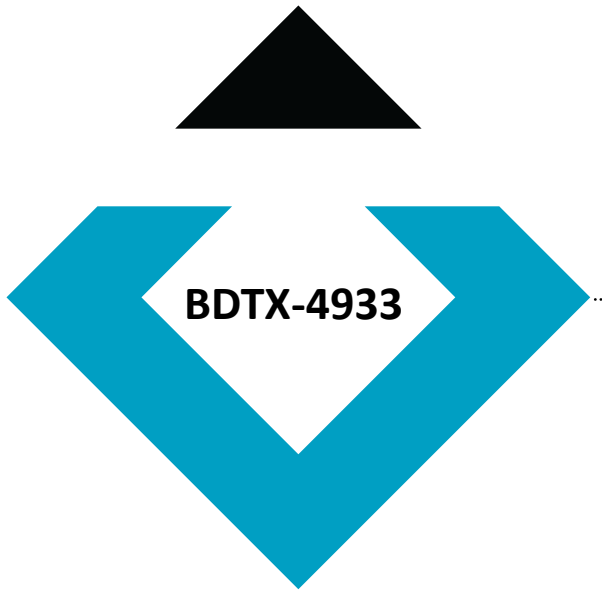
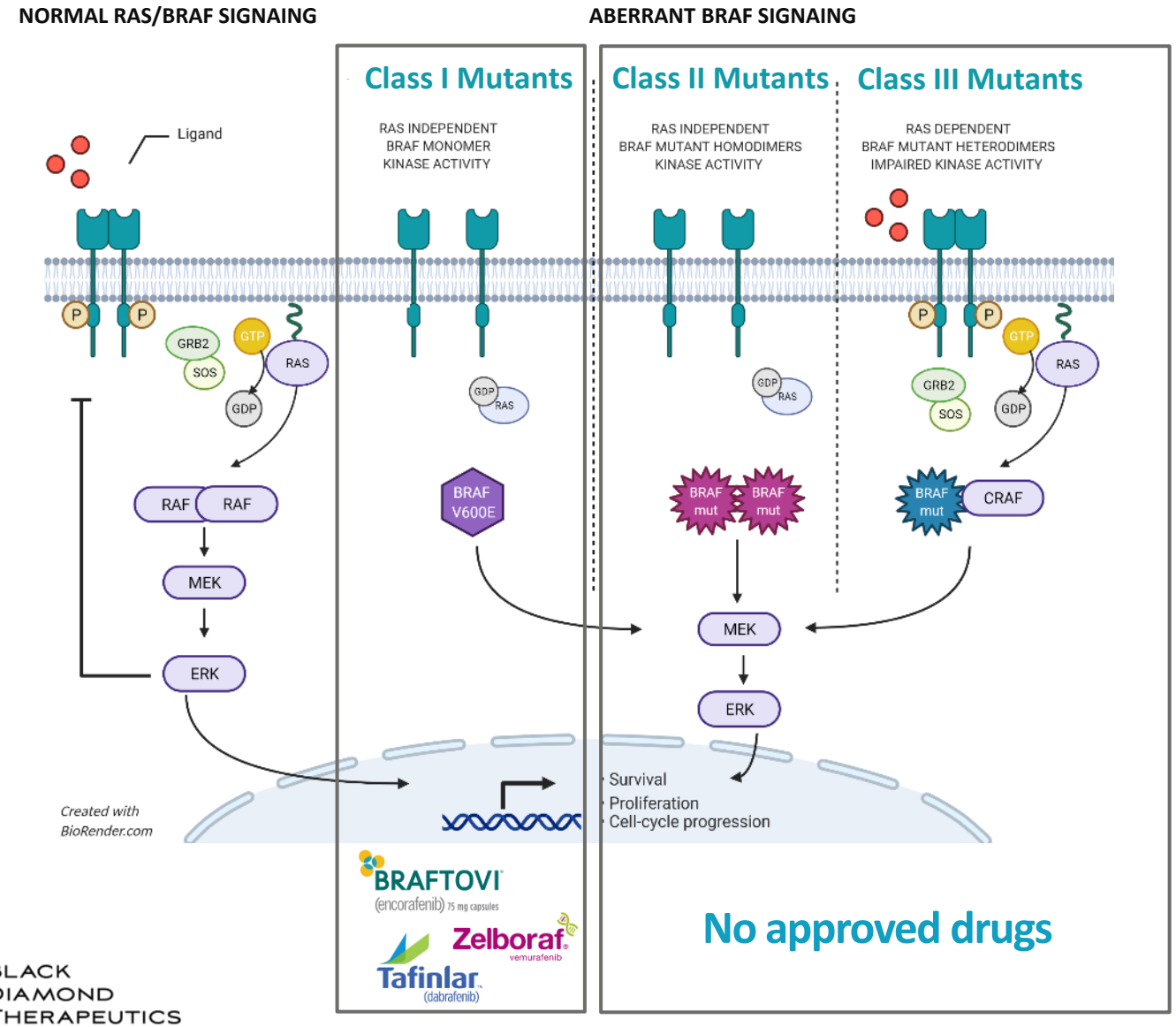
BDTX-4933: Oral, Brain Penetrant RAF MasterKey Inhibitor



MasterKey Family	Designed for potent and selective inhibition of BRAF Class I, II, and III and RAS mutations
Brain Penetrant	Designed to be brain penetrant to treat CNS tumors
Avoids Paradoxical Activation	Inhibits dimerized RAF kinases and avoids paradoxical activation
Status	IND-enabling studies initiated

BRAF Alterations Drive Oncogenesis Through Hyperactivation of the MAP Kinase Pathway



- MAPK signaling is a central pathway regulating cellular proliferation, cell-cycle progression, and survival
- Hyperactivation responsible for >40% of human cancer cases
- Activating BRAF alterations are associated with various cancers including melanoma and NSCLC
- Currently approved BRAF inhibitors only address Class I V600 mutations and lack CNS activity

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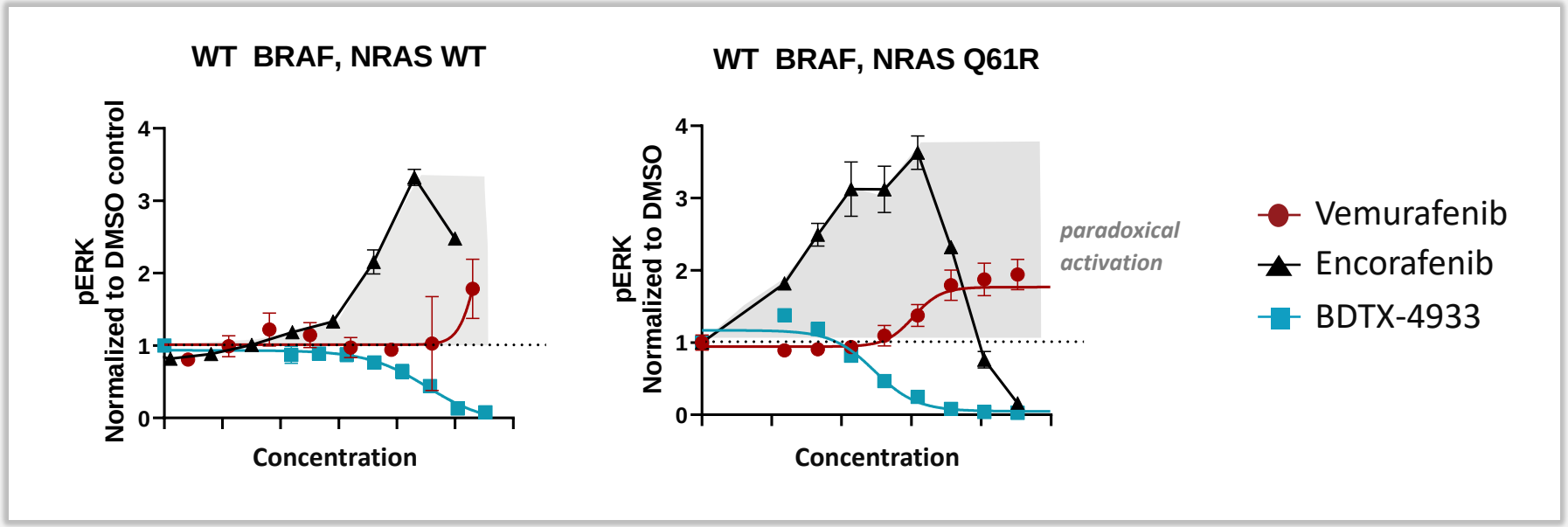
BDTX-4933 Designed to Deliver Superior Activity by Avoiding Paradoxical Activation Independent of Context

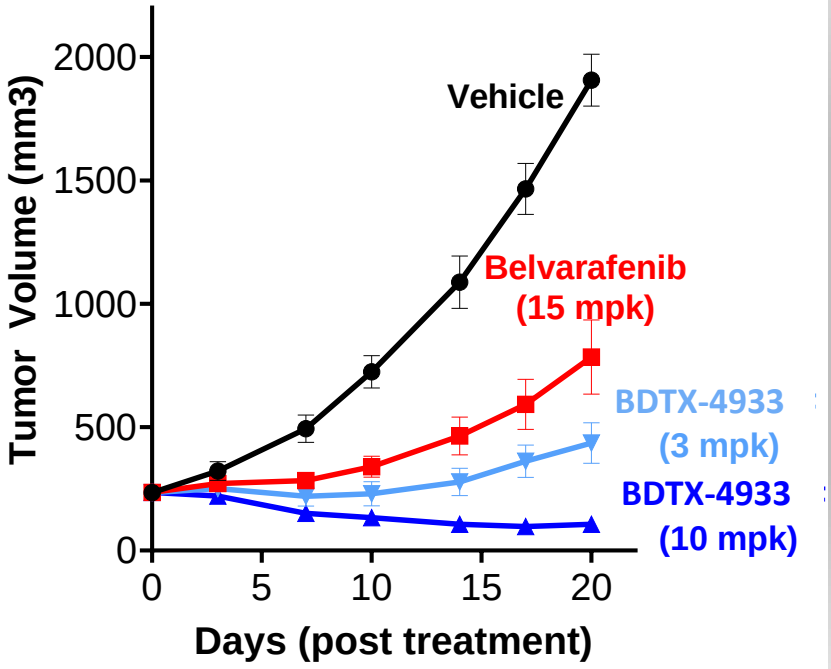
Avoidance of Paradoxical Activation



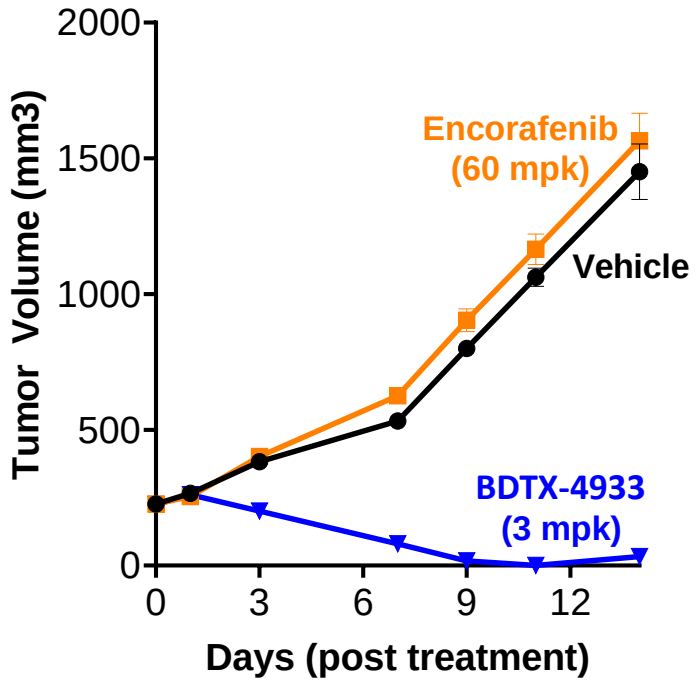
- Paradoxical activation occurs through activation of the non-inhibited RAF molecule in dimer
  —Limits efficacy through secondary malignancies and/or cutaneous toxicities
- Approved BRAF inhibitors demonstrate paradoxical activation
- Some investigational “paradox breaker” agents demonstrate context-dependent paradoxical activation

BDTX-4933 Exhibits Strong Anti-Tumor Activity Across All BRAF Mutation Classes in *In Vivo* Models

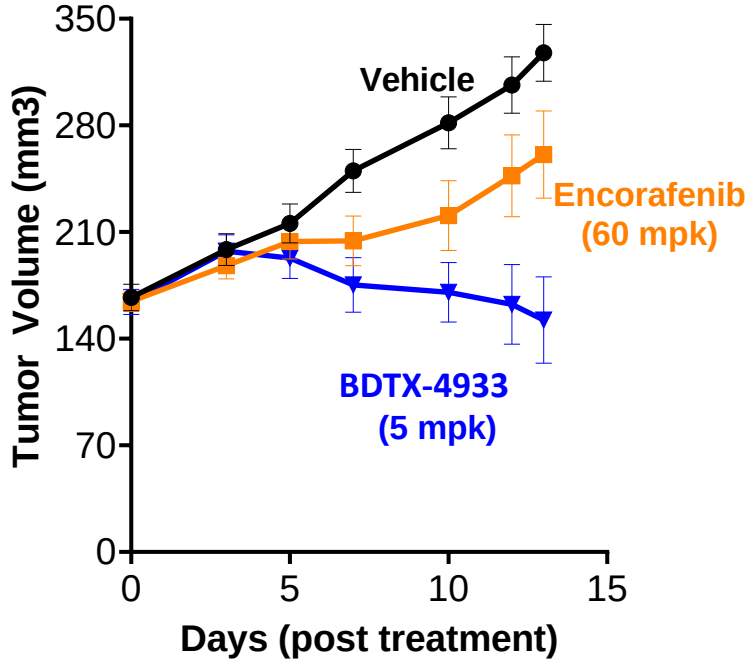
BRAF Class I
Mutant Tumor Model



BRAF Class II
Mutant Tumor Model

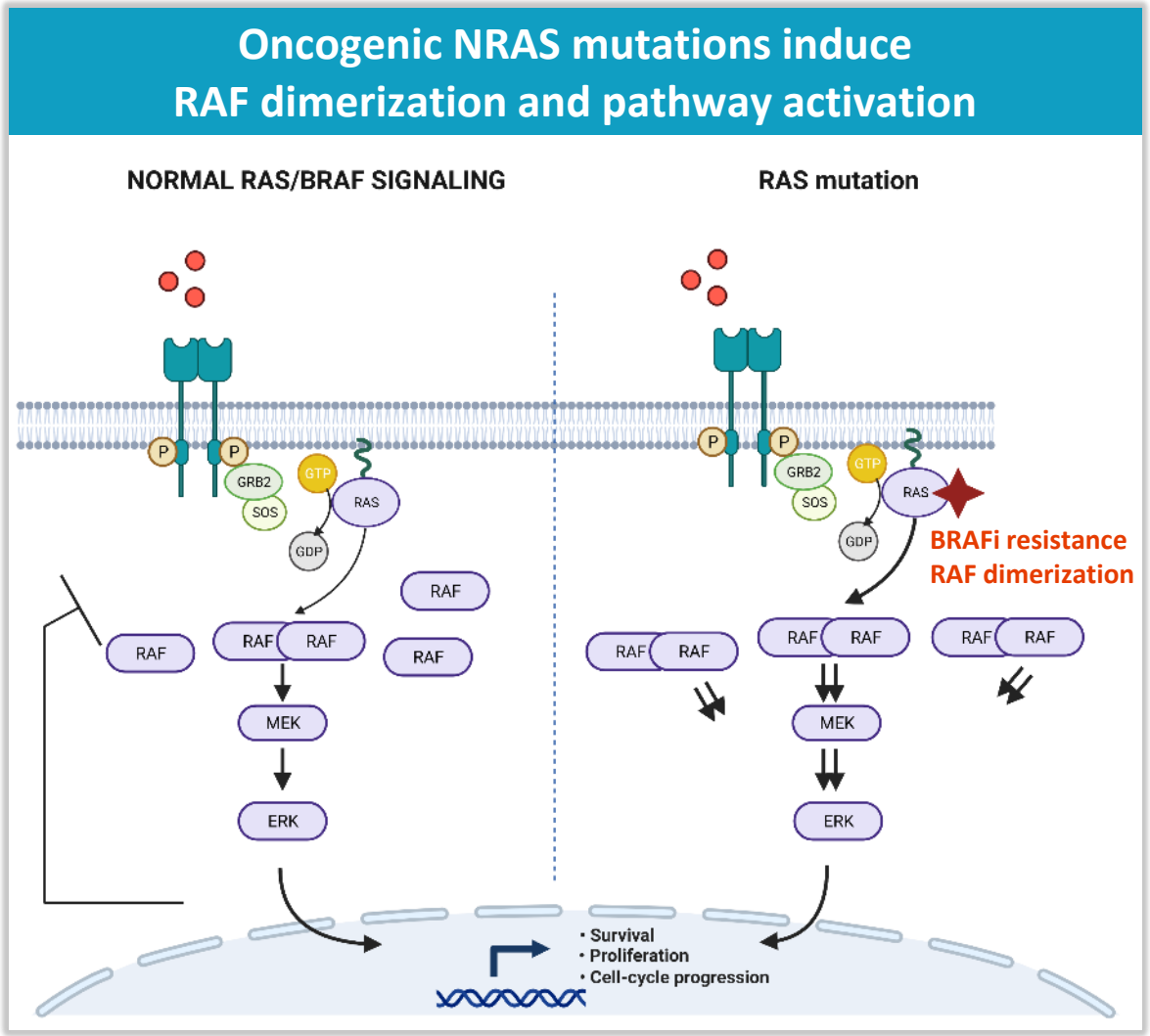


BRAF Class III
Mutant Tumor Model



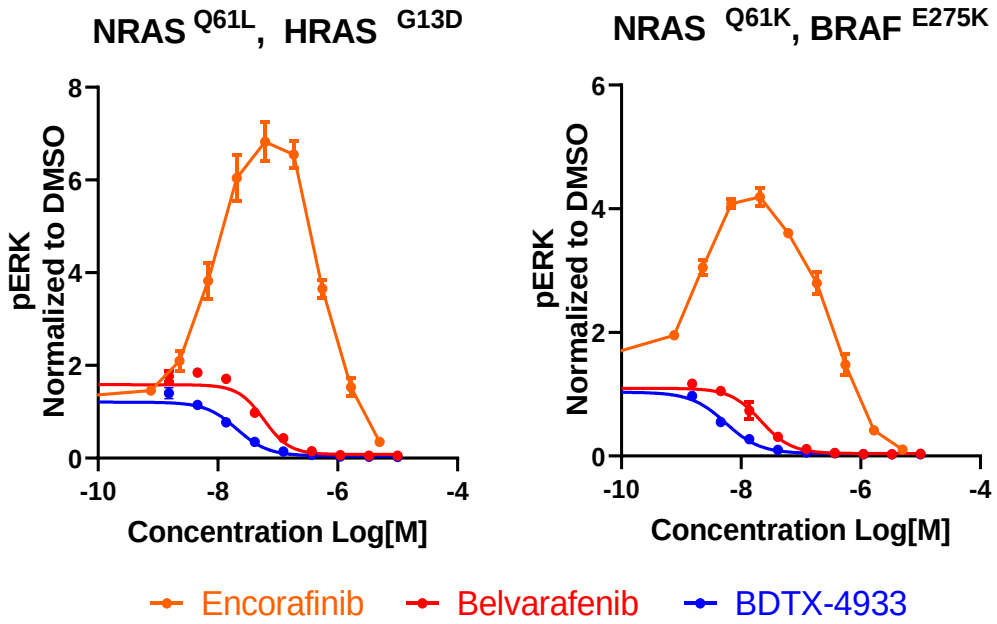
Daily oral dosing

NRAS-mutant Driven Cancers: Additional Clinical Opportunity for BDTX-4933

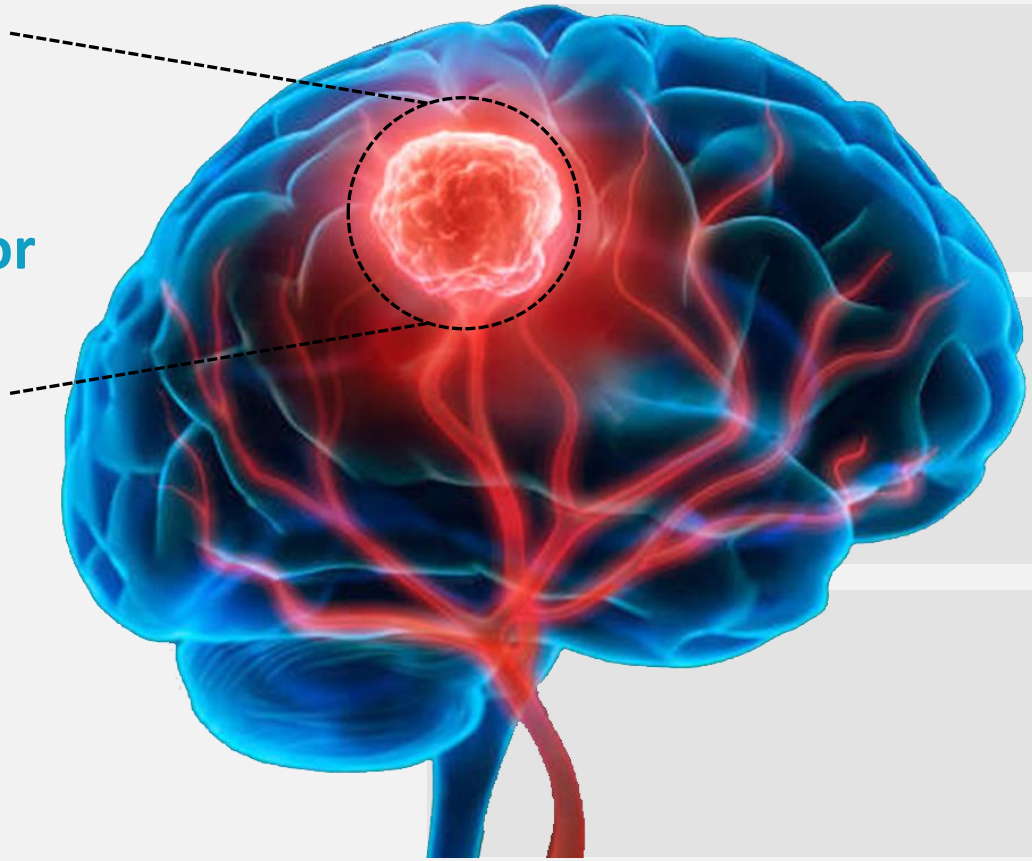


Created by BioRender

- NRAS-mutant melanoma represent ~20% of melanomas
- Acquired NRAS mutations associated with BRAF inhibitor use and brain metastases
- Clinical proof of concept: Belvarafenib in NRAS-mutant melanoma trial



BDTX-4933 Designed to be Brain Penetrant to Treat CNS Disease

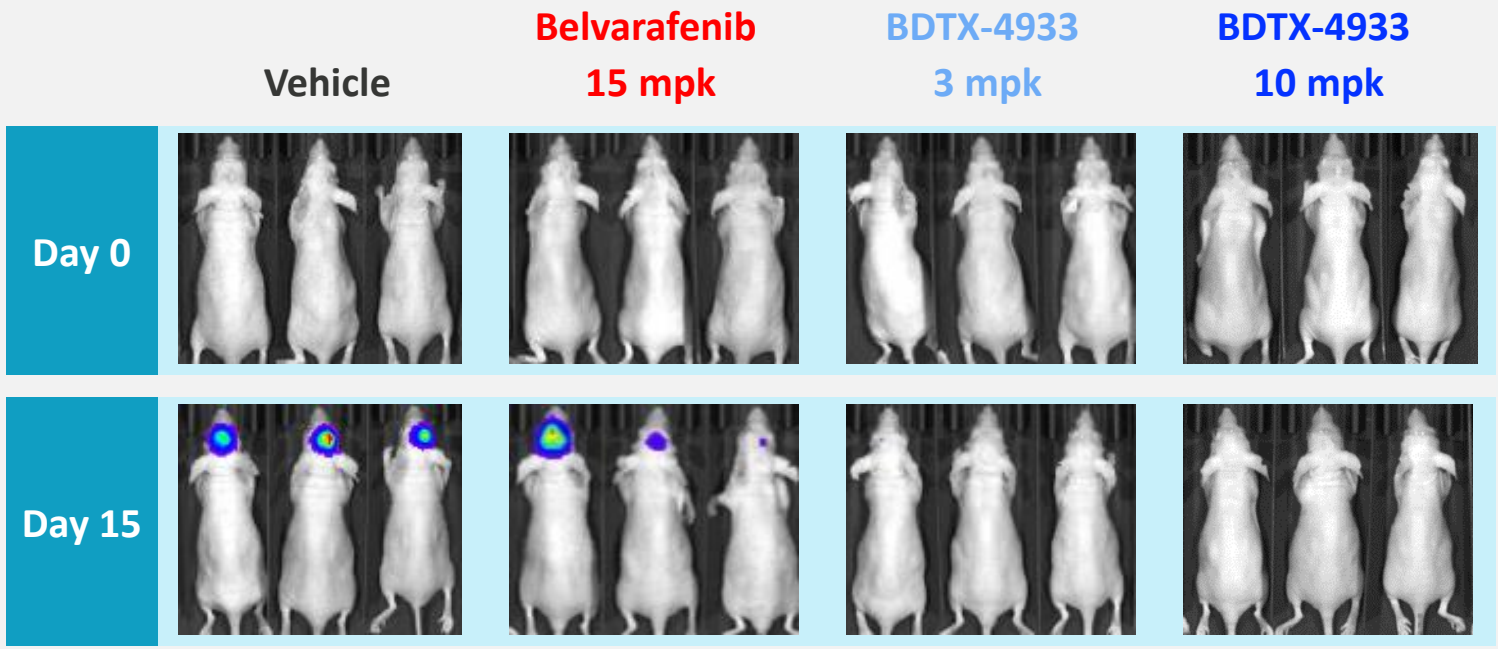


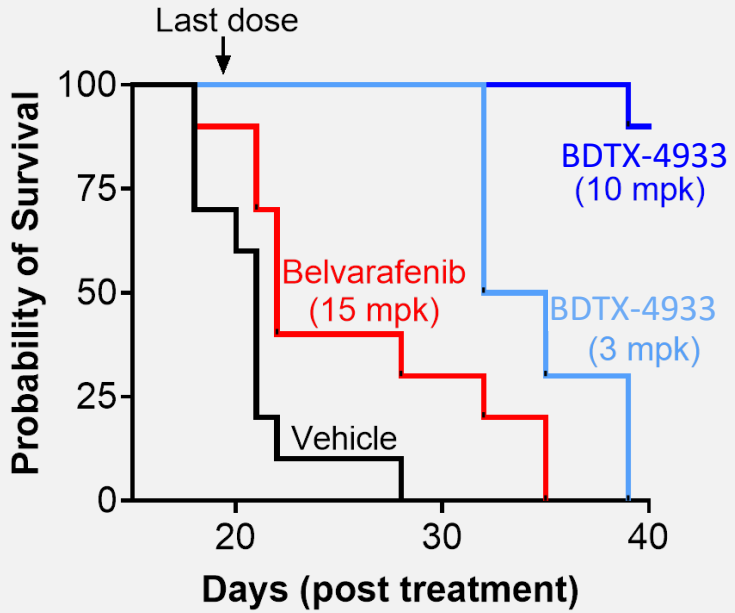
- CNS metastasis occurs in ~30-40%[1] of BRAF driven cancers
  - ~17,000[2] patients/year in the US
- BRAF and RAS mutations drive primary CNS tumors (e.g., glioma) in ~1,500[2] patients/year in the US
- Currently approved therapies are not brain penetrant

[1]Management of brain metastases in melanoma - UpToDate
[2]EvaluatePharma Epi for incidence by tumor type (2021, US), publications and GENIE/TCGA datasets for mutation prevalence by tumor type

BDTX-4933 Is Brain Penetrant and Exhibits Robust Activity in Treating CNS Disease in *in vivo* models

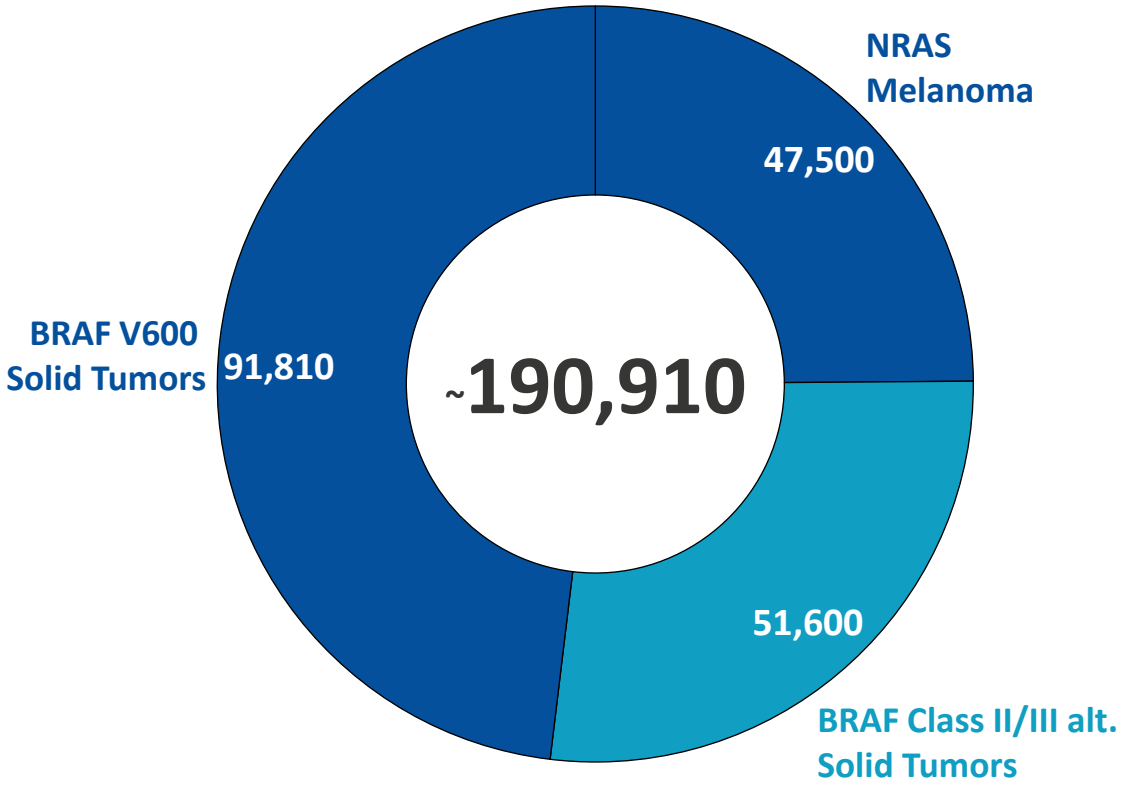
BDTX-4933 prolongs survival in BRAF-V600E intracranial tumor model



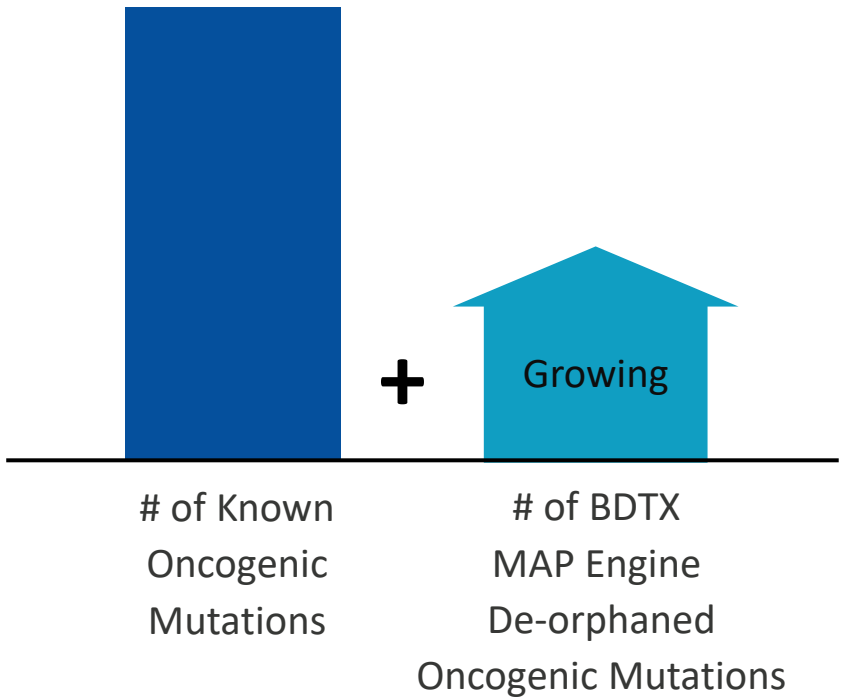


BDTX-4933: Potential *Best-in-Class*, RAF Masterkey Inhibitor For A Greater Number Of Patients With Overlooked Oncogenic Mutations

Addressable US / EU / JP Patient Population



BDTX Is Growing The Addressable Patient Population By De-Orphaning of Overlooked Mutations

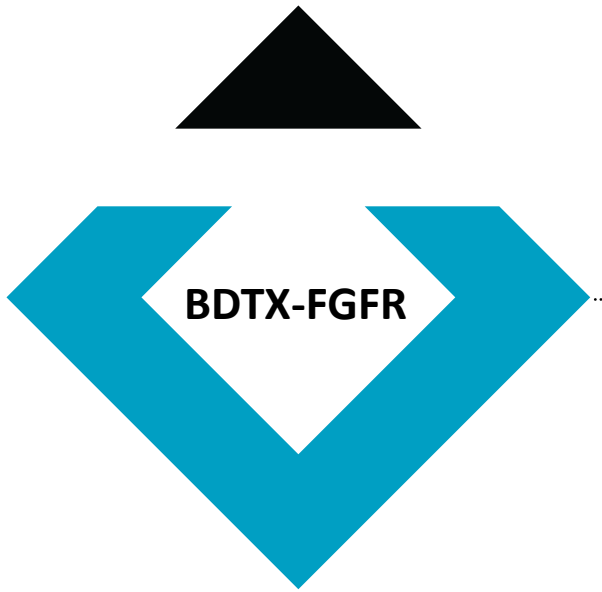


Sources: EvaluatePharma Epi and GENIE/TCGA

FGFR2/3 Selective Inhibitor Program

Black Diamond Therapeutics

BDTX-FGFR: Oral, Selective Small-Molecule FGFR2 & FGFR3 Inhibitor



Unique Activity Profile	**Potency against families of FGFR2 & FGFR3 alterations and amplifications**
Selective	**Designed to be FGFR1 & FGFR4 sparing, allowing maximum efficacy while minimizing dose limiting toxicities**
Preclinical PoC	**Robust *in vivo* efficacy demonstrated in bladder (FGFR3) and gastric (FGFR2) xenograft models without hyperphosphatemia**
Status	**Progressing toward development candidate nomination**

MAP Drug Discovery Engine

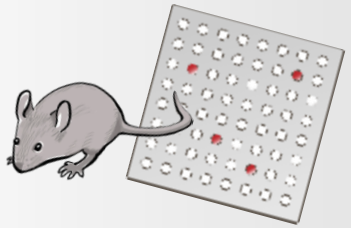
Black Diamond Therapeutics

MAP Drug Discovery Engine Unlocks Precision Medicine with a "MasterKey"

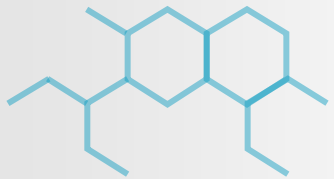
Proprietary MAP scoring *in silico*

Genomics + *Proteomics*

Validate novel oncogenic driver mutations and targets



Develop MasterKey inhibitors against mutation families



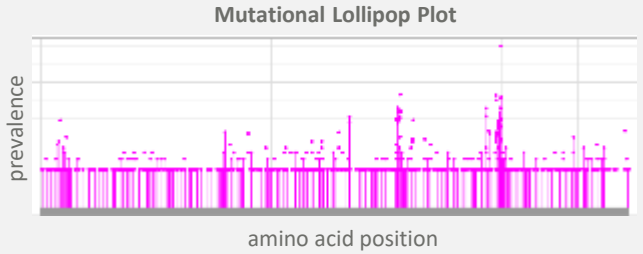
Employ structural and dynamic methods to identify oncogenic mutation families

BLACK DIAMOND THERAPEUTICS

MAP Drug Discovery Engine: A Scaled Approach to Extract Oncogenic **MasterKey Mutation** Families

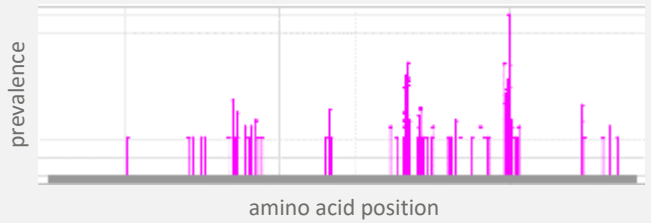
Population level clinical mutation landscape

Thousands



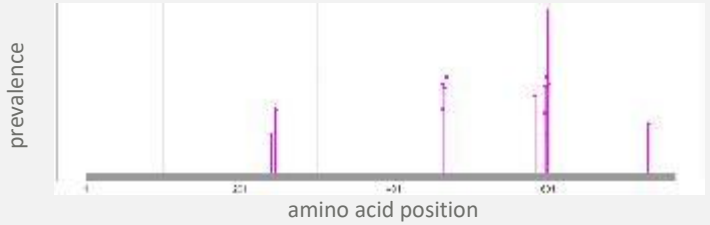
Computational *in-silico* oncogenicity prediction

Hundreds

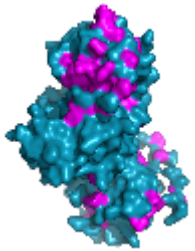


Experimentally validated oncogenic MasterKey mutations

Tens



Oncogene



Corporate Overview

Black Diamond Therapeutics

Deep Oncology and Small Molecule Drug Discovery and Development Experience

Leadership Team

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

(OSI) pharmaceuticals
astellas
DukeNUS Medical School

Liz Buck, Ph.D.
Chief Scientific Officer

(OSI) pharmaceuticals
astellas

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

VERSANT ventures
Roche

Sergey Yurasov
Chief Medical Officer

Nuvation Bio
IMMUNE DESIGN
CLOVIS ONCOLOGY
Lilly
Roche

Brent Hatzis-Schoch, J.D.
COO and General Counsel

Radius
MERZ
PHARMACIA

Elizabeth L. Montgomery
Chief People Officer

CLEARVIEW Healthcare Partners
Boston Scientific
IQVIA

Board of Directors

Ali Behbahani, M.D.
General Partner, NEA

Kapil Dhingra, M.D.
Managing Member, KAPital Consulting

Wendy Dixon, Ph.D.
Former Global Marketing Head, Bristol Myers Squibb

David M. Epstein, Ph.D.
CEO, Black Diamond Therapeutics, Inc.

Bob Ingram – Chairman
General Partner, Hatteras Ventures

Sam Kulkarni, Ph.D.
CEO, CRISPR Therapeutics AG

Alex Mayweg, Ph.D.
Managing Director, Versant Ventures

Garry Menzel
CEO, TCR2

Rajeev Shah
Managing Director, RA Capital

Mark Velleca, M.D., Ph.D.
CEO, StrideBio, Inc.

Cash Runway Expected to Enable Multiple Upcoming Milestones

Upcoming program milestones

- BDTX-1535 clinical data update in 2023
- BDTX-4933 IND filing in 1H 2023
- FGFR program progressing toward development candidate nomination
- Undisclosed program development candidate nomination in 2023

Strong balance sheet

- Approximately $144.2 mm in cash, cash equivalents and investments as of September 30, 2022
- Cash runway into 3Q 2024

Expanding the Reach of Precision Medicine Through the Development of MasterKey Therapies

MasterKey therapies address oncogene mutation families; providing precision oncology medicines to greater numbers of patients with genetically defined tumors

Clinical and late-preclinical pipeline of MasterKey inhibitors derived from our MAP drug discovery engine targeting oncogenic EGFR, RAF, FGFR2/3 and additional undisclosed targets

Our proprietary **MAP drug discovery engine** is designed to:

- Predict and validate novel oncogenic mutant families from population level tumor genomics
- Pioneer mutant family conformation-based MasterKey drug design
- Provide opportunities beyond oncology and small molecules

BDTX-1535: a brain-penetrant, mutant selective, irreversible EGFR MasterKey inhibitor, currently in Phase 1 development for treatment of patients with GBM and NSCLC driven by EGFR intrinsic & acquired resistance mutations

BDTX-4933: a brain-penetrant RAF MasterKey inhibitor targeting oncogenic BRAF Class I, II, III and RAS mutations, currently in IND-enabling studies

Thank You

Partnership: partnership@bdtx.com

Investors: investors@bdtx.com

Media: media@bdtx.com

Black Diamond Therapeutics