UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or Section 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 10, 2022

Black Diamond Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-39200**	**81-4254660**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

One Main Street, 10th Floor **Cambridge, MA** (Address of principal executive offices)	**02142** (Zip Code)

Registrant's telephone number, including area code: 617-252-0848

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation to the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	BDTX	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On January 10, 2022, Black Diamond Therapeutics, Inc., (the "Company") issued a press release titled, "*Black Diamond Therapeutics Announces Strategic Priorities and Expected Milestones for 2022*" and updated its corporate presentation for use in meetings with investors, analysts and others. A copy of the press release and a copy of the corporate presentation are furnished as Exhibits 99.1 and 99.2, respectively, to this Current Report on the Form 8-K.

The information furnished under this Item 7.01, including Exhibits 99.1 and 99.2, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01. Other Events.

BDTX-1535

On January 10, 2022, the Company announced the submission of its Investigational New Drug application to the US Food and Drug Administration ("FDA") for BDTX-1535 and expects to initiate the Phase 1 study of BDTX-1535 in the first quarter of 2022, subject to allowance of the IND by the FDA. The Company expects to provide a clinical data update on BDTX-1535 in the second half of 2023.

BDTX-189

The Company also announced that, due to the rapid evolution of the treatment landscape in non-small cell lung cancer harboring either EGFR or HER2 Exon 20 insertion mutations, the Company has decided to enroll additional patients into the MasterKey-01 Phase 1 safety expansion cohort to obtain more clinical data and inform future development of BDTX-189. The Company expects to provide further guidance on the BDTX-189 program in 2022.

Financial Guidance

The Company announced that it ended 2021 with approximately $210 million in cash, cash equivalents and investments, which the Company believes is sufficient to fund its anticipated operating expenses and capital expenditure requirements into 2024.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits:

Exhibit No.	Description
99.1	Press Release issued by Black Diamond Therapeutics, Inc., dated January 10, 2022.
99.2	Corporate Presentation of Black Diamond Therapeutics, Inc., dated January 10, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document contained in Exhibit 104).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

January 10, 2022

BLACK DIAMOND THERAPEUTICS, INC.

By: /s/ Brent Hatzis-Schoch
Name: Brent Hatzis-Schoch
Title: Chief Operating Officer and General Counsel

Exhibit 99.1

Black Diamond Therapeutics Announces Strategic Priorities and Expected Milestones for 2022

- *Company announces IND submission for BDTX-1535 for the treatment of GBM and NSCLC including those with CNS tumors;*

- *Company to enroll additional patients into MasterKey-01 Phase 1 safety expansion cohort to obtain more clinical data and inform future development of BDTX-189;*

- *Company anticipates initiation of IND-enabling studies for its CNS-penetrant Class I,II,III BRAF program in 2022;*

- *Existing resources to be prioritized in the near-term for advancement of MasterKey pipeline programs BDTX-1535, BRAF, FGFR and the MAP discovery engine; cash runway extended to 2024*

CAMBRIDGE, Mass. And NEW YORK, January 10, 2022 (GLOBE NEWSWIRE) – Black Diamond Therapeutics, Inc. (Nasdaq: BDTX), a precision oncology medicine company pioneering the discovery and development of MasterKey therapies, today announced a strategic pipeline update and outlined its expected upcoming milestones.

“MasterKey inhibitors target mutation families and are designed to address the unmet medical need of cancer patients with genetically defined cancers for whom precision therapies are not available,” said David Epstein, Ph.D., Chief Executive Officer of Black Diamond Therapeutics. “We are incredibly pleased to have submitted the IND ahead of schedule for BDTX-1535, a next generation CNS penetrant MasterKey inhibitor designed to target EGFR driver mutations found in certain patients with GBM and NSCLC. The oncogenic alterations of EGFR, particularly those associated with GBM, result in distinct conformations which impart unique pharmacology and drug resistance. BDTX-1535 is designed to exploit this mechanism as a critical point of attack. We believe Black Diamond is uniquely positioned to deliver a pipeline of truly differentiated MasterKey programs as we leverage our expertise in cancer genomics, onco-protein function and drug discovery.”

“As a result of the rapid evolution of the treatment landscape in NSCLC harboring EGFR or HER2 Exon 20 insertion mutations, we have decided to obtain further clinical data from the BDTX-189 safety expansion cohort at the recommended Phase 2 dose in 2022 in order to inform the future development of our BDTX-189 program, gating the start of a Phase 2 trial. The revised strategy enables near-term prioritization of BDTX-1535 clinical development and further investment in our pipeline, while allowing us to obtain more clinical data on BDTX-189, and simultaneously extends our cash runway into 2024.”

Pipeline Updates and Expected Milestones:

BDTX-1535

- Black Diamond announced ahead of schedule the submission of its Investigational New Drug (IND) application to the US Food and Drug Administration (FDA) for BDTX-1535 and expects to initiate the Phase 1 study of BDTX-1535 in the first quarter of 2022, subject to allowance of the IND by the FDA.
- BDTX-1535 is designed as a potent, selective, brain-penetrant and irreversible MasterKey inhibitor of epidermal growth factor receptor (EGFR) mutations expressed in glioblastoma multiforme (GBM) and of intrinsic and acquired resistance EGFR mutations to third generation EGFR inhibitors in NSCLC.
- In pre-clinical studies, Black Diamond has demonstrated that oncogenic alterations of EGFR, particularly those associated with GBM, result in distinct conformations which impart unique pharmacology and drug resistance. BDTX-1535 is designed to exploit this mechanism and has demonstrated anti-cancer activity and growth regressions across a panel of patient-derived xenograft models including intracranial tumor models.
- It is estimated that approximately 50% of GBM patients harbor an oncogenic EGFR alteration that has the potential to be addressed by BDTX-1535, representing a potential patient population of greater than 60,000 patients annually across the US, EU, Japan and China.
- It is estimated that across the US, EU, Japan and China there are approximately 20,000 patients who are diagnosed annually with non-small cell lung cancer (NSCLC) harboring an EGFR intrinsic or acquired resistance mutation.
- The Company expects to provide a clinical data update on BDTX-1535 in the second half of 2023.

BDTX-189

- BDTX-189 is designed as a MasterKey inhibitor targeting families of oncogenic mutations in EGFR and HER2.
- Clinical data obtained from the MasterKey-01 study to date have demonstrated a favorable safety profile for BDTX-189 and early signs of clinical activity in patients whose tumors are driven by MasterKey mutation families, including two confirmed partial responses in heavily pretreated patients who have remained on treatment for more than 10 months.
- Due to the rapid evolution of the treatment landscape in NSCLC harboring either EGFR or HER2 Exon 20 insertion mutations, the Company has decided to gate the initiation of the Phase 2 portion of the MasterKey-01 study and determine next steps in development based on further clinical data obtained from the safety expansion cohort at the recommended Phase 2 dose.
- The Company expects to provide further guidance on the BDTX-189 program in 2022.

BRAF Program

- Black Diamond is developing a CNS-penetrant BRAF inhibitor against a family of Class I, II, III canonical and non-canonical mutations. The Company's lead BRAF compound is designed to be highly selective, potent and to avoid paradoxical activation.
- In cell-based assays, Black Diamond's lead BRAF compound demonstrated potent inhibition of a wide spectrum of BRAF mutations and fusions and exhibited dose-dependent inhibition of protein kinase RNA-like endoplasmic reticulum kinase downstream signaling.

- In preclinical BRAF-driven tumor models, daily dosing of the lead compound demonstrated dose-dependent tumor growth inhibition, tumor regression and survival consistent with potent on-target and on-pathway inhibition.
- The Company's lead BRAF compound demonstrated robust brain penetration properties and achieved intracranial tumor growth inhibition in pre-clinical studies.
- It is estimated that across the US, EU, and Japan there are approximately 190,000 patients with solid tumors who are diagnosed annually with BRAF oncogenic mutations.
- Black Diamond anticipates the initiation of IND-enabling studies for the BRAF program in 2022.

MAP Discovery Engine

- The Company continues to focus on building its Mutation-Allostery-Pharmacology (MAP) Discovery Engine to exploit mutant onco-protein conformations for the delivery of selective MasterKey therapies, with a focus on developing a MasterKey inhibitor that spares wild type fibroblast growth factor receptor 1 (FGFR1) while inhibiting FGFR2 and FGFR3 mutant families, as well as other preclinical stage programs.
- The Company plans to integrate new molecular dynamic modeling tools from its strategic partnership with OpenEye Scientific.

Financial Guidance

- Black Diamond ended 2021 with approximately $210 million in cash, cash equivalents and investments, which the Company believes is sufficient to fund its anticipated operating expenses and capital expenditure requirements into 2024.

About Black Diamond

Black Diamond Therapeutics is a precision oncology medicine company pioneering the development of novel MasterKey therapies. Black Diamond is addressing the significant unmet need for novel precision oncology therapies for patients with genetically defined cancers who have limited treatment options. Black Diamond is built upon a deep understanding of cancer genetics, onco-protein function, and drug discovery. The Company's proprietary Mutation-Allostery-Pharmacology, or MAP drug discovery engine, is designed to allow Black Diamond to analyze population-level genetic sequencing tumor data to predict and validate oncogenic mutations that promote cancer across tumor types as MasterKey mutations. Black Diamond discovers and develops selective MasterKey therapies against these families of oncogenic mutations. Black Diamond was founded by David M. Epstein, Ph.D., and Elizabeth Buck, Ph.D. For more information, please visit www.blackdiamondtherapeutics.com.

Forward-Looking Statements
Statements contained in this press release regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding: the continued development and advancement of BDTX-1535, including expectations for IND allowance and plans for initiating the Phase 1 trial of BDTX-1535, the continuation of the BDTX-189 safety expansion cohort and the resulting data, the continued development of the BRAF program, including the timing for initiating IND-enabling studies, the continued development of the FGFR program, including plans for nominating a development candidate, the continued development of the MAP discovery engine and the Company’s cash runway. Any forward-looking statements in this statement are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include: the success, cost, and timing of the Company’s product candidate development activities and planned IND-enabling studies and clinical trials, the Company’s ability to execute on its strategy, regulatory developments in the United States, the Company’s ability to fund operations, and the impact that the current COVID-19 pandemic will have on the Company’s clinical trials and preclinical studies, supply chain, and operations, as well as those risks and uncertainties set forth in its Annual Report on Form 10-K for the year ended December 31, 2020, filed with the United States Securities and Exchange Commission and in its other filings filed with the United States Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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Black Diamond Therapeutics, Inc.
Pioneering the Development of MasterKey Therapies
BLACK
DIAMOND
THERAPEUTICS
JANUARY 2022

Important Notice and Disclaimers

This presentation contains "forward-looking statements" of Black Diamond Therapeutics, Inc. ("Black Diamond," "we" or "our") within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements include, but are not limited to, express or implied statements regarding our ability to advance and expand the MAP drug discovery engine, the potential timing and advancement of our clinical trial and preclinical studies, including the initiation of our clinical trial for BDTX-1535 and the continuation of our clinical trial for BDTX-189, the timing and potential achievement of milestones to advance our product candidate pipeline, including initiation of additional investigational new drug ("IND")-enabling studies, filing and allowance of INDs and product candidate nomination, and the potential commercial opportunities, including value and market, for our product candidates. Any forward-looking statements in this presentation are based on management's current expectations and beliefs of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Our actual future results may be materially different from what we expect due to factors largely outside our control, including the results of clinical trials, clinical trial patient enrollment, changes in regulatory requirements or decisions of regulatory authorities, commercialization plans and timelines if approved, the actions of our third party clinical research organizations, suppliers and manufacturers, and the impact that the current COVID-19 pandemic will have on our clinical trials, pre-clinical studies, and operations. 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 2020 annual report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in our other filings with the Securities and Exchange Commission. All information in this presentation is as of the date hereof, and we undertake no duty to update this information unless required by law.

Certain information contained in this presentation relates to, or is based on, studies, publications, surveys and other data obtained from third party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.


Black Diamond Therapeutics Overview
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THERAPEUTICS

Expanding Precision Medicine Through the Development of MasterKey Therapies

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

Proof-of-principle mutation family selective inhibitors; clinical and late-preclinical pipeline of MasterKey inhibitors derived from our MAP drug discovery engine: EGFR, HER2, BRAF, and FGFR

BDTX-1535, an irreversible, mutant selective, brain-penetrant EGFR inhibitor entering Phase 1 for the treatment of GBM and NSCLC driven by EGFR intrinsic & acquired resistance mutations

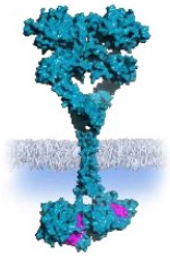
BDTX-189, a mutant selective EGFR/HER2 inhibitor in Phase 1 Safety Expansion study in patients expressing targeted oncogenic mutations

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

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

Classic/Current Approach:
Targeting active site kinase domain mutations

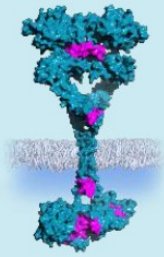


Targeting single mutations in individual tumor types

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 Classes of Precision Medicines

Target	Drug Candidate	Indication	Discovery	Optimization	IND-Enabling	Phase 1	Phase 2	Phase 3
EGFR	BDTX-1535	GBM, NSCLC ± CNS mets	**Clinical Data** (2023)					
EGFR HER2	BDTX-189	NSCLC, breast	**Safety Expansion Update** (2022)					
BRAF	Undisclosed	Targeted solid tumors ± CNS mets	**Initiate IND-Enabling Studies** (2022)					
FGFR	Undisclosed	Targeted solid tumors	**Development Candidate Selection** (2022)					

EGFR=Epidermal Growth Factor Receptor; HER2= Human Epidermal Growth Factor Receptor 2; FGFR=Fibroblast Growth Factor Receptor; IND=Investigational New Drug


MAP Drug Discovery Engine
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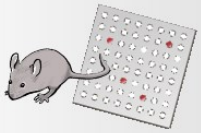
MAP Drug Discovery Engine Unlocks Precision Medicine with a “MasterKey”

Proprietary MAP scoring *in silico*

Genomics + *Proteomics*

Validate novel oncogenic driver mutations and targets



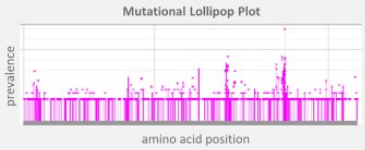
Develop MasterKey inhibitors against mutation families

Employ structural and dynamic methods to identify oncogenic mutation families

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

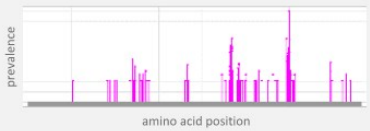
Population level clinical mutation landscape

Thousands



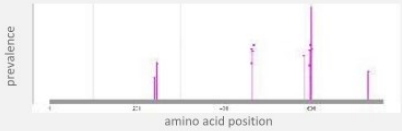
Computational *in-silico* oncogenicity prediction

Hundreds



Experimentally validated oncogenic MasterKey mutations

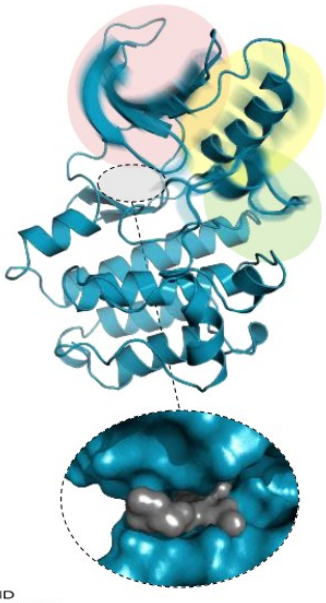
Tens



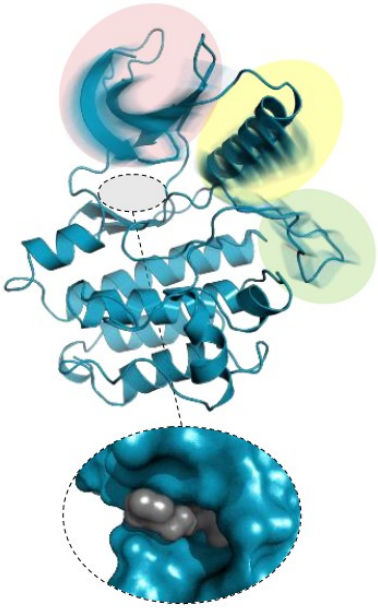
Oncogene

Conformation Based Drug Design Enabled by MAP Drug Discovery Engine

WILD TYPE



MASTERKEY MUTATION FAMILIES



MasterKey mutations drive global **conformation change**

MasterKey Inhibitors designed to exploit this vulnerability

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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** — IND submitted for Phase 1 study in patients with either GBM or NSCLC with and without CNS tumors

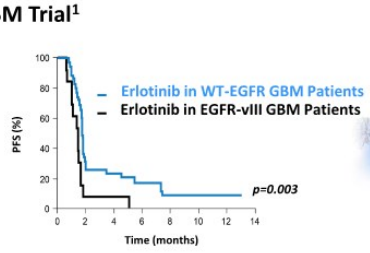
CNS=Central Nervous System; WT=Wild-Type; GBM=Glioblastoma Multiforme; NSCLC=Non-Small Cell Lung Cancer

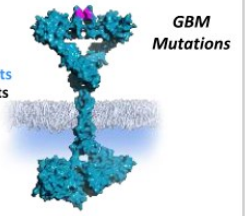
Reversible EGFR Inhibitors Show Potentially Detrimental Pharmacology in EGFR Driven GBM

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

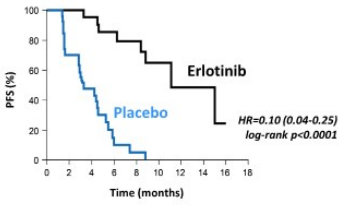
EGFR TKIs Extend PFS in Patients with Kinase Domain Mutations

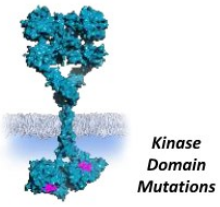
GBM Trial[1]



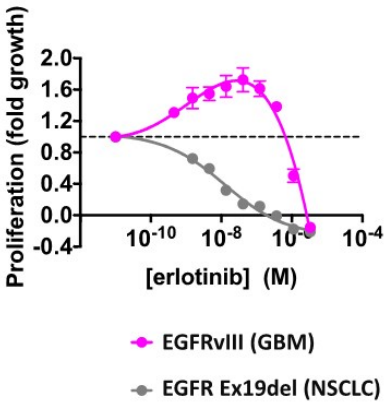


NSCLC Trial[2]





Paradoxical Activation of EGFR in GBM



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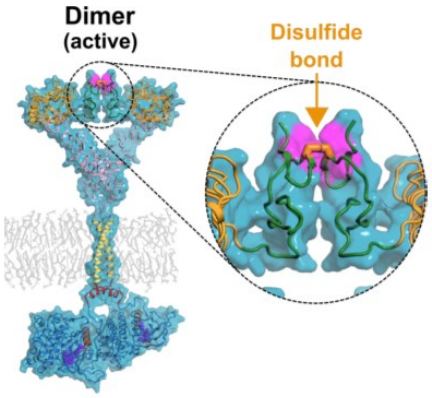
[1] Van den Bent et al JCO 2009
[2] Capuzzo et al Lancet 2010

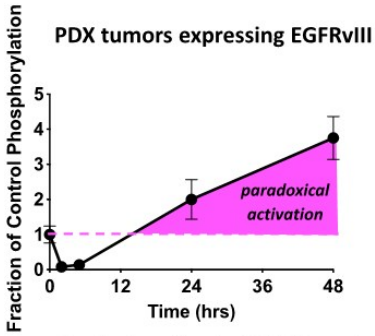
TKIs=Tyrosine Kinase Inhibitors.

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



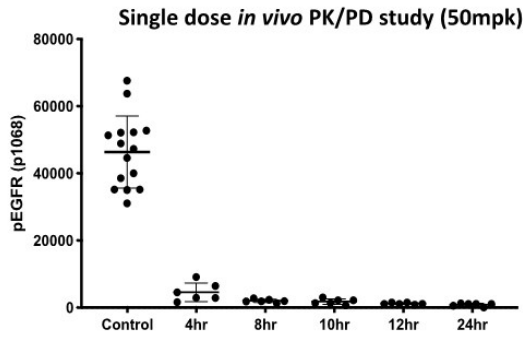
Single dose *in vivo* PK/PD study

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

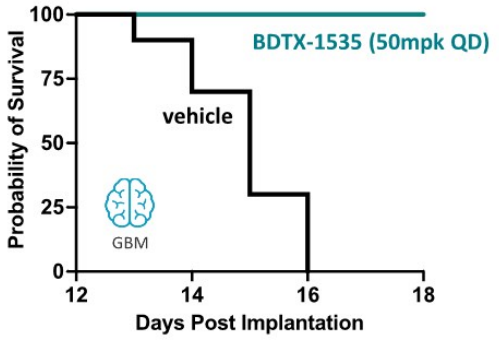
PK=Pharmacokinetics; PD=Pharmacodynamics; PDX=Patient-Derived Xenografts

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 PDX tumors

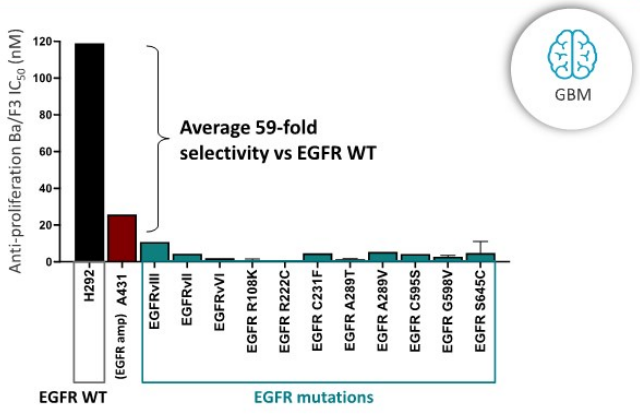


Average oral unbound brain fraction (Kp_{uu}) = 0.55 in Rats

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

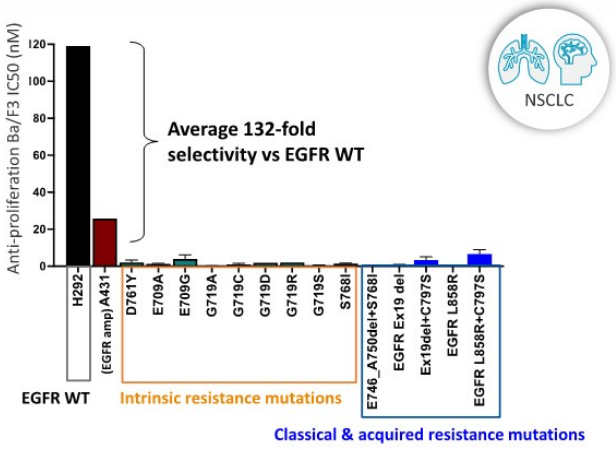
BDTX-1535 Optimized to Address a Wide Range of Oncogenic EGFR MasterKey Mutations and Amplification in GBM and NSCLC

EGFR variants and mutations prevalent in GBM



Average IC_{50} = 3.8 nM

EGFR mutations of intrinsic resistance and acquired resistance in NSCLC

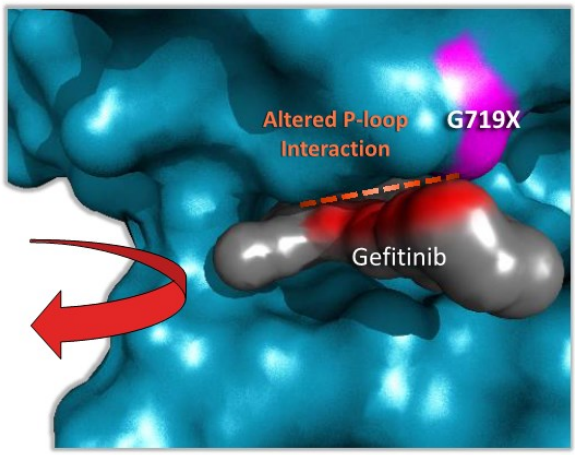


Average IC_{50} = 3.5 nM

BDTX-1535 Designed to Potently Inhibit EGFR Intrinsic and Acquired Resistance Mutations in NSCLC

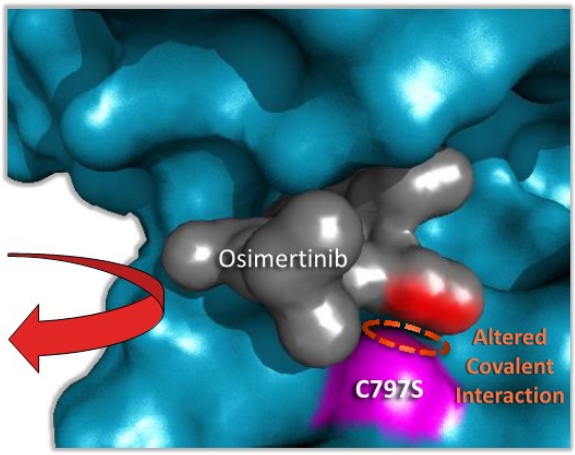
Intrinsic Resistance Mutations

Designed for potent & selective inhibition across mutant families



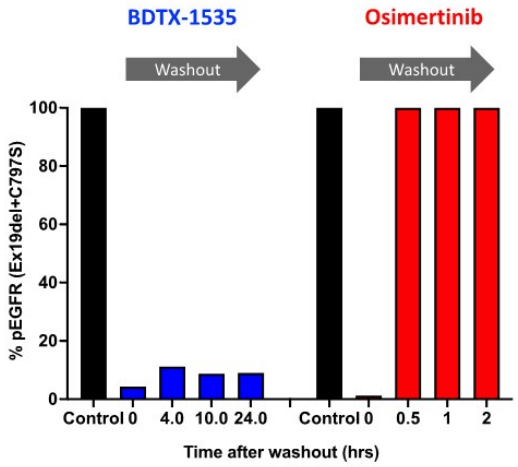
Acquired Resistance Mutations

Designed to covalently target C797 & C797S

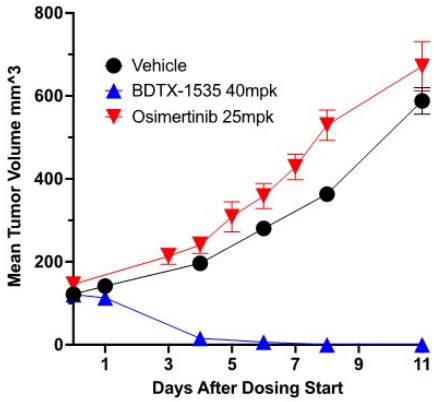


BDTX-1535 Achieves Dose-dependent Tumor Regression in EGFR Mouse Models, Including Acquired Resistance Mutation C797S

BDTX-1535 retains irreversible binding against C797S mutant



BDTX-1535 demonstrates dose-dependent tumor regression in EGFR Ex19del / C797S tumor model



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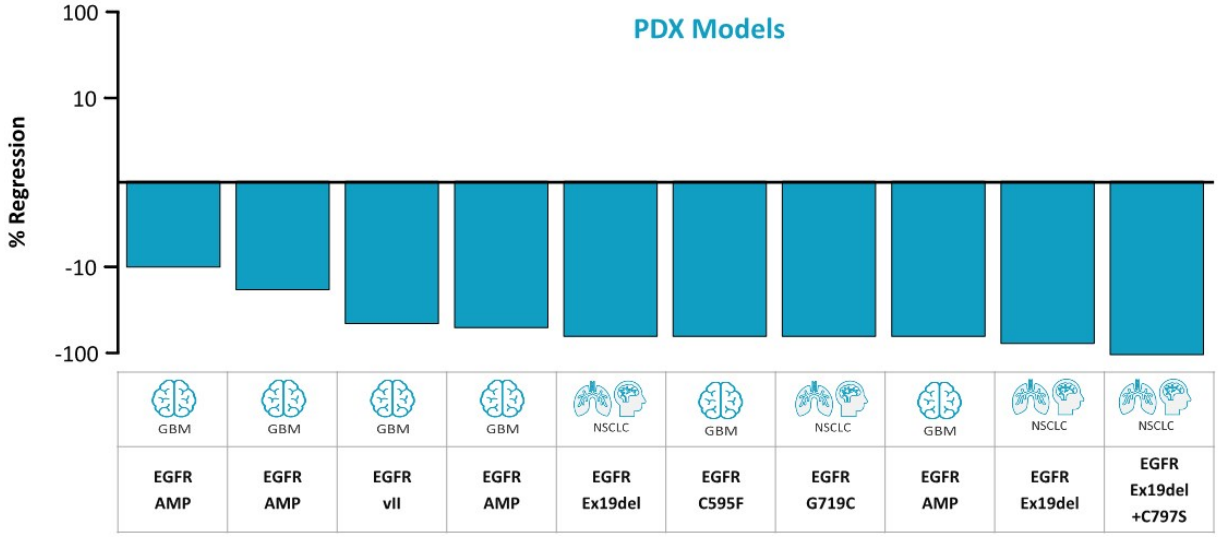
BDTX-1535 Promotes Regression Across Range of GBM & NSCLC PDX Tumors Expressing MasterKey EGFR Mutations & EGFR Amplification



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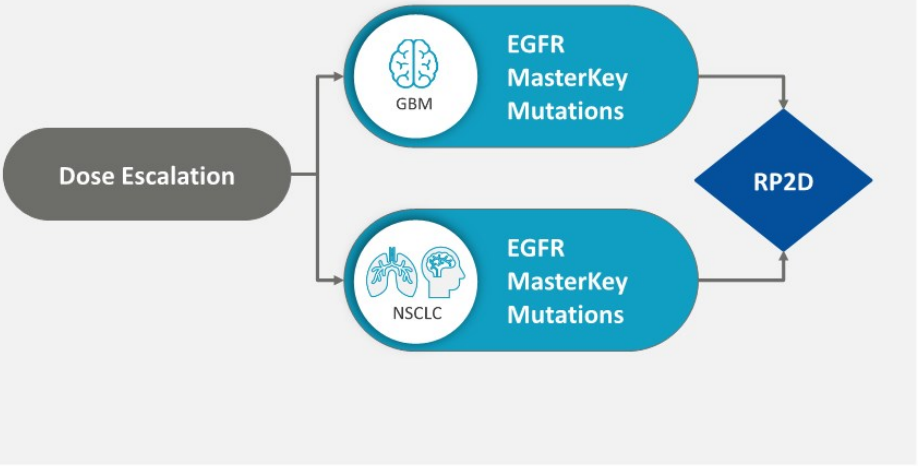
AMP=Amplification

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



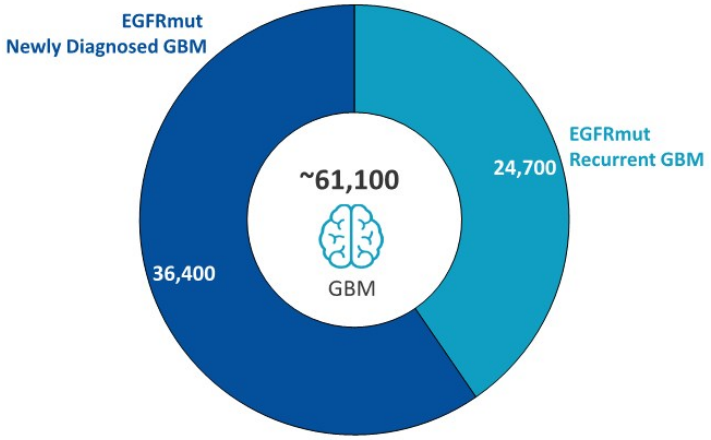
Selected Patient Population

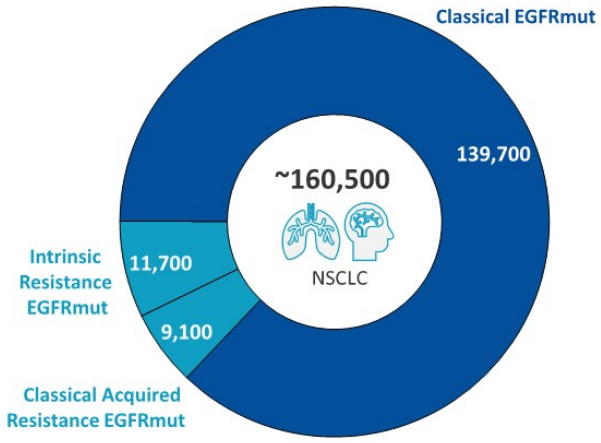
- GBM Patients with EGFR alterations
- NCSLC Patients with EGFR intrinsic resistance mutations
- NCSLC Patients with acquired EGFR resistance mutations

RP2D=Recommended Phase 2 Dose

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 Well Positioned to Address Unmet Needs in EGFR Mutant GBM/NSCLC

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

- Irreversible inhibition of GBM mutations to avoid paradoxical activation
- Irreversible binding to C797 and C797S acquired resistance in NSCLC
- Regression across panel of PDX tumor models harboring EGFR mutations in GBM and NSCLC

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

- Unbound brain fraction (Kp_{uu}) = 0.55 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-189
Inhibitor Targeting MasterKey EGFR/HER2 Mutations
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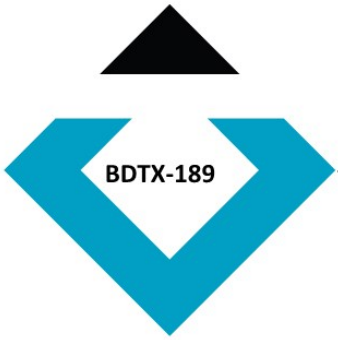
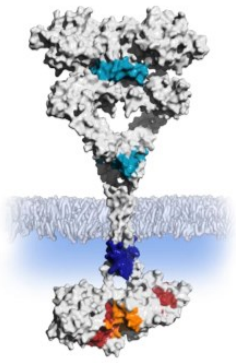
BDTX-189: MasterKey EGFR/HER2 Inhibitor, Early Proof-of-Concept Demonstrated



RP2D Achieved	FDA endorsed RP2D 800 mg QD non-fasting PK in-line with preclinical predictions
Favorable Safety	Well-tolerated, minimal evidence of systemic WT-EGFR related adverse events
Activity Observed	Anti-tumor activity in NSCLC EGFR Ex20ins and in HER2 amplified solid tumors
MasterKey-01 Clinical Trial	Continuing enrollment into Safety Expansion cohort to gate next steps in development

BDTX-189 is a Potent and Selective Inhibitor Across EGFR/HER2 MasterKey Mutation Family

Oncogenic MasterKey Mutation Family



EGFR/HER2

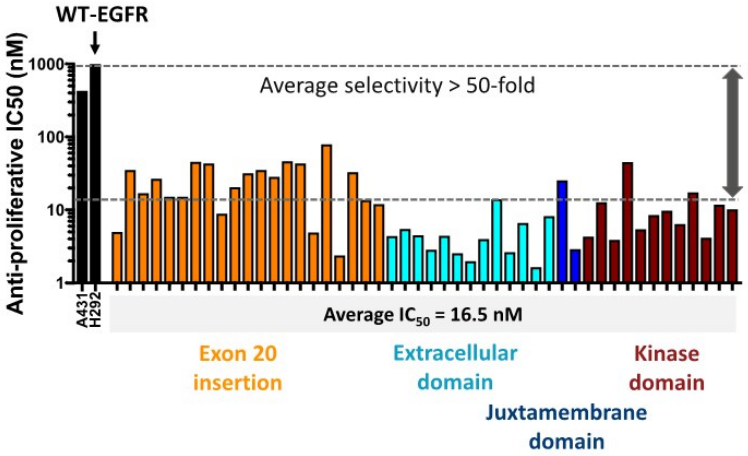
EC domain
17 mutants

JM domain
2 mutants

Ex 20 ins
24 mutants

Kinase domain
18 mutants

Phenotypic Activity Against MasterKey Mutation Family & Selectivity vs WT-EGFR



EC domain, extracellular domain; JM domain, juxtamembrane domain; Ex 20 ins, Exon 20 insertions

MasterKey-01 Dose Escalation Complete; Safety Expansion Enrolling

Safety Summary

- Safety dataset dose escalation QD cohorts n=59*
- n=18 at 800 mg QD fasting
- n=13 at 800 mg QD non-fasting

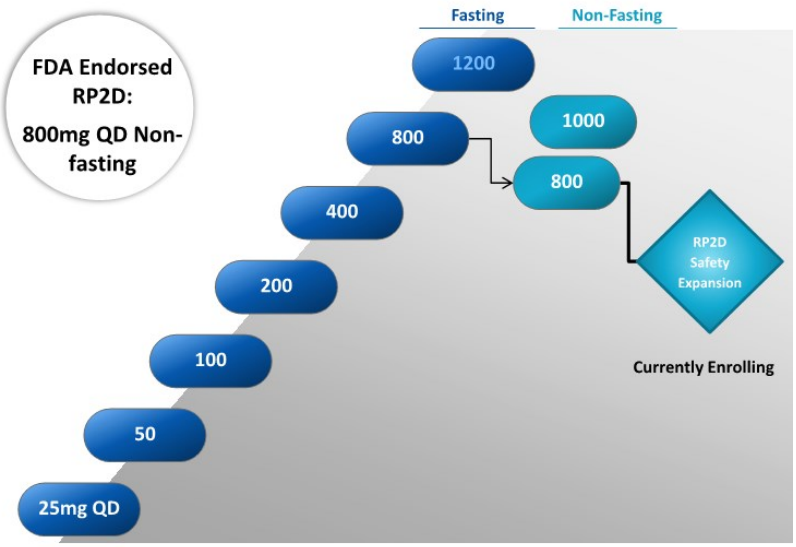
Recommended Phase 2 Dose (RP2D)

- 800 mg QD non-fasting
- Well tolerated, no DLTs at RP2D
- Most common AE grade 1 diarrhea, no AE ≥ grade 2
- Low rate of rash

Safety Expansion Cohort

- Gate future development as single agent and in combination

Phase 1 QD Dose Escalation



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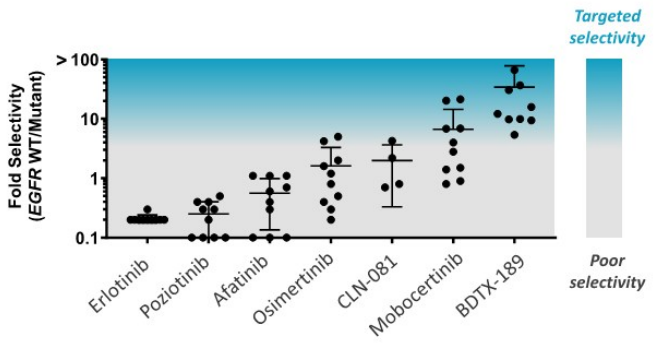
*Includes 18 patients from food-effect cohort; DLT=dose limiting toxicity; AE=adverse events

Improved Selectivity Drives Improved Safety – Potential to Limit Overlapping Toxicities in Combination

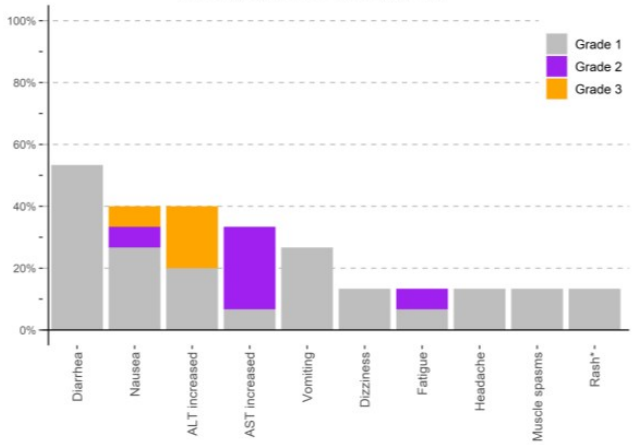
BDTX-189 designed for superior selectivity profile



Mutations assessed: *HER2* S310F, *HER2* P95, *HER2* R678Q, *HER2* L755S, *HER2* V777L, *HER2* YVMA, *HER2* GSP, EGFRvIII, *EGFR* NPH, *EGFR* ASV

Improved Safety - Limited skin and manageable gastro-intestinal toxicity at RP2D

Treatment related AEs by max grade observed in >10% of patients 800 mg QD, Non-fasting (N=15)



NCT04209465 is an ongoing study and is undergoing active data entry and cleaning. Includes AEs with start date prior to Oct. 30, 2021

*Rash = Dermatitis acneiform and Rash

NSCLC EGFR Ex 20 Ins: 51-year-old Woman with 53% Tumor Reduction at Week 12 and Improved Diffuse Lung Disease

Genomic alteration: EGFR Ex20ins (SVD), HER2-amp

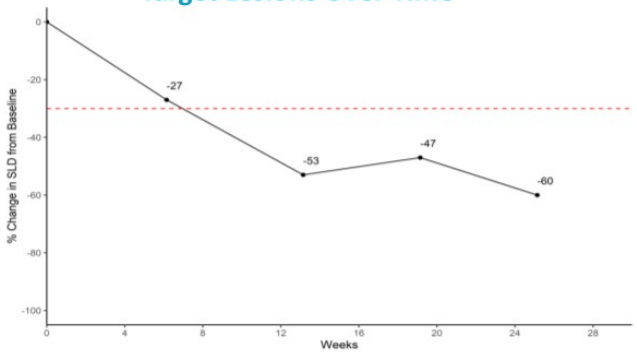
Prior therapy:

- Poziotinib with PR and toxicity followed by PD
- Carboplatin and pemetrexed

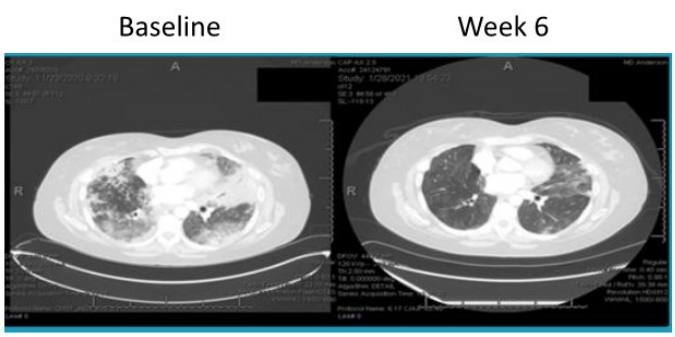
Response to BDTX-189:

- BDTX-189, 800 mg QD non-fasting
- Controlled, low-grade diarrhea
- Off oxygen starting at ~9 weeks
- On study with PR, beyond 14+ Cycles (10 months)

Target Lesions Over Time



Radiologic Scans



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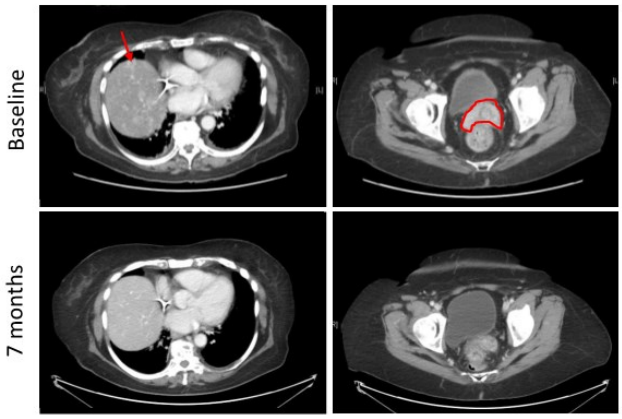
SLD=Sum of longest diameter; PR=partial response; PD=progressive disease

NCT04209465 is an ongoing study and is undergoing active data entry and cleaning. Includes data prior to 30 Oct 2021

Early PoC Achieved for BDTX-189 in Solid Tumors with HER2-Amp with Deep and Durable Confirmed PR Observed

Radiologic Scans



Cancer of Unknown Primary[a] (HER2 Amplification):
73-year-old Woman with Deep and Durable Confirmed PR

Genomic alteration: HER2-amplification

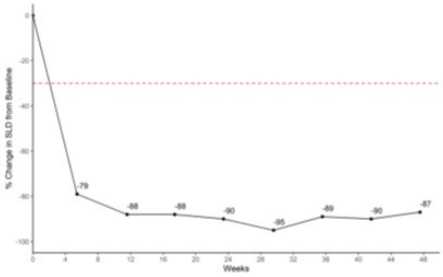
Prior therapy:

- Carbo/taxol, FOLFIRINOX, Everolimus

Response to BDTX-189:

- BDTX-189 800 mg QD fasting
- Had brief episodes of Grade 1 diarrhea
- Off study due to PD after 17+ Cycles (12 months)

Target Lesions Over Time



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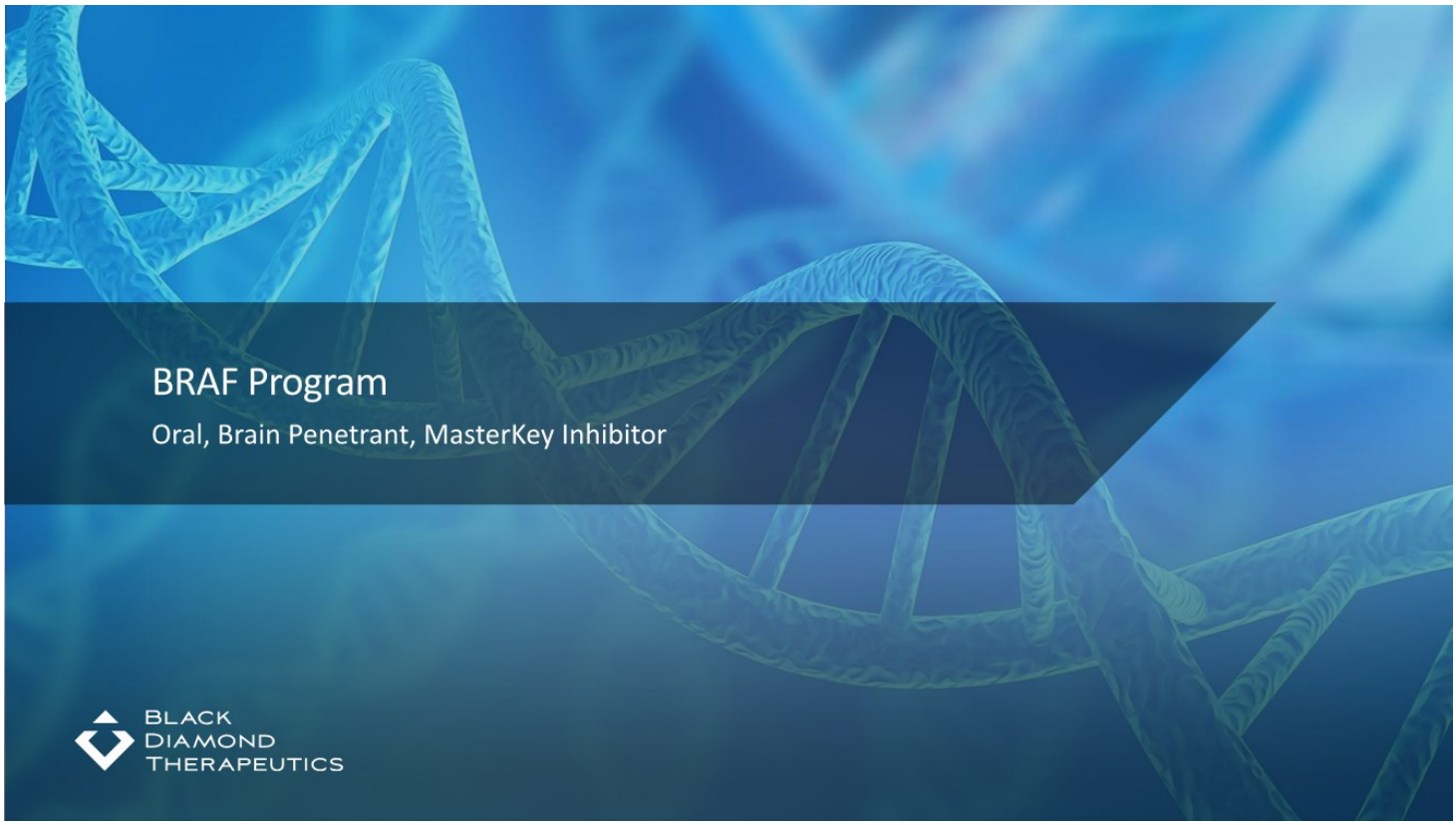
[a]CUP presumed by the investigator of this patient to be of breast cancer, pancreato-biliary or upper gastrointestinal origin.

NCT04209465 is an ongoing study and is undergoing active data entry and cleaning. Includes data prior to Oct. 30, 2021


BRAF Program
Oral, Brain Penetrant, MasterKey Inhibitor
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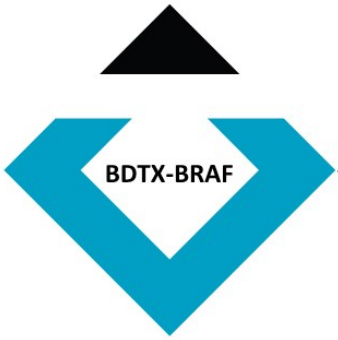
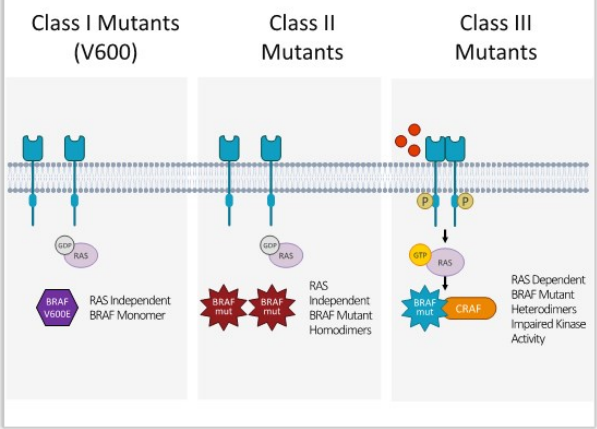
BDTX-BRAF: Oral, Brain Penetrant, Inhibitor of Oncogenic BRAF Mutations



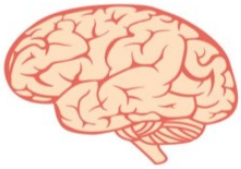
MasterKey Family	Designed for potent and selective inhibition of Class I, II, and III BRAF mutations
Brain Penetrant	Designed to be brain penetrant to treat CNS tumors
Avoids Paradoxical Activation	Inhibits dimerized RAF kinases and avoids paradoxical activation
Status	Initiation of IND-enabling studies expected in 2022

BDTX-BRAF: Designed with Potential *Best-In-Class* Target Product Profile

Potent Inhibition of All Three Class I / II / III BRAF Mutations



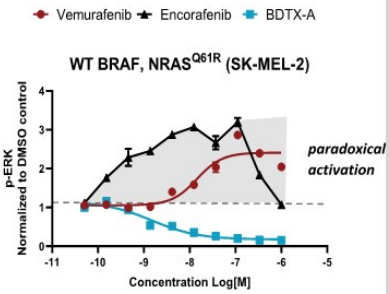
Brain Penetration



High incidence of CNS metastasis among tumors express BRAF mutations (lung, melanoma)

High prevalence of BRAF mutations in primary CNS malignancies (glioma)

Avoidance of Paradoxical Activation

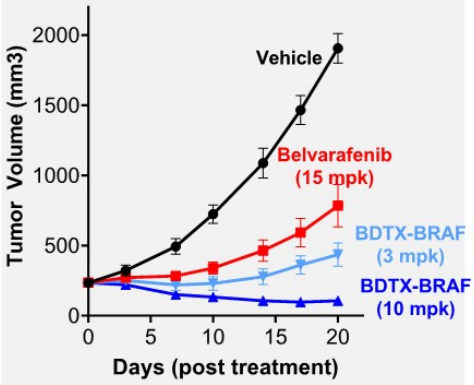


Designed for

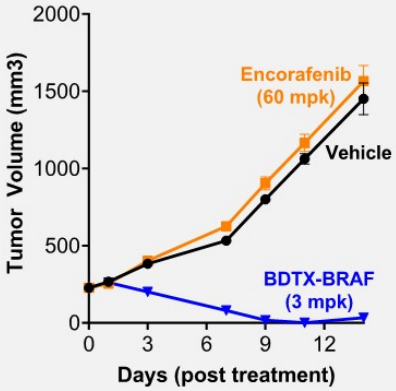
- Superior breadth & depth of activity
- Lack of cutaneous toxicity

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

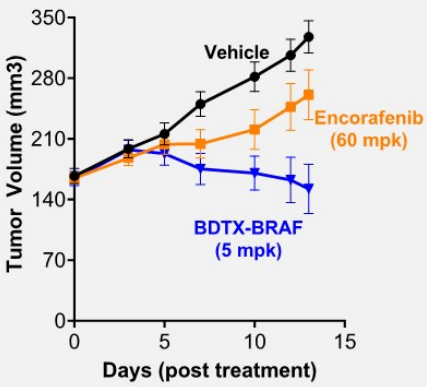
BRAF Class I
Mutant Tumor Model



BRAF Class II
Mutant Tumor Model

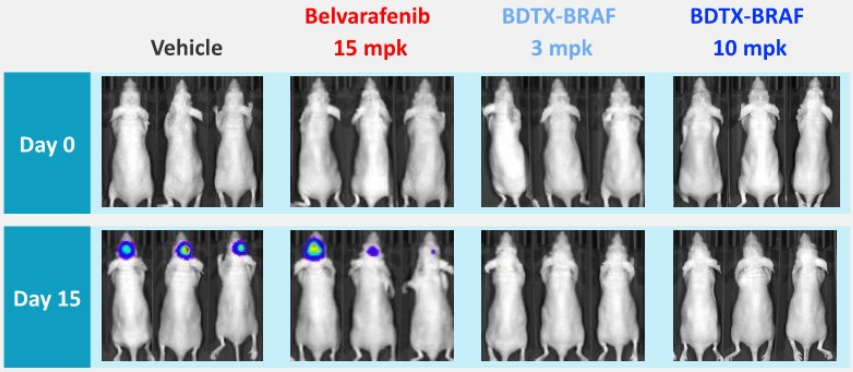


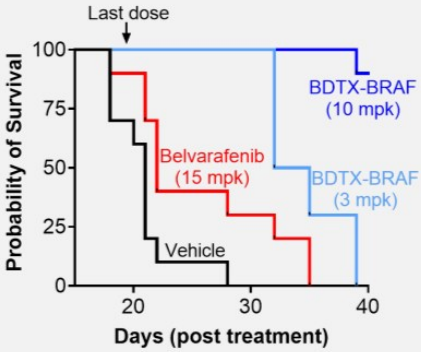
BRAF Class III
Mutant Tumor Model



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

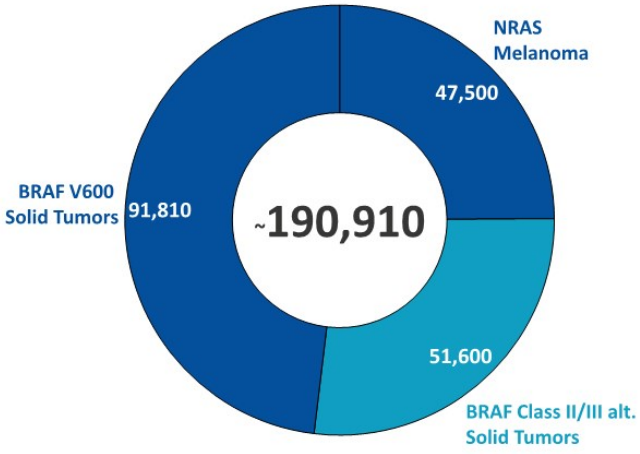
BDTX-BRAF prolongs survival in BRAF-V600E intracranial tumor model



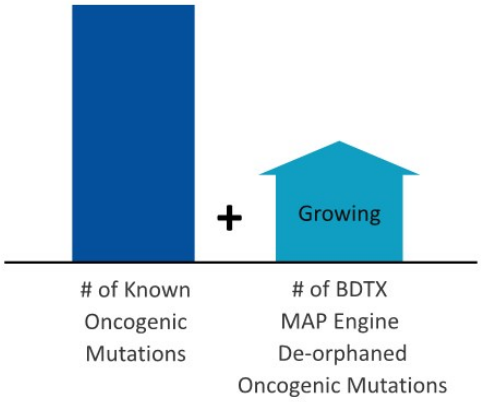


BDTX BRAF: Potential *Best-in-Class*, Masterkey Inhibitor For A Greater Number Of Patients With Overlooked Oncogenic Mutations

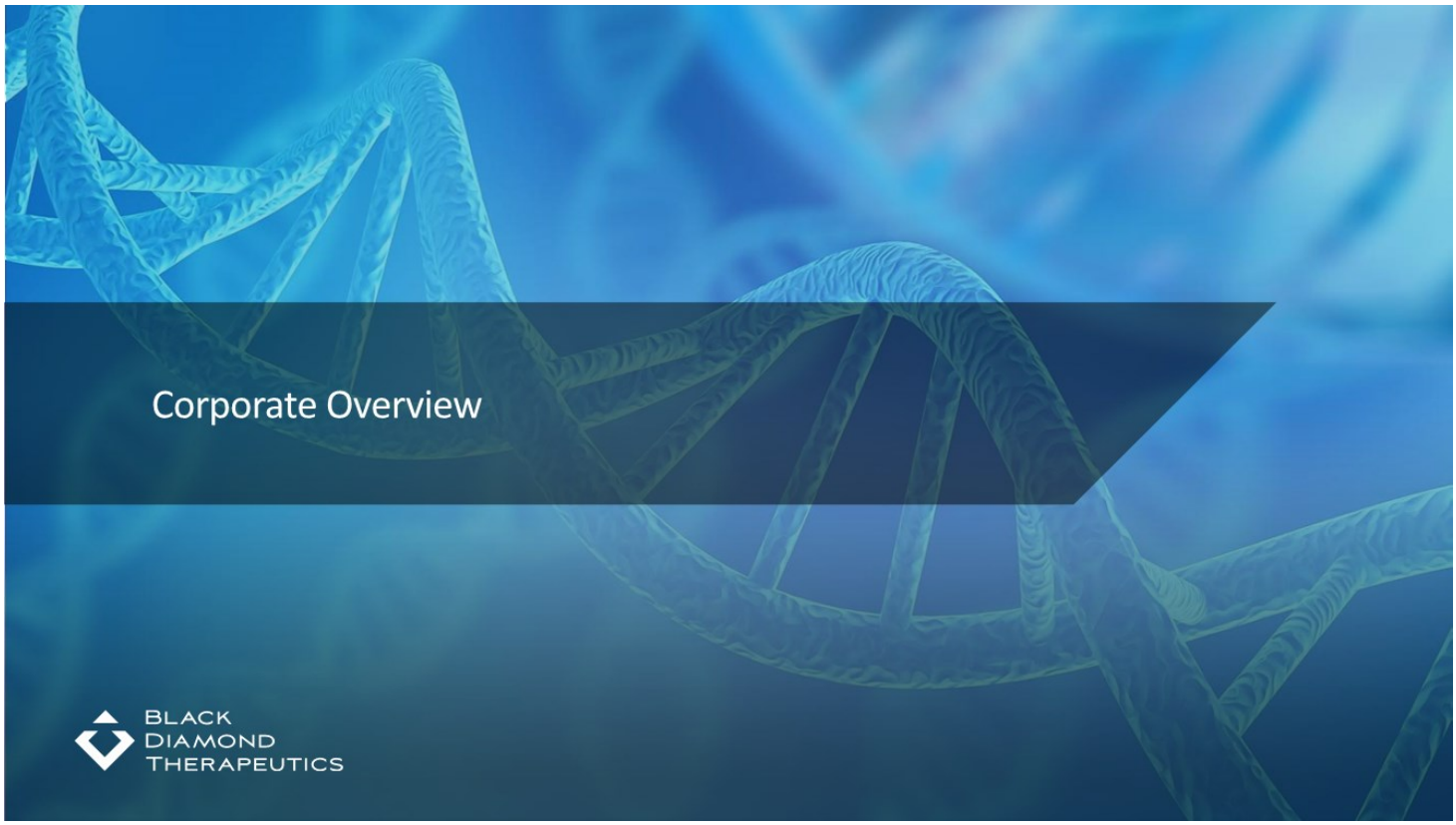
Addressable US / EU / JP Patient Population



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



Sources: EvaluatePharma Epi and GENIE/TCGA


Corporate Overview
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Deep Oncology and Small Molecule Drug Discovery and Development Experience

Leadership Team

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

OSI pharmaceuticals
Astellas
Duke-NUS 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

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

Radius
MERZ PHARMACIA

Karsten Witt, M.D.
Interim Chief Medical Officer

OSI pharmaceuticals
ARRAY BIOPHARMA
GILEAD

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General Partner, Hatteras Ventures

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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.
Venture Partner, Hatteras Ventures

Expanding Precision Medicine Through the Development of MasterKey Therapies

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

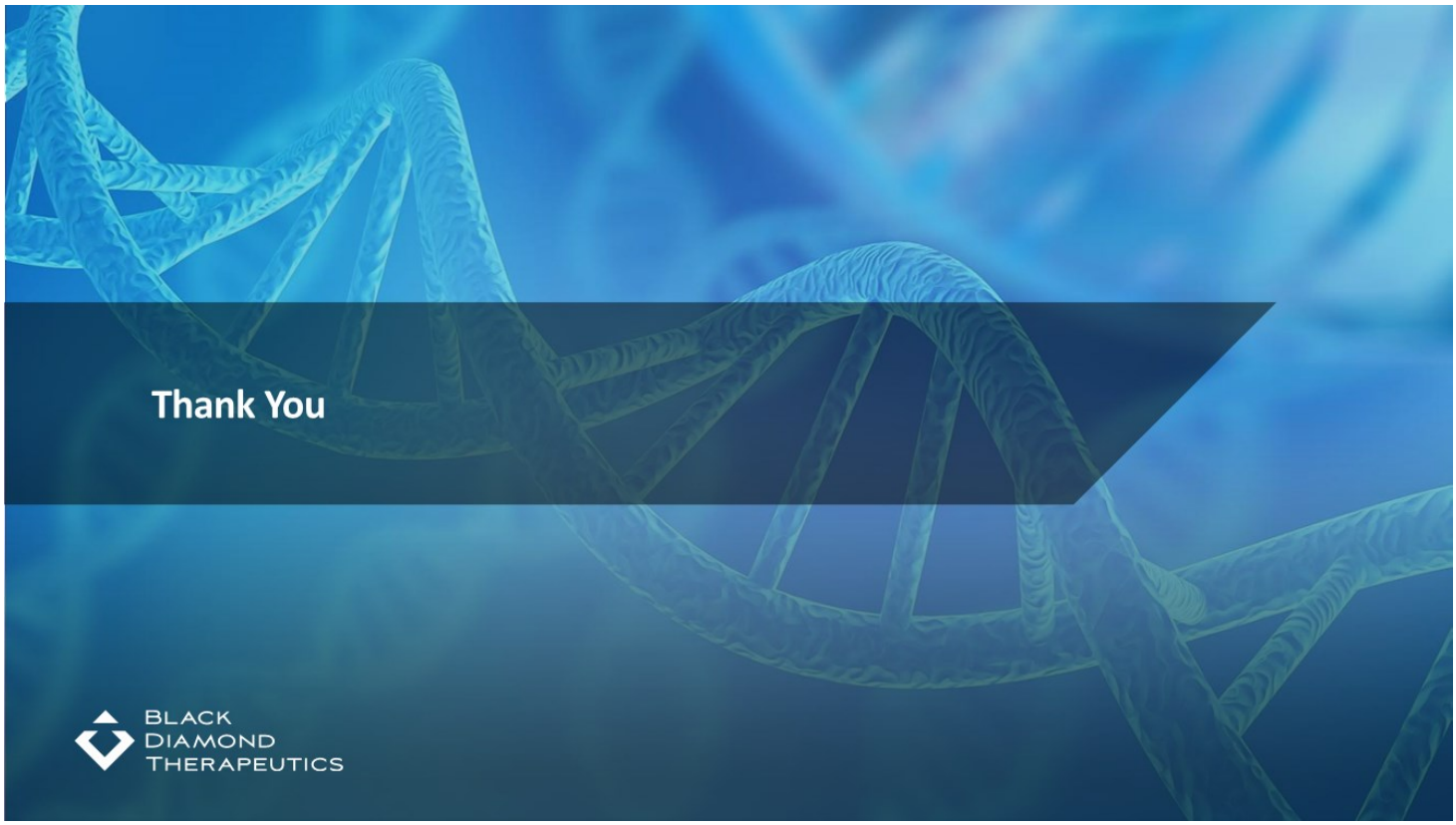
Proof-of-principle mutation family selective inhibitors; clinical and late-preclinical pipeline of MasterKey inhibitors derived from our MAP drug discovery engine: EGFR, HER2, BRAF, and FGFR

BDTX-1535, an irreversible, mutant selective, brain-penetrant EGFR inhibitor entering Phase 1 for the treatment of GBM and NSCLC driven by EGFR intrinsic & acquired resistance mutations

BDTX-189, a mutant selective EGFR/HER2 inhibitor in Phase 1 Safety Expansion study in patients expressing targeted oncogenic mutations

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
- Provides opportunities beyond oncology and small molecules


Thank You
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