Black Diamond Therapeutics Announces Initial Dose Escalation Data Demonstrating Anti-Tumor Activity of BDTX-1535 in Non-Small Cell Lung Cancer Patients Across Multiple EGFR Mutation Families

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- *BDTX-1535, an epidermal growth factor receptor (EGFR) MasterKey inhibitor, demonstrates clinical proof of activity for MasterKey mutation-targeting approach based on radiographic tumor responses and circulating tumor DNA changes in NSCLC patients with acquired resistance and intrinsic driver EGFR mutations*
- *Confirmed radiographic partial response by RECIST 1.1 achieved across predicted therapeutic doses in 5 of 12 NSCLC patients in subgroup with measurable disease, who underwent post baseline tumor assessment by RECIST1.1; one additional patient demonstrated unconfirmed PR awaiting confirmation, while the remaining six patients had stable disease*
- *Expansion cohorts expected to commence in second half of 2023 to assess ORR by RECIST 1.1 in NSCLC patients with EGFR-acquired resistance and intrinsic driver mutations after progression on a third-generation EGFR inhibitor*
- *Favorable tolerability profile observed with once-daily therapeutic doses to be further explored in NSCLC expansion cohorts*
- *Update on Phase 1 dose escalation data in GBM cohort anticipated in the fourth quarter of 2023*
- *Company to host investor conference call and webcast today at 8:00 a.m. ET*

CAMBRIDGE, Mass. and NEW YORK, June 27, 2023 (GLOBE NEWSWIRE) -- Black Diamond Therapeutics, Inc. (Nasdaq: BDTX), a clinical-stage precision oncology company developing MasterKey therapies that target families of oncogenic mutations in patients with genetically defined cancers, today announced initial clinical data from the dose escalation portion of the Phase 1 clinical study of BDTX-1535. BDTX-1535 is an investigational fourth-generation epidermal growth factor receptor (EGFR) MasterKey inhibitor being developed for the treatment of non-small cell lung cancer (NSCLC) and glioblastoma multiforme (GBM). The new data from the dose escalation portion of the Phase 1 study demonstrated clinical proof of activity of BDTX-1535 in NSCLC patients harboring both acquired resistance and intrinsic driver EGFR mutations.

“These initial safety and clinical activity data support the continued development of BDTX-1535 as a potential first and best-in-class treatment option for osimertinib-resistant NSCLC patients. Importantly, BDTX-1535 is the first EGFR TKI to show radiographic responses across NSCLC patients whose cancers are driven by diverse mutation families including acquired resistance mutations after osimertinib therapy, as well as in patients whose cancers are driven by classical and intrinsic driver mutations, providing clinical validation for our MasterKey approach of targeting families of mutations with a single drug,” said Sergey Yurasov, M.D., Ph.D., Chief Medical Officer of Black Diamond Therapeutics. “With a favorable tolerability profile in dose escalation, a long half-life to support once-daily dosing and ease of administration, we believe that BDTX-1535 has the potential to become an important treatment option for patients suffering from EGFR-mutated NSCLC. With these data in hand, we look forward to working with the FDA to define our recommended Phase 2 dose selection strategy and, ultimately, discussing a path to potential accelerated approval in NSCLC patients with newly diagnosed and recurrent intrinsic and acquired resistance EGFR mutations.”

“Intrinsic and acquired resistance to osimertinib remains a significant challenge for patients with EGFR-mutant lung cancers. There is a large unmet need to personalize therapies based on acquired EGFR resistance mechanisms post treatment with osimertinib but also an equally important unmet need to address intrinsic resistance, with a focus on EGFR mutation subtypes that do worse with current therapies such as EGFR L858R or atypical EGFR mutations such as EGFR exon 18 mutations. That is why a fourth-generation EGFR TKI that addresses intrinsic and acquired resistance by effectively targeting these EGFR alterations - combined with ease of administration and brain penetrance - may be an impactful treatment option for patients. I am eager to see BDTX-1535 continue to advance in the clinic,” said Helena Yu, M.D., Associate Attending Physician at Memorial Sloan Kettering Cancer Center.

BDTX-1535 Phase 1 Study Design

This Phase 1 first-in-human, open-label clinical trial of BDTX-1535 consists of dose escalation followed by dose expansion cohorts. The dose escalation part is based on a Bayesian Optimal Interval adaptive design to evaluate the safety, pharmacokinetics (PK), and preliminary anti-tumor activity of BDTX-1535 in adult patients with either advanced/metastatic NSCLC harboring EGFR mutations with or without central nervous system (CNS) disease, or recurrent GBM expressing EGFR alterations. Following the dose escalation portion, the study includes several disease specific expansion cohorts to assess objective response rate (ORR), CNS ORR and progression-free survival and further evaluate safety, tolerability and PK.

Initial Phase 1 Dose Escalation Data

As of the data cutoff date of May 20, 2023, a total of 51 patients (24 patients with recurrent EGFR+ NSCLC and 27 patients with recurrent GBM with EGFR alterations) were treated with BDTX-1535 in the dose-escalation portion of the Phase 1 clinical trial at seven dose levels ranging from 15mg to 400mg once-daily (QD). NSCLC patients (n=24) were heavily pretreated with a median of two prior therapies (range 1-9); all patients received prior treatment with EGFR TKI with the majority receiving osimertinib (79%) as first- or second-line treatment, 67% of patients receiving prior chemotherapy,

and 42% of patients receiving prior anti-angiogenesis drug or checkpoint inhibitors. All glioblastoma patients had a recurrent disease after standard of care surgery, radiation and chemotherapy. The Company will provide a clinical update on BDTX-1535 Phase 1 dose escalation data in recurrent GBM patients in the fourth quarter of 2023.

- The BDTX-1535 PK profile obtained during dose escalation in NSCLC and GBM patients showed a linear increase in exposure with an average half-life of approximately 15 hours that supports a daily dosing schedule with sufficient and sustained steady state target mutation coverage achieved at 100 mg QD dose level and above.
- BDTX-1535 was generally well tolerated by NSCLC and GBM patients and the overall safety profile was consistent with the EGFR tyrosine kinase inhibitor (TKI) class of drugs. The most common drug-related adverse events were mild to moderate rash, diarrhea, stomatitis, paronychia, nausea and fatigue. No patients experienced dose limiting toxicity at 15-200 mg QD doses. One of 15 patients treated at the 300 mg QD dose experienced dose limiting diarrhea and 5 of 12 patients at the 400 mg QD dose experienced dose limiting toxicity (diarrhea, 2 patients; rash, stomatitis, fatigue and decreased appetite, 1 patient each). No unexpected safety signal was identified during dose escalation.
- Based on additional data updates as of June 16, 2023, 5 of 12 NSCLC patients in a subgroup, who had measurable disease at study start, and underwent post baseline tumor assessment by RECIST1.1, demonstrated radiographic confirmed partial response (PR). One additional patient demonstrated unconfirmed PR awaiting confirmation, while the remaining six patients had stable disease.
- Confirmed PRs were observed in NSCLC patients with a wide range of EGFR mutations including classical and intrinsic driver mutations and acquired C797S resistance mutation, as well as complex mutations that include a combination of classical, intrinsic, and acquired resistance mutations. Radiographic improvement of CNS metastasis was documented in 2 NSCLC patients.
- Based on emerging PK, safety, tolerability and radiographic response data, enrollment will commence at the BDTX-1535 200 mg QD dose in two expansion cohorts of NSCLC patients with acquired resistance or intrinsic driver mutations who received up to two prior lines of therapy including a third-generation EGFR TKI. Additional doses may be further evaluated after review of the totality of dose escalation data during a meeting with the U.S. Food and Drug Administration (FDA) later in 2023. The objective of expansion cohorts will be ORR by RECIST 1.1 and durability of response to support future discussion with the FDA of a potential accelerated approval path in EGFR-mutated NSCLC. In addition, BDTX plans to open an expansion cohort in newly diagnosed NSCLC patients with intrinsic driver mutations after discussion with the FDA.

Black Diamond anticipates the following key milestones for BDTX-1535:

- Initiation of the dose expansion cohorts of NSCLC patients with EGFR acquired resistance and intrinsic driver mutations after progression on third generation EGFR TKI with the objective of ORR by RECIST 1.1 in the second half of 2023
- Presentation of the full BDTX-1535 dose escalation data in NSCLC at a medical conference in the fourth quarter of 2023
- Meeting with the FDA in the fourth quarter of 2023 to align on dosing strategy to enable a potential accelerated approval pathway in NSCLC
- Initiation of an expansion cohort in newly diagnosed NSCLC patients with intrinsic driver mutations after discussion with the FDA
- Clinical update on BDTX-1535 Phase 1 dose escalation data in recurrent GBM patients in the fourth quarter of 2023

Conference Call Information

Black Diamond will host a conference call and webcast on Tuesday, June 27, 2023, at 8:00 a.m. ET to discuss the initial results from the Phase 1 dose escalation study of BDTX-1535 in patients with NSCLC. The webcast may be accessed online here or by visiting the Events page in the Investors section of the Company's website at www.blackdiamondtherapeutics.com.

A replay of the webcast will be available for 30 days on the Investors section of Black Diamond's website.

About Black Diamond Therapeutics

Black Diamond Therapeutics is a clinical-stage precision oncology medicine company focused on the development of MasterKey therapies that target families of oncogenic mutations in clinically validated targets. Black Diamond leverages a deep understanding of cancer genetics and onco-protein structure and function, to discover and develop innovative MasterKey therapies. The Company's MasterKey therapies are designed to overcome resistance, minimize on-target, wild-type mediated toxicities, and be brain-penetrant to address significant unmet medical needs of patients with genetically defined cancers. The Company is advancing a robust pipeline with lead clinical-stage program BDTX-1535, targeting MasterKey mutations in both EGFR mutant-positive NSCLC and in GBM, and BDTX-4933, a program targeting RAF MasterKey mutations in solid tumors, as well as discovery-stage research programs. The Company's proprietary MAP drug discovery engine is designed to allow Black Diamond to analyze population-level genetic sequencing tumor data and validate MasterKey mutations. 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 BDTX-1535 development program, including the initiation of the dose expansion cohorts of BDTX-1535 in NSCLC patients, presentation of the full BDTX-1535 dose escalation data in NSCLC, a potential accelerated approval pathway for BDTX-1535 in NSCLC and the upcoming clinical update on BDTX-1535 in recurrent GBM patients. 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 those risks and uncertainties set forth in its Annual Report on Form 10-K for the year ended December 31, 2022, filed with the United States Securities and Exchange Commission and in its subsequent 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.

Contacts

For Investors:
Julie Seidel, Stern Investor Relations
(212) 362-1200
investors@bdtx.com

For Media:
Kathy Vincent
kathy@kathyvincent.com
media@bdtx.com