Black Diamond Therapeutics Announces First Patients Dosed in Phase 1 Clinical Trial Expansion Cohorts Evaluating BDTX-1535 in Patients with Intrinsic Driver and Acquired Resistance EGFR Mutation Positive Non-Small Cell Lung Cancer

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Company to present BDTX-1535 dose escalation data in NSCLC at the AACR-NCI-EORTC Conference in October 2023

CAMBRIDGE, Mass. and NEW YORK, Sept. 11, 2023 (GLOBE NEWSWIRE) -- Black Diamond Therapeutics, Inc. (Nasdaq: BDTX), a clinical-stage precision oncology company developing therapies that target families of oncogenic mutations in patients with genetically defined cancers, today announced the first patients dosed in mutation matched expansion cohorts of non-small cell lung cancer (NSCLC) in the ongoing Phase 1 clinical study evaluating BDTX-1535.

BDTX-1535, a fourth-generation, brain-penetrant epidermal growth factor receptor (EGFR) MasterKey tyrosine kinase inhibitor (TKI), is under investigation for the treatment of NSCLC harboring intrinsic driver and/or acquired resistance (post-osimertinib) EGFR mutations and glioblastoma multiforme (GBM) with multiple EGFR alterations. The BDTX-1535 expansion cohort portion of the study will assess single-agent objective response rate (ORR) in a second- or third-line setting in NSCLC patients with EGFR intrinsic driver and/or acquired resistance mutations, who have received prior treatment with approved EGFR TKI.

The dosing of the first patients in the expansion cohorts follows the Company's initial data readout from the dose escalation portion of the BDTX-1535 Phase 1 clinical study, which demonstrated clinical proof of activity through radiographic responses in NSCLC patients harboring diverse types of EGFR mutations including intrinsic driver and post-osimertinib acquired resistance EGFR mutations.

"The Phase 1 expansion cohorts will assess objective response rate and durability of response in NSCLC patients whose disease has progressed after prior EGFR inhibitor therapy, including prior osimertinib, and who have evidence of a variety of EGFR driver or resistance mutations that are targeted by BDTX-1535," said Sergey Yurasov, M.D., Ph.D., Chief Medical Officer of Black Diamond Therapeutics. "In conjunction with establishing an optimal dose for a future pivotal study, these efficacy data will be essential for establishing a regulatory pathway for BDTX-1535. Despite significant recent advances in treating lung cancer, there is a large unmet medical need for a targeted therapy for these EGFR mutation-positive NSCLC patients, for whom chemotherapy is still the most common treatment option."

"Dosing of the first patients in the BDTX-1535 dose expansion cohorts represents an important step towards offering an oral therapeutic with manageable side effects as a potential alternative to chemotherapy-based regimens following progression on osimertinib for patients with treatment-resistant lung cancer," said David Epstein, Ph.D., President and Chief Executive Officer of Black Diamond Therapeutics. "The population of EGFR mutation-positive NSCLC is genetically heterogeneous – which has presented challenges in the development of effective therapies. BDTX-1535 was designed to disrupt the limited existing treatment paradigm by addressing real-world patterns of patient-specific EGFR mutations, and we remain focused on the rapid advancement of this novel MasterKey inhibitor."

The discovery and development of BDTX-1535 was informed by the Company's powerful Mutation-Allostery-Pharmacology (MAP) drug discovery engine, which leverages critical genomic profiling to expand the addressable patient population by targeting families of mutations with a single drug. Emergence of intrinsic driver and acquired resistance EGFR mutations to osimertinib represents a significant unmet need for patients with EGFR-mutant lung cancer. Thirteen percent of patients in the U.S. with EGFR mutation-positive NSCLC show presence of intrinsic driver mutations, which are associated with worse clinical outcomes when treated with currently approved EGFR TKIs. Fifteen percent of patients in the U.S. whose disease has progressed after osimertinib therapy show evidence of acquired resistance EGFR mutations (e.g., C797S) for which currently there is no approved EGFR TKI.

The Company is advancing BDTX-1535 as a potential targeted therapy option for patients with this broad spectrum of EGFR mutations in second-line NSCLC, and plans to investigate safety and efficacy in a first-line setting in NSCLC patients with intrinsic driver EGFR mutations after discussion with the U.S. Food and Drug Administration (FDA).

BDTX-1535 Phase 1 Clinical Study Design
The Phase 1 first-in-human, open-label clinical trial of BDTX-1535 (NCT05256290) consists of a dose escalation portion that evaluated the safety, pharmacokinetics (PK), and preliminary anti-tumor activity of BDTX-1535 followed by dose expansion cohorts. The trial is evaluating BDTX-1535 in patients with advanced/metastatic NSCLC harboring EGFR mutations with or without central nervous system (CNS) disease, or with recurrent GBM expressing EGFR alterations. The Phase 1 dose escalation portion of the study in NSCLC and GBM patients has been completed and the study is now progressing to evaluate BDTX-1535 as a single agent, second-line or third-line therapy in two cohorts of EGFR mutation-positive NSCLC patients with progressive disease after prior therapy with EGFR TKI (e.g., osimertinib) to assess ORR, CNS ORR, duration of response, and progression-free survival and further evaluate safety, tolerability and PK:

- Second- or third-line NSCLC patients with acquired EGFR resistance mutations +/- CNS metastasis; and
- Second- or third-line NSCLC patients with EGFR intrinsic driver mutations +/- CNS metastasis.

About Black Diamond Therapeutics
Black Diamond Therapeutics is a clinical-stage precision oncology medicine company focused on the development of 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 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. 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 continuation of the BDTX-1535 dose expansion cohorts in EGFR mutation positive NSCLC patients, the expected timing for data updates for BDTX-1535 and presentation of the full BDTX-1535 dose escalation data in NSCLC, and the continued development of the MAP drug discovery engine. 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.

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