Black Diamond Therapeutics Presents Trial in Progress Poster for BDTX-1535 and Preclinical Data on BDTX-1535 and BDTX-4933 at the 2023 American Association of Cancer Research Annual Meeting

April 17, 2023

- *BDTX-1535 Phase 1 dose escalation ongoing in NSCLC harboring sensitizing EGFR mutations with or without CNS disease and recurrent GBM expressing EGFR alterations; Dose expansion cohorts expected to open in 2023*
- *In preclinical tumor models, BDTX-4933 exhibits potent inhibition of aberrantly activated RAF as result of BRAF Class I, II, III and RAS mutations, as well as high brain penetration demonstrating survival benefit in intracranial BRAF mutant tumor model; Phase 1 clinical study expected to initiate in the second quarter of 2023*

CAMBRIDGE, Mass and NEW YORK, April 17, 2023 (GLOBE NEWSWIRE) -- Black Diamond Therapeutics, Inc. (Nasdaq: BDTX), a clinical-stage precision oncology medicine company developing MasterKey therapies designed to overcome limitations of existing therapies by targeting families of oncogenic driver mutations in patients with genetically defined cancers, today announced the presentation of three posters highlighting the design of the phase 1 clinical study of BDTX-1535 and new preclinical data on BDTX-1535 and BDTX-4933 at the 2023 American Association of Cancer Research (AACR) Annual Meeting being held in Orlando, Florida.

“Black Diamond’s MasterKey approach to precision oncology medicines is grounded in our deep understanding of the characterization of oncogenic mutations, and these presentations highlight the depth of our work to expand the addressable patient population for precision oncology. With an everchanging treatment landscape for genetically defined cancers, we believe that our approach to grouping our targets into druggable oncogene families presents a truly differentiated opportunity to address the continuing unmet need of patients,” said Elizabeth Buck, Ph.D., Chief Scientific Officer of Black Diamond. “Our MAP Drug Discovery Engine has enabled us to intricately design MasterKey inhibitors based on extensive preclinical and real-world data, elucidating what we believe to be the necessary attributes for effectively targeting shared, activated conformations used by oncogenic drivers for tumor growth. Our fourth-generation irreversible brain penetrant EGFR MasterKey inhibitor, BDTX-1535, has demonstrated its ability to achieve potent anti-tumor activity against EGFR alterations and amplifications in a broad range of preclinical NSCLC and GBM models and we look forward to continuing to advance its development in the clinic and providing a first clinical update in the second half of this year. Our next most advanced program, BDTX-4933 was designed to be brain penetrant and selectively inhibits aberrant RAF signaling as result of BRAF class I, II, III and RAS oncogenic mutations without inducing paradoxical activation. We are encouraged by the results shared today, which support its potentially best-in-class profile.”

BDTX-1535 Program:

Black Diamond presented two posters highlighting BDTX-1535’s preclinical development as well as the ongoing Phase 1 study.

In a poster titled, “Discovery of BDTX-1535, a novel brain penetrant, irreversible, potent, wild type sparing EGFR MasterKey inhibitor that targets oncogenic kinase domain mutations as well as extracellular domain alterations for the treatment of NSCLC and GBM,” Black Diamond outlined the unmet need for next generation EGFR inhibitors that target classical driver mutations as well as acquired and intrinsic resistance mutations expressed in the context of EGFR driver mutations in non-small cell lung cancer (NSCLC), and EGFR alterations expressed in glioblastoma multiforme (GBM). Additional highlights include:

- While EGFR C797S substitution is a frequently reported post-osimertinib resistance mutation, real world evidence indicates the emergence of other EGFR alterations that lead to resistance to osimertinib including EGFR kinase domain mutations (e.g., S768I), extracellular domain alterations (e.g., EGFRvIII, A289X), and EGFR amplification.
- A family of extracellular domain EGFR alterations occurs in nearly 50% of GBM patients and these alterations are clinically resistant to all current generation inhibitors.
- Real world data in GBM demonstrates EGFR alterations often co-occur and persist throughout treatment with current standard of care therapy. Black Diamond observed that the oncogenic isoform of EGFR in GBM is a covalent homo-dimer which can be formed and paradoxically activated by the binding of reversible EGFR inhibitors.
- Black Diamond concluded that an effective EGFR inhibitor should meet four design principles and be: 1) potent and selective against a broad family of intracellular, extracellular EGFR oncogenic alterations and amplification, 2) wild type EGFR sparing, 3) irreversible to avoid paradoxical activation, and 4) central nervous system (CNS) penetrant.

In a poster titled, “A Phase 1 Study to Assess BDTX-1535, an Oral EGFR Inhibitor, in Patients with Glioblastoma or Non-Small Cell Lung Cancer,” Black Diamond outlined its ongoing Phase 1, open-label, multicenter study to assess the safety, tolerability, pharmacokinetics, CNS penetrance and preliminary antitumor activity of BDTX-1535 in recurrent GBM (rGBM) or locally advanced or metastatic NSCLC with or without CNS disease. Key highlights include:

- The monotherapy dose escalation portion will evaluate BDTX-1535 in patients with either rGBM expressing EGFR alterations or locally advanced/metastatic NSCLC harboring sensitizing EGFR mutations with or without CNS disease.
- Patients with rGBM must have previously received available standard therapy of surgical resection followed by

chemoradiotherapy and/or temozolomide (TMZ). Eligible NSCLC patients must have EGFR mutated NSCLC that has progressed following standard of care EGFR inhibitor therapy.

- Following the establishment of a provisional recommended Phase 2 dose, BDTX-1535 monotherapy will be explored in the following dose expansion cohorts to further evaluate safety, pharmacokinetics (PK), and preliminary assessment of efficacy: 1) rGBM with confirmed EGFR alterations, 2) NSCLC with uncommon EGFR mutations following EGFR inhibitor therapy, and 3) NSCLC with acquired EGFR resistance mutation(s) following a 3rd generation EGFR inhibitor in the first-line setting. NSCLC patients may enroll with or without CNS metastases and must not be known to express excluded resistance mutations such as EGFR T790M or MET.
- BDTX-1535 will also be studied in combination with TMZ to assess safety, tolerability, and a recommended combination dose for the treatment of patients with rGBM harboring EGFR mutations or variants.
- Enrollment was initiated in 2022 and dose escalation is ongoing. Dose Expansion cohorts are expected to open in 2023.

Black Diamond remains on track to provide a clinical update on BDTX-1535 in the second half of 2023.

BDTX-4933 Program:

In a poster titled, “Preclinical characterization of a brain penetrant RAF inhibitor, BDTX-4933, targeting oncogenic BRAF Class I/II/III and RAS mutation,” Black Diamond outlined its approach to characterizing BRAF, RAS and MAPK pathway in addition to the design and preclinical development of BDTX-4933:

- Mutations in BRAF and RAS are often oncogenic and lead to a constitutively active MAPK pathway that promotes aberrant cell proliferation and tumor growth.
- BDTX-4933 is a potent, reversible, CNS penetrant RAF MasterKey inhibitor designed to target a large family of oncogenic BRAF class I, II, III and RAS mutants.
- In a panel of cancer cell lines that endogenously express BRAF or RAS mutations, BDTX-4933 demonstrated inhibition of the MAPK pathway signaling without paradoxical activation, resulting in potent inhibition of cellular proliferation.
- In tumor models in vivo, BDTX-4933 showed target engagement, inhibiting ERK phosphorylation, achieving strong anti-tumor activity and tumor regression across tumor models driven by either BRAF or RAS mutations.
- BDTX-4933 exhibits high CNS exposure leading to dose-dependent tumor growth inhibition, and survival benefit in an intracranial tumor model harboring oncogenic BRAF mutation.
- Based on preclinical data, BDTX-4933 has a potential best-in-class profile to treat cancer patients harboring oncogenic BRAF Class I, II, III and RAS mutations, with or without brain disease.

Black Diamond expects to initiate a Phase 1 clinical trial of BDTX-4933 in patients with tumors harboring all-class BRAF or RAS mutations in the second quarter of 2023.

The posters from the AACR Annual Meeting are available on the “Scientific Presentations and Publications” section of the Black Diamond Therapeutics 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 non-small cell lung cancer (NSCLC) and in glioblastoma multiforme (GBM), and BDTX-4933, a program targeting RAF MasterKey mutations in solid tumors, as well as discovery-stage research programs. 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 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 continued development and advancement of BDTX-1535 and BDTX-4933, including the ongoing Phase 1 clinical trial and the expected timing for data updates for BDTX-1535 and the timing for initiating a Phase I clinical trial of BDTX-4933. 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.

Contact:

Julie Seidel, Stern Investor Relations

(212) 362-1200

investors@bdtx.com

media@bdtx.com