Black Diamond Therapeutics Presents Dose Escalation Data Demonstrating Durable Responses in Patients with NSCLC from Phase 1 Trial of BDTX-1535

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Initial results from BDTX-1535 dose escalation show durable activity in patients with NSCLC across heterogeneous EGFR mutation subtypes

No new safety or tolerability signal reported across all three active once daily doses of 100mg, 200mg and 300mg

Initial NSCLC expansion cohort data expected in 2024

Initial GBM dose escalation data expected later this year

CAMBRIDGE, Mass. and NEW YORK, Oct. 14, 2023 (GLOBE NEWSWIRE) -- Black Diamond Therapeutics, Inc. (Nasdaq: BDTX), a clinical-stage oncology company developing MasterKey therapies that target families of oncogenic mutations in patients with genetically defined cancers, today presented results demonstrating encouraging response durability of BDTX-1535 in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC). BDTX-1535, a fourth-generation, brain-penetrant epidermal growth factor receptor (EGFR) inhibitor, is under investigation in a Phase 1 clinical trial for patients with NSCLC or glioblastoma multiforme (GBM). The NSCLC results were disclosed in a poster presentation on October 14, 2023 at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Boston.

The findings expand upon the initial dose escalation results disclosed on June 27, 2023, which showed anti-tumor activity of BDTX-1535 in patients with NSCLC across heterogeneous EGFR mutation subtypes (including acquired resistance C797S mutation, intrinsic driver mutations, e.g., L747P, L718Q, as well as complex mutations). Data shared at the 2023 AACR-NCI-EORTC conference reflects 27 patients with advanced/metastatic NSCLC who received a range of doses spanning 25mg to 400mg once daily. A poster titled “Phase 1 Study of BDTX-1535, an Oral 4th Generation Inhibitor, in Patients with Non-Small Cell Lung Cancer and Glioblastoma: Preliminary Dose Escalation Results” shows that BDTX-1535 achieved:

- **Drug exposures providing target coverage.** Pharmacokinetic (PK) analyses demonstrated that doses at or above 100mg provide sufficient drug levels to cover all relevant mutations over a 24-hour period following once daily oral administration.
- **Favorable emerging safety profile.** The majority of adverse events (AEs) at doses of 100mg and 200mg were mild or moderate, and no unexpected safety signals were identified. No dose limiting toxicities (DLTs) were observed at or below 200mg dose level.
- **Circulating tumor DNA (ctDNA) clearance.** Eradication of targeted variant alleles and significant ctDNA reductions were observed for all NSCLC EGFR mutation subtypes in patients treated across dose levels. ctDNA reduction has been shown to be predictive of clinical response.
- **Radiographic responses in patients with NSCLC at starting dose of 100mg or above**. Five of the 13 patients with either intrinsic driver, acquired resistance or complex mutations had a confirmed partial response (PR) by RECIST1.1. One patient remains an unconfirmed PR and continues on study with no sign of tumor progression, and six patients have stable disease at doses at or above 100mg once daily. Evidence of reduction in brain metastases was observed, including a patient with more than three prior therapies.
- **Durable clinical responses in patients with NSCLC who have had multiple lines of prior therapy.** Three responders continue on therapy for greater than six months (two confirmed PRs, one uPR). One patient with confirmed PR remained on therapy for six months. Two additional patients with stable disease continue on therapy for greater than 12 months.

“These results point to a highly active compound that has the potential to fill a substantial unmet need for an oral, well-tolerated precision therapy option in the current NSCLC therapeutic landscape for patients who progressed on a third-generation EGFR inhibitor,” said Helena Yu, M.D., Associate Attending Physician at Memorial Sloan Kettering Cancer Center. “We are most encouraged by the durable responses observed, as they underscore the potential of BDTX-1535 for patients with NSCLC who have progressed on prior tyrosine kinase inhibitors (TKIs).”

Black Diamond is currently enrolling patients in the expansion cohorts evaluating BDTX-1535 at doses of 100mg and 200mg in patients with intrinsic driver and acquired resistance EGFR mutation positive NSCLC assessing objective response rate (ORR) by RECIST 1.1. The Company expects to share initial results from this portion of the study in 2024.

“These dose escalation results underscore that the well-tolerated and durable clinical activity of BDTX-1535 could have important implications for patients with EGFR mutant NSCLC,” said Sergey Yurasov, M.D., Ph.D., Chief Medical Officer of Black Diamond Therapeutics. “As real-world evidence shows, C797S is the most prevalent on-target resistance mutation, co-occurring with an increasingly heterogeneous set of other EGFR-acquired resistance mutations, intrinsic drivers, and classical drivers, highlighting the need for an agent like BDTX-1535 to address the complex combination of mutations. We look forward to results from the dose expansion cohorts in patients with NSCLC in 2024 and our End of Phase 1 meeting with the FDA later this year.”

Black Diamond also presented two additional posters outlining the study design of the ongoing Phase 1 clinical trial of BDTX-1535 in NSCLC and preclinical data for BDTX-4933, a brain-penetrant MasterKey RAF inhibitor targeting KRAS, NRAS and BRAF alterations in solid tumors. Key

preclinical findings from the BDTX-4933 presentation include:

- BDTX-4933 potently and selectively inhibited the proliferation of tumor cells expressing a range of KRAS, NRAS and BRAF mutations in cell lines, suggesting potential best-in-class potency compared to other RAF inhibitors.
- BDTX-4933 demonstrated strong anti-tumor activity and regression across cell line and patient-derived xenograft models expressing several MAPK pathway mutations, including KRAS G12D, KRAS G12V, and KRAS G13C mutant NSCLC models.
- BDTX-4933 exhibited high central nervous system (CNS) exposure leading to dose-dependent tumor growth inhibition and survival benefit in mice implanted intracranially with xenograft BRAF mutant tumors.

Black Diamond initiated a Phase 1 clinical trial for BDTX-4933 with emphasis on KRAS mutant NSCLC in the second quarter of 2023.

About BDTX-1535
BDTX-1535 is an oral, brain-penetrant MasterKey inhibitor of oncogenic epidermal growth factor receptor (EGFR) mutation in non-small cell lung cancer (NSCLC), including families of intrinsic driver mutations (e.g., L747P, L718Q), acquired resistance C797S mutation, and complex mutations. BDTX-1535 is a fourth-generation TKI that potently inhibits, based on preclinical data, greater than 50 oncogenic EGFR mutations and alterations expressed across a diverse group of patients with NSCLC in multiple lines of therapy. Based on preclinical data, BDTX-1535 also inhibits EGFR extracellular domain mutations and alterations commonly expressed in glioblastoma multiforme (GBM) and avoids paradoxical activation observed with earlier generation reversible TKIs. The ongoing BDTX-1535 Phase 1 clinical trial is currently in dose expansion for NSCLC and dose escalation for GBM (NCT05256290).

About BDTX-4933
BDTX-4933 is an oral, brain-penetrant RAF MasterKey inhibitor designed to target oncogenic alterations in KRAS, NRAS and BRAF, while also avoiding paradoxical activation. In preclinical studies, BDTX-4933 has demonstrated a potential best-in-class profile, showing potent target engagement, inhibition of MAPK signaling and strong anti-tumor activity/tumor regression across tumor models driven by either KRAS, NRAS or BRAF mutations and alterations. BDTX-4933 also exhibits high central nervous system (CNS) exposure leading to dose-dependent tumor growth inhibition and a survival benefit in an intracranial tumor model harboring oncogenic BRAF mutation. The ongoing BDTX-4933 Phase 1 clinical trial is currently in dose escalation with emphasis on KRAS mutant NSCLC patients (NCT05786924).

About Black Diamond Therapeutics
Black Diamond Therapeutics is a clinical-stage oncology company focused on the development of MasterKey therapies that address families of oncogenic mutations in clinically validated targets. The Company's MasterKey therapies are designed to address broad genetically defined patient populations, overcome resistance, minimize on-target/wild-type mediated toxicities, and be brain-penetrant to treat CNS metastases. The Company is advancing two clinical stage programs: BDTX-1535, a brain-penetrant fourth-generation EGFR MasterKey inhibitor targeting EGFR mutant NSCLC and GBM, and BDTX-4933, a brain penetrant RAF MasterKey inhibitor targeting KRAS, NRAS and BRAF alterations 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 BDTX-1535 development program, including clinical updates on the dose expansion cohorts of BDTX-1535 in NSCLC patients and on dose escalation data for BDTX-1535 in recurrent GBM patients, the timing of meeting with regulatory agencies, and the potential of BDTX-1535 to address an unmet medical need of patients with EGFR-mutant NSCLC. 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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