Black Diamond Therapeutics Presents Novel Real-World Evidence of the Evolving EGFR Mutation Landscape in NSCLC and the Opportunity for BDTX-1535 in an Oral Presentation at the 2024 American Association of Cancer Research Annual Meeting

April 07, 2024

Real-world data demonstrate non-classical mutations are present in 20-30% of all patients with EGFRm NSCLC

Emerging data show non-classical EGFR mutations can be co-expressed with the classical L858R mutation, a setting characterized by shorter duration of response to osimertinib

BDTX-1535 profile differentiated as the most advanced fourth-generation oral TKI in clinical development addressing the full spectrum of classical, non-classical, and C797S resistance EGFR mutations

CAMBRIDGE, Mass., April 07, 2024 (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 cancer, presented real-world evidence of the evolving epidermal growth factor receptor (EGFR) mutation landscape in non-small cell lung cancer (NSCLC), and the potential of BDTX-1535 to address a broader range of mutations compared to existing therapies. The results were disclosed in an oral presentation on April 7, 2024, at the 2024 American Association of Cancer Research (AACR) Annual Meeting held in San Diego, California.

The oral presentation, titled “BDTX-1535 – A MasterKey EGFR Inhibitor Targeting Classical, Non-Classical and the C797S Resistance Mutation to Address the Evolved Landscape of EGFR Mutant NSCLC,” evaluated more than 235,000 sequenced cases of NSCLC sourced from Guardant Health (GuardantINFORM™) and Foundation Medicine (FoundationInsights™). The analyses reveal a broad spectrum of non-classical mutations, as well as an increased prevalence of the acquired resistance mutation, C797S. Over 100 unique non-classical EGFR oncogenic driver mutations were identified in newly diagnosed patients with NSCLC, and these non-classical EGFR mutations were present in 20-30% of patients across all lines of treatment.

“The landscape of EGFR mutations in NSCLC continues to evolve, revealing classical and non-classical driver mutations,” said John Heymach, M.D., Ph.D., Chair of Thoracic/Head and Neck Medical Oncology at MD Anderson Cancer Center. “Non-classical mutations fall into categories including kinase domain PACC mutations and ectodomain mutations; therefore, next generation EGFR targeted therapies must effectively cover multiple subgroups of mutations.”

“Novel targeted therapies are still needed to continue to improve clinical outcomes for patients with EGFR-mutant lung cancers,” added Xiuning Le, M.D., Ph.D., Associate Professor, Thoracic/Head and Neck Medical Oncology at MD Anderson Cancer Center. “To extend survival for our patients, newer drugs need to have good mutational coverage, good tolerability, and good brain penetrance.”

Preclinical data demonstrated that BDTX-1535 potently inhibits more than 50 clinically relevant, non-classical EGFR mutations (as well as the classical L858R and exon19-del mutations) while sparing wild-type EGFR. The compound also potently inhibits the drug resistance C797S mutation, which emerges following treatment with third-generation EGFR inhibitors, including osimertinib. Real-world data indicate non-classical EGFR mutations can be co-expressed with classical mutation L858R, a setting that has been characterized by shorter duration of response to osimertinib first-line therapy. Preclinical data show that BDTX-1535 potently inhibits these co-expressed non-classical mutations.

“BDTX-1535 was designed to address a broad spectrum of more than 50 non-classical oncogenic EGFR mutations, as well as the C797S resistance mutation,” said Elizabeth Buck, Ph.D., Chief Scientific Officer and co-founder of Black Diamond Therapeutics. “We believe that the potency of BDTX-1535 against the full spectrum of classical, non-classical, and C797S mutations positions the compound as the first and best-in-class fourth-generation EGFR inhibitor potentially offering NSCLC patients a well-tolerated, brain-penetrant, oral therapy across various lines of treatment.”

Phase 1 proof-of-concept data demonstrating durable responses in recurrent NSCLC patients with both non-classical and acquired resistance C797S mutations were presented in October 2023. Black Diamond is currently advancing BDTX-1535 in a Phase 2 trial for patients with EGFRm NSCLC across multiple lines of therapy. Patients are being enrolled both in a first-line (1L) setting (for those expressing EGFR non-classical mutations) and in second- and third-line (2L/3L) settings following prior treatment with an EGFR inhibitor. Initial results from 2L/3L patients are anticipated in the third quarter of 2024.

About BDTX-1535
BDTX-1535 is an oral, brain-penetrant MasterKey inhibitor of oncogenic epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer (NSCLC), including classical driver mutations, non-classical driver mutations, and the acquired resistance C797S mutation. BDTX-1535 is a fourth-generation tyrosine kinase inhibitor (TKI) that potently inhibits, based on preclinical data, more than 50 oncogenic EGFR mutations 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 (GBM) and avoids paradoxical activation observed with earlier generation reversible TKIs. A “window of opportunity” trial of BDTX-1535 in patients with GBM is ongoing (NCT06072586) and a Phase 2 trial is ongoing in patients with NSCLC (NCT05256290).

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 wild-type mediated toxicities, and be brain penetrant to treat CNS disease. 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 potential of BDTX-1535 to address a broader range of mutations compared to existing therapies, the position of BDTX-1535 as compared to other fourth-generation EGFR inhibitors, the timing of clinical updates for BDTX-1535 in patients with NSCLC and in patients with recurrent GBM, and the potential of BDTX-1535 to benefit patients with 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, 2023, 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:
Mario Corso, Head of Investor Relations, Black Diamond Therapeutics
mcorso@bdtx.com

For Media:
media@bdtx.com