UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or Section 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 19, 2021

Black Diamond Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-39200**	**81-4254660**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

One Main Street, 10th Floor **Cambridge, MA**	**02142**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: 617-252-0848

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation to the registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	BDTX	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On May 19, 2021, Black Diamond Therapeutics, Inc. (the "Company") issued a press release to announce initial data from the Phase 1 dose-escalation portion of its MasterKey-01 clinical trial of BDTX-189. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information furnished under this Item 7.01, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On May 19, 2021, the Company announced initial pharmacokinetics, safety and preliminary efficacy data from its Phase 1, first-in-human, open-label dose escalation study of BDTX-189 in patients with advanced solid tumors harboring any one of more than 48 oncogenic alterations in the epidermal growth factor receptor ("EGFR") and human epidermal growth factor receptor 2 ("HER2") oncogenes.

As of the data cut-off date of April 2, 2021, 55 patients from the once-daily ("QD") regimen were dosed across the dosing range, 25-400 mg QD fasting (n = 12), 800 mg QD fasting (n = 21), 800 mg QD non-fasting (n = 9), 1000 mg QD fasting (n = 7), and 1200 mg QD fasting (n = 6).

Pharmacokinetics

The pharmacokinetic data for the BDTX-189 QD regimen demonstrated dose-dependent increases in exposure up to 800 mg QD, achieving the predicted efficacious exposure at 800 mg QD. BDTX-189 was rapidly absorbed, with a short elimination half-life of 1.3-4.4 hours, consistent with pre-clinical predictions. No apparent accumulation or change in exposure at steady state was observed.

Safety

BDTX-189 demonstrated a favorable tolerability profile, with no dose-limiting toxicities at doses of ≤800 mg QD fasting and non-fasting in the dose-escalation cohorts. 800 mg non-fasting was selected as the preliminary recommended Phase 2 dose for the QD regimen.

Efficacy

In a heavily pre-treated patient population, including patients who had received prior EGFR/HER2 tyrosine kinase inhibitors, evidence of anti-cancer activity was observed. Among all cancer type/genomic alteration pairs, two had ≥ three RECIST-evaluable patients dosed at ≥800 mg QD: non-small cell lung cancer ("NSCLC") harboring either EGFR Exon 20 mutations (n = 3) or HER2 Exon 20 mutations (n = 3). In the separate group of patients with solid tumors harboring HER2-amplification, six patients dosed at ≥800 mg QD were RECIST-evaluable.

- Three patients with NSCLC EGFR Exon 20 dosed at ≥800 mg QD (all at 800 mg QD) were evaluable by RECIST at the time of data cut-off, all of whom had received prior EGFR/HER2-targeted therapy. One confirmed partial response was observed in a patient who had previously responded and then progressed on poziotinib (at the data cut-off, 53% tumor regression observed and treatment with BDTX-189 ongoing 13+ weeks). One patient with stable disease and one patient with progressive disease were observed.
- Three patients with NSCLC HER2 Exon 20 dosed at ≥800 mg QD (all at 800 mg QD) were evaluable by RECIST at the time of data cut-off, two of whom had received prior EGFR/HER2-targeted therapy. All three patients demonstrated stable disease.
- Six patients with HER2-amplification across a range of tumor types dosed at ≥800 mg QD were evaluable by RECIST at the time of data cut-off, two-thirds of whom had received prior EGFR-/HER2-targeted therapy. One confirmed partial response (cancer of unknown primary; at data cut-off, 90.3% tumor reduction and treatment with BDTX-189 ongoing >24 weeks), one unconfirmed partial response (NSCLC), two patients with stable disease (ovarian and pancreatic), and two patients with progressive disease were observed.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits:

Exhibit No.	Description
99.1	Press Release issued by Black Diamond Therapeutics, Inc., dated May 19, 2021.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

May 19, 2021

BLACK DIAMOND THERAPEUTICS, INC.

By: /s/ Thomas Leggett
Name: Thomas Leggett
Title: Chief Financial Officer and Principal Financial Officer

Exhibit 99.1

Black Diamond Therapeutics Presents Phase 1 Pharmacokinetic, Safety, and Preliminary Efficacy Data of BDTX-189 in Advanced Solid Tumors Harboring EGFR or HER2 Alterations

Once-daily (QD) dose escalation completed; pharmacokinetic (PK) profile consistent with design principles and preclinical predictions

Generally well-tolerated with medically manageable toxicities observed; safety profile compares favorably in the context of other agents in the class; preliminary recommended Phase 2 dose (RP2D) selected for the QD regimen

Preliminary anti-cancer activity observed in heavily pre-treated patients (prior EGFR/HER2-directed and/or I/O agents) in a variety of tumor types and genomic alterations in EGFR or HER2, including confirmed partial responses

Conference call and webcast to be held today at 6:00 PM ET

CAMBRIDGE, Mass. and NEW YORK, *May 19, 2021* – Black Diamond Therapeutics, Inc. (Nasdaq: BDTX), a precision oncology medicine company pioneering the discovery and development of small molecule, MasterKey therapies, today announced initial data from the Phase 1 dose-escalation portion of the MasterKey-01 trial of BDTX-189 in patients with advanced solid tumors harboring any one of more than 48 oncogenic alterations in the epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2) oncogenes. These data provide early proof-of-concept for BDTX-189, including evidence of anti-cancer activity and a safety profile that is in-line with the Company's preclinical expectations. The data announced today will be presented in poster presentations at the upcoming 2021 American Society of Clinical Oncology (ASCO) Annual Meeting, taking place June 4-8, 2021.

"These encouraging Phase 1 safety and anti-cancer activity data provide early proof-of-concept for BDTX-189 as a differentiated MasterKey inhibitor of undrugged oncogenic mutants of EGFR, including EGFR Exon 20 insertion mutations and oncogenic mutants of HER2," said Rachel Humphrey, M.D., Chief Medical Officer of Black Diamond Therapeutics. "We look forward to the continued advancement of BDTX-189 through clinical development and remain on track to initiate the potentially pivotal Phase 2 portion of the MasterKey-01 trial in the second half of 2021."

"These initial data suggest BDTX-189 may provide meaningful clinical benefit to patients with advanced solid tumors, including those with allosteric EGFR and HER2 mutations," said Alison Schram, M.D., Medical Oncologist, Memorial Sloan Kettering Cancer Center. "The favorable tolerability profile demonstrated thus far supports the potential of BDTX-189 to address the unmet need in this patient population, for which there are no currently approved targeted therapies and where other in-clinic agents are limited by toxicity."

MasterKey-01 Part A Dose-Escalation Study Design

Part A is a Phase 1, first-in-human, open-label dose escalation study, comprised of initial single-patient, accelerated titration cohorts followed by multiple-patient cohorts utilizing a Bayesian Optimal Interval (BOIN) design. Part A is designed to determine the recommended Phase 2 dose and schedule for the QD and twice-daily (BID) regimens in patients with solid tumors with an allosteric HER2 or HER3 mutation; EGFR or HER2 Exon 20 insertion mutation; HER2 amplified or overexpressing tumor; or EGFR Exon 19 deletion or L858R mutation.

Initial Study Results

As of the data cut-off date of April 2, 2021, 55 patients from the QD regimen were dosed across the dosing range, 25-400 mg QD fasting (n = 12), 800 mg QD fasting (n = 21), 800 mg QD non-fasting (n = 9), 1000 mg QD fasting (n = 7), and 1200 mg QD fasting (n = 6). The dose-escalation portion successfully enrolled patients with a broad range of tumor types and genomic alterations. Tumor types enrolled included non-small cell lung cancer (NSCLC), breast, colorectal (CRC), ovary, biliary, pancreas, cervical, cancer of unknown primary, kidney, salivary, prostate, signet ring cell, liver, and bladder. Genomic alterations enrolled included HER2 amplification and the following mutations: allosteric HER2, EGFR Exon 20 insertion, HER2 Exon 20 insertion, EGFR Exon 19 del./L858R, and HER3.

PK

The PK data for the BDTX-189 QD regimen demonstrated dose-dependent increases in exposure up to 800 mg QD, achieving the predicted efficacious exposure at 800 mg QD. BDTX-189 was rapidly absorbed, with a short elimination half-life of 1.3-4.4 hours, consistent with preclinical predictions. No apparent accumulation or change in exposure at steady state was observed.

Safety

BDTX-189 demonstrated a favorable tolerability profile, with no dose-limiting toxicities at doses of ≤800 mg QD fasting and non-fasting in the dose-escalation cohorts. 800 mg non-fasting was selected as the preliminary RP2D for the QD regimen.

The most common drug-related adverse events were gastrointestinal in nature, the majority of which were low grade and generally medically manageable. At 800 mg QD fasted or non-fasted (n = 30), the most common drug-related adverse events were diarrhea (50%, 7% Gr3), nausea (50%, 7% Gr3), vomiting (30%, 3% Gr3), ALT increased (20%, 10% Gr3), AST increased (13%, 3% Gr3), fatigue (20%, 0% Gr3), skin disorders (13%, 0% Gr3), and decreased appetite (10%, 0% Gr3).

Efficacy

In a heavily pre-treated patient population, including patients who had received prior EGFR/HER2 tyrosine kinase inhibitors (TKI), evidence of anti-cancer activity was observed. Among all cancer type/genomic alteration pairs, two had ≥ three RECIST-evaluable patients dosed at ≥800 mg QD: NSCLC harboring either EGFR Exon 20 mutations (n = 3) or HER2 Exon 20 mutations (n = 3). In the separate group of patients with solid tumors harboring HER2-amplification, six patients dosed at ≥800 mg QD were evaluable by RECIST.

- Three patients with NSCLC EGFR Exon 20 dosed at ≥800 mg QD (all at 800 mg QD) were evaluable by RECIST at the time of data cut-off, all of whom had received prior EGFR/HER2-targeted therapy. One confirmed partial response was observed in a patient who had previously responded and then progressed on poziotinib (at the data cut-off, 53% tumor regression observed and treatment with BDTX-189 ongoing 13+ weeks). One patient with stable disease and one patient with progressive disease were observed.
- Three patients with NSCLC HER2 Exon 20 dosed at ≥800 mg QD (all at 800 mg QD) were evaluable by RECIST at the time of data cut-off, two of whom had received prior EGFR/HER2-targeted therapy. All three patients demonstrated stable disease.
- Six patients with HER2-amplification across a range of tumor types dosed at ≥800 mg QD were evaluable by RECIST at the time of data cut-off, two-thirds of whom had received prior EGFR/HER2-targeted therapy. One confirmed partial response (cancer of unknown primary; at data cut-off, 90% tumor reduction and treatment with BDTX-189 ongoing 24+ weeks), one unconfirmed partial response (NSCLC), two patients with stable disease (ovarian and pancreatic), and two patients with progressive disease were observed.

“We’re incredibly encouraged by the rapid progress of the MasterKey-01 study and promising proof-of-concept data for BDTX-189. These preliminary data support the differentiated profile of BDTX-189 as a MasterKey inhibitor of diverse oncogenic alterations in EGFR and HER2, as well as initial validation of Black Diamond’s proprietary MAP drug discovery engine and MasterKey approach to drug development,” said David M. Epstein, President and Chief Executive Officer of Black Diamond Therapeutics. “We’d like to thank all the patients, their families, and their caregivers for participating in this study.”

Black Diamond is continuing to dose patients in the ongoing QD dose-escalation portion and the food effect cohort, as well as enrolling and dosing patients in the BID dose-escalation portion. The Company will initiate the safety expansion cohort ahead of the Phase 2 portion of the MasterKey-01 study, which remains on track for initiation in the second half of 2021.

Part B is a Phase 2, open-label, multi-center study designed to determine anti-cancer activity and safety in adult patients with solid tumors harboring an allosteric HER2 mutation or EGFR or HER2 Exon 20 insertion mutation. This portion of the trial will enroll patients in focused tumor/mutation cohorts and is designed to be potentially pivotal. Additionally, based on early proof-of-concept data, Black Diamond is exploring the potential for further clinical development in the HER2-amplified setting.

The data announced today will be presented in poster presentations at the upcoming ASCO meeting:

Title: Safety and Preliminary Efficacy from the Phase 1 Portion of MasterKey-01: A First-in-Human Dose-Escalation Study to Determine the Recommended Phase 2 Dose (RP2D), Pharmacokinetics (PK), and Preliminary Antitumor Activity of BDTX-189, an Inhibitor of Allosteric ErbB mutations, in Patients with Advanced Solid Malignancies
Session Type: Poster Session
Session: Developmental Therapeutics – Molecularly Targeted Agents and Tumor Biology
Date and Time: Friday, June 4, 9:00 AM ET
Abstract ID: 3086

Title: Clinical pharmacokinetics of BDTX-189, an inhibitor of allosteric ErbB mutations, in patients with advanced solid malignancies in MasterKey-01 study
Session Type: Poster Session
Session: Developmental Therapeutics – Molecularly Targeted Agents and Tumor Biology
Date and Time: Friday, June 4, 9:00 AM ET
Abstract ID: 3097

Conference Call and Webcast:

In connection with today's announcement, Black Diamond's management team will host a conference call and live audio webcast at 6:00 PM ET today, Wednesday, May 19, 2021.

The live audio webcast and accompanying slides may be accessed through the Events page in the Investors section of the Company's website at www.blackdiamondtherapeutics.com. Alternatively, the conference call may be accessed as follows:

Conference ID: 1979666
Domestic Dial-in Number: 1-833-730-3983
International Dial-in Number: 1-720-405-2158

For those unable to participate in the conference call or webcast, a replay will be available for 30 days on the Investors section of the Company's website.

About BDTX-189

BDTX-189 is an orally available, irreversible, and ATP competitive small molecule inhibitor that is designed to block the function of a family of oncogenic epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2) proteins across a range of tumor types. BDTX-189 is designed as a MasterKey inhibitor targeting a family of previously undrugged and functionally similar oncogenic mutations in a tumor-agnostic manner. These mutations include extracellular domain allosteric mutations of HER2, as well as EGFR and HER2 kinase domain Exon 20 insertions, and additional activating oncogenic drivers of EGFR and HER2. BDTX-189 is also designed to spare normal, or wild-type, EGFR, which we believe has the potential to improve upon the toxicity profiles of current EGFR/HER2 kinase inhibitors. Currently, there are no medicines approved by the U.S. Food and Drug Administration (FDA) to target all of these oncogenic mutations with a single therapy.

BDTX-189 is currently being evaluated in a Phase 1/2 clinical trial (MasterKey-01) in adult patients with advanced solid tumors expressing a range of alterations of EGFR and HER2 receptors, including oncogenic MasterKey mutations, HER2-WT amplification, HER3 mutation, EGFR Exon 19 deletion, and L858R mutation who have no standard therapy available or for whom standard therapy is considered unsuitable or intolerable. In July 2020, the FDA granted Fast Track designation to BDTX-189 for the treatment of adult patients with solid tumors harboring an allosteric HER2 mutation or an EGFR or HER2 Exon 20 insertion mutation who have progressed following prior treatment and who have no satisfactory treatment options.

About Black Diamond Therapeutics

Black Diamond Therapeutics is a precision oncology medicine company pioneering the discovery of small molecule, MasterKey therapies. Black Diamond targets undrugged mutations in patients with genetically defined cancers. Black Diamond is built upon a deep understanding of cancer genetics, protein structure and function, and medicinal chemistry. The Company's proprietary technology platform and drug discovery engine, Mutation-Allostery-Pharmacology, or MAP, platform, is designed to allow Black Diamond to analyze population-level genetic sequencing data to identify oncogenic mutations that promote cancer across tumor types, group these mutations into families, and develop a single small molecule therapy that targets a specific family of mutations, termed a MasterKey therapy. Black Diamond was founded by David M. Epstein, Ph.D., and Elizabeth Buck, Ph.D. 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 of BDTX-189 and the timing for initiating and completing the safety expansion cohort or starting the Phase 2 portion of the ongoing clinical trial of BDTX-189. 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: the success, cost, and timing of the Company's product candidate development activities and planned IND-enabling and clinical trials, the Company's ability to execute on its strategy, regulatory developments in the United States, the Company's ability to fund operations, and the impact that the current COVID-19 pandemic will have on the Company's clinical trials and preclinical studies, supply chain, and operations, as well as those risks and uncertainties set forth in its 2020 annual report on Form 10-K filed with the United States Securities and Exchange Commission and its other 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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