BioXcel Therapeutics Presents Positive Data from Phase 2 Trial of BXCL701 in Aggressive Forms of Prostate Cancer at 2022 ASCO Genitourinary Cancers Symposium

February 14, 2022

BXCL701 plus KEYTRUDA® (pembrolizumab) demonstrates encouraging composite response rates in SCNC (33%) and adenocarcinoma (21%) cohorts

Company plans to continue evaluation of BXCL701 combination as potentially differentiated approach for mCRPC patients

Results support BXCL701's potential to extend checkpoint inhibitor therapy into cold tumor settings

NEW HAVEN, Conn., Feb. 14, 2022 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. (Nasdaq: BTAI), a clinical-stage biopharmaceutical company utilizing artificial intelligence approaches to develop transformative medicines in neuroscience and immuno-oncology, today announced results from its ongoing Phase 2 trial of BXCL701, the Company's investigational, oral innate immunity activator, in metastatic castration-resistant prostate cancer (mCRPC) patients with either adenocarcinoma or small cell neuroendocrine carcinoma (SCNC) phenotype. Results will be highlighted in two poster presentations at the 2022 ASCO Genitourinary Cancers Symposium on February 17, 2022.

"There are, unfortunately, very few treatment options available for patients with mCRPC, especially those with SCNC, for which there are no approved therapies," said Rahul Aggarwal, M.D., Associate Director for Clinical Sciences, UCSF Helen Diller Family Comprehensive Cancer Center and Associate Professor of Hematology/Oncology, UCSF. "These data demonstrate the potential of BXCL701 plus pembrolizumab to redefine the standard of care for patients with advanced disease. The results were particularly encouraging given that patients were not preselected on the basis of predictors of immune response in prostate cancer."

KEY SCNC FINDINGS

- In the evaluable patient cohort (n = 15), 5 (33%) patients achieved a composite response at the planned interim analysis.
- In patients with measurable disease (n = 12), RECIST-defined partial response was observed in 4 (33%) patients (3 confirmed responses) and the disease control rate, defined as complete response (CR) + partial response (PR) + stable disease (SD), was 58% (7 patients).
- 3 (17%) patients experienced serious adverse events (AEs) possibly related to BXCL701 or pembrolizumab, and 4 (22%) patients discontinued any drug due to AEs.

KEY ADENOCARCINOMA FINDINGS

- In the evaluable patient cohort (n = 29), 6 (21%) patients achieved a composite response.
- In patients with measurable disease (n = 18), RECIST-defined partial response was observed in 4 (22%) patients (3 confirmed responses) and the disease control rate was 83% (15 patients); all responders experienced a decrease in tumor size from baseline.
- In the 29 patients who had at least 1 post-baseline PSA measurement, the PSA_{50} was 17% including 5 patients who showed a -100% to -57% PSA decrease.
- From historic data, single agent pembrolizumab showed an objective response rate of 3% to 5%, a disease control rate of 12% and a PSA_{50} response of 6%.[1]
- 5 (12%) patients experienced serious AEs possibly related to BXCL701 or pembrolizumab, and 2 (5%) patients discontinued any drug due to AEs.
- Results support randomized trial expansion to evaluate BXCL701 monotherapy vs. BXCL701-KEYTRUDA combination therapy.

"We are pleased that BXCL701 in combination with pembrolizumab has shown strong clinical activity in these heavily pre-treated mCRPC patients with both adenocarcinoma or SCNC phenotypes, which are particularly aggressive tumors," said Vincent J. O'Neill, M.D., Senior Vice President and Chief Medical Officer of BioXcel Therapeutics. "We are excited about the broad potential of BXCL701 to extend the activity of checkpoint therapy into cold tumor settings and look forward to initiating the randomized trial extension in patients with adenocarcinoma and continuing patient enrollment in SCNC."

The Phase 2a trial is an open-label, multicenter study to evaluate the safety and efficacy of BXCL701 in combination with pembrolizumab in men with mCRPC presenting with either adenocarcinoma or SCNC phenotypes. Eligibility criteria include progression as defined by PCWG3[2] criteria and at least 1 but no more than 2 androgen signaling inhibitors (ASI) and at least 1 prior line of taxane chemotherapy for inclusion in the adenocarcinoma cohort, or at least 1 prior line of chemotherapy for inclusion in the SCNC cohort. 29 evaluable mCRPC patients with adenocarcinoma and 15 evaluable mCRPC patients with SCNC received 0.3 mg of BXCL701 twice daily (BID) on days 1 through 14 of a 21-day cycle (0.2 mg BID the first week of Cycle 1) plus 200 mg of pembrolizumab administered intravenously on day 1 and every subsequent 21 days. The primary endpoint of the trial is composite response rate defined as RECIST 1.1 ± PSA_{50} ± CTC count conversion. Secondary endpoints include duration of response, progression-free survival,

overall survival, and biomarker evaluation as measured by changes in circulating cytokines and correlation of outcome with baseline tumor characteristics.

POSTER PRESENTATION DETAILS

Title: BXCL701: First-in-class oral activator of systemic innate immunity combined with pembrolizumab, in patients with metastatic castration-resistant prostate cancer (mCRPC) of adenocarcinoma phenotype—Phase 2a results.
Poster Session: Poster Session A: Prostate Cancer
Date/Time: February 17, 2022, 11:30 AM-1:00 PM; 5:45 PM-6:45 PM PST
Poster Number: 125

Title: BXCL701: First-in-class oral activator of systemic innate immunity combined with pembrolizumab, in patients with metastatic castration-resistant prostate cancer (mCRPC) of small-cell neuroendocrine carcinoma (SCNC) phenotype—Phase 2a interim results
Poster Session: Poster Session A: Prostate Cancer
Date/Time: February 17, 2022, 11:30 AM-1:00 PM; 5:45 PM-6:45 PM PST
Poster Number: 126

The abstracts are currently available on the ASCO GU website. At the start of the poster sessions, the posters will be available in the "News & Media" section of the Company's website at www.bioxceltherapeutics.com.

About BXCL701

BXCL701 is an investigational orally administered innate immune activator designed to initiate inflammation in the tumor microenvironment. Approved and experimental immunotherapies often struggle to address cancers that appear "cold" or uninflamed. Therefore, BXCL701 may render "cold" tumors "hot," making them more detectable by the adaptive immune system and thereby facilitating the development of a strong anti-cancer immune response. BioXcel Therapeutics' preclinical data supports BXCL701's synergy with both current checkpoint inhibitor-based therapies and emerging immunotherapies directed to activate T-cells, such as IL-2.

BXCL701 is currently being developed as therapy for metastatic castration-resistant prostate cancer (mCRPC) of adenocarcinoma and small cell neuroendocrine carcinoma (SCNC) phenotypes (both "cold" tumors) and other advanced solid cancers that are "hot" or have become resistant to checkpoint inhibitors.

About BioXcel Therapeutics, Inc.

BioXcel Therapeutics, Inc. is a clinical-stage biopharmaceutical company utilizing artificial intelligence approaches to develop transformative medicines in neuroscience and immuno-oncology. The Company's drug re-innovation approach leverages existing approved drugs and/or clinically validated product candidates together with big data and proprietary machine learning algorithms to identify new therapeutic indices. BioXcel Therapeutics' two most advanced clinical development programs are BXCL501, an investigational, proprietary, orally dissolving thin film formulation of dexmedetomidine for the treatment of agitation associated with psychiatric and neurological disorders, and BXCL701, an investigational, orally administered, systemic innate immunity activator in development for the treatment of aggressive forms of prostate cancer and advanced solid tumors that are refractory or treatment naïve to checkpoint inhibitors. For more information, please visit www.bioxceltherapeutics.com.

Forward-Looking Statement

This press release includes "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements in this press release include but are not limited to the timing, trial design and data from clinical trials for BXCL701, the Company's plans to initiate an extension of its Phase 2 trial and the potential benefits of treatment with BXCL701. When used herein, words including "anticipate," "being," "will," "plan," "may," "continue," and similar expressions are intended to identify forward-looking statements. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements are based upon the Company's current expectations and various assumptions. The Company believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. The Company may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various important factors, including, without limitation, its limited operating history; its incurrence of significant losses; its need for substantial additional funding and ability to raise capital when needed; its limited experience in drug discovery and drug development; its dependence on the success and commercialization of BXCL501 and BXCL701 and other product candidates; the failure of preliminary data from its clinical studies to predict final study results; failure of its early clinical studies or preclinical studies to predict future clinical studies; its ability to receive regulatory approval for its product candidates; its ability to enroll patients in its clinical trials; undesirable side effects caused by the Company's product candidates; its approach to the discovery and development of product candidates based on EvolverAI is novel and unproven; its exposure to patent infringement lawsuits; its ability to comply with the extensive regulations applicable to it; impacts from the COVID-19 pandemic; its ability to commercialize its product candidates; and the other important factors discussed under the caption "Risk Factors" in its Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2021, as such factors may be updated from time to time in its other filings with the SEC, which are accessible on the SEC's website at www.sec.gov. These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While the Company may elect to update such forward-looking statements at some point in the future, except as required by law, it disclaims any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this press release.

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Source: BioXcel Therapeutics, Inc.

[1] Antonarakis et al. "Pembrolizumab for Treatment-Refractory Metastatic Castration-Resistant Prostate Cancer: Multicohort, Open-Label Phase II KEYNOTE-199 Study." *Journal of Clinical Oncology* 38, no. 5 (February 10, 2020) 395-405. DOI: 10.1200/JCO.19.01638.

[2] Prostate Cancer Working Group 3 (PCWG3) is an international working group of clinical and translational experts in prostate cancer who issued Consensus Guidelines on key principles of trial conduct for trials in castration-resistant prostate cancer.