BioXcel Therapeutics Announces BXCL501 Met Primary Endpoint in Phase 1b Placebo-Controlled Trial in the Treatment of Agitation in Patients with Schizophrenia

July 22, 2019

Statistically significant mean reduction in PEC score at two hours compared to placebo following a single dose of 180 mcg (p<0.0001), with rapid and durable reductions in PEC score maintained for 4 to 6 hours

Approximately 90% of patients met response criteria at 180 mcg with a reduction in PEC score (≥40%)

Results from secondary analyses were consistent with results observed for the primary endpoint and statistically significant for calming as measured by ACES at two hours compared to placebo following a single dose of 180 mcg (p<0.0001)

Well-tolerated with no serious or severe adverse events across the entire dose range

Data support progressing BXCL501 program potentially to Phase 3 pivotal trials, subject to ongoing discussions with FDA

Conference call scheduled today, July 22, 2019 at 8:30 EDT

NEW HAVEN, Conn., July 22, 2019 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. (“BTI”) (Nasdaq: BTAI), a clinical-stage biopharmaceutical development company utilizing novel artificial intelligence approaches to identify and advance the next wave of medicines in neuroscience and immuno-oncology, today announced positive top-line results from the adaptive Phase 1b, randomized, double-blind, placebo-controlled, multi-center, U.S. trial, evaluating multiple doses of BXCL501 for acute treatment of agitation in 135 patients with schizophrenia. In the trial, a reduction in the PEC score (PANSS or the Positive and Negative Syndrome Scale, Excitatory Component) for agitation was observed with rapid calming without excessive sedation at two hours and at earlier time-points. The 80 mcg, 120 mcg and 180 mcg doses of BXCL501 showed reductions of PEC scores of -7.1, -9.2 and -10.8, respectively, compared to -4.5 for placebo at two hours. The results for these three doses were statistically significant in patients treated compared to placebo (80 mcg; p=0.0152), (120 mcg; p=0.0003), and (180 mcg; p<0.0001) with clinically meaningful, rapid and durable reductions in PEC score. BTI also observed clinically meaningful but not statistically significant reductions in PEC scores of -6.0 following 60 mcg at two hours (p=0.1227). The Company believes that these results suggest a predictable and dose-dependent response for BXCL501.

The secondary evaluations included assessment using ACES (Agitation-Calmness Evaluation Scale) which evaluated the potential calming effects of BXCL501. The ACES assessment was consistent with the analysis of the primary endpoint, and met statistically significance for calming as measured by ACES at two hours compared to placebo in the three highest doses evaluated (80mcg; p=0.0156), (120 mcg; p=0.0005) and (180 mcg; p<0.0001). BXCL501 was well-tolerated with no serious or severe adverse events across the entire dose range; the most common treatment-related adverse events were mild somnolence and dry mouth. BXCL501 was granted Fast-Track Designation by the U.S. Food and Drug Administration (FDA) in December 2018.

“We need better treatments for agitation episodes in medical settings. It would be best if novel treatments could be administered non-invasively and demonstrate a rapid onset of action,” said Professor John Krystal, MD, Chairman, Department of Psychiatry, Yale University School of Medicine. “The BTI Phase 1b data suggest that BXCL501, rapidly and non-invasively calmed agitated schizophrenia patients without requiring intramuscular administration and without producing excessive sedation. If successfully developed and approved, BXCL501 could offer psychiatrists and Emergency Medicine physicians a new tool for treating agitation in their patients.”

As previously announced, BTI anticipates enrolling approximately 600 to 700 patients (300-350 each in schizophrenia and bipolar disorder) for BTI’s first pivotal trial, designed to measure reduction in PEC at two hours as the primary endpoint, as discussed with the FDA and used in clinical trials of other approved agents. With the statistically significant results observed in multiple doses in this trial, BTI plans to meet with the FDA to obtain additional feedback on progressing to a Phase 3 pivotal trial.

“These very encouraging data provide supportive evidence regarding BXCL501’s potential to treat agitation in patients with schizophrenia and additionally, provides support for the drug’s broad potential across multiple neuropsychiatric disorders,” said Vimal Mehta, Ph.D., Chief Executive Officer of BioXcel Therapeutics. “There has been little advancement in the discovery and development of acute treatment for agitation associated with neuropsychiatric disorders in the last several decades. The positive results observed in this study support advancing the program into late stage clinical development.”

Norepinephrine is a brain hormone that regulates the fight or flight response. It is released during stress and is the core causal mechanism for producing agitation. BXCL501 is an investigational, highly selective alpha 2A adrenergic receptor agonist that is being developed as a non-invasive rapid treatment for agitation in a variety of neuropsychiatric disorders. BXCL501 is designed to treat agitation by reducing the activity of brain norepinephrine to drive the agitation response independent of the underlying disease conditions.

“Currently there are significant gaps in the management of agitation in multiple disease settings and our development goal at BioXcel Therapeutics is to potentially transform the treatment landscape with BXCL501, if approved, by offering a non-invasive treatment with a non-antipsychotic or non-benzodiazepine mechanism,” said Robert Risinger, M.D., Vice President, Clinical Development of BTI. “We believe our data meets those expectations with the positive results observed with multiple doses in this trial. We expect to select two doses that showed clinically meaningful reductions in PEC scores and were well tolerated during the trial. The planned Phase 3 pivotal trial will be powered using these results.”

About Conference Call:
BTI will host a conference call today, July 22, 2019, at 8:30 a.m. Eastern Time to discuss the results of this study and BXCL501 Program. Interested

investors can access the call by dialing 866-575-6539 in the U.S. and Canada, or 323-794-2423 internationally. The call, along with a slide presentation to accompany the call, will be available via a live, listen-only webcast at http://public.viavid.com/index.php?id=135530 and archived for 30 days. For those unable to participate, a replay of the call will be available until August 22, 2019. To access the replay, please dial 844-512-2921 in the U.S. and Canada, or 412-317-6671 internationally and enter passcode 5862088.

About the Placebo-controlled Phase 1b trial of BXCL501 in Agitated Schizophrenia:
In the randomized, double-blind, placebo-controlled trial, 135 eligible patients (with a minimum score of 14 on the PANSS-Excitatory Component scale for Agitation) were sequentially randomized to receive BXCL501 (five dose strengths of film ranging from 20 mcg to 180mcg) or matching placebo (in a 2:1 ratio with 27 subjects per dose group; 18 BXCL501: 9 placebo). All doses were self-administered by the agitated patient. The study consisted of a screening period followed by a treatment day, and a 7-day follow-up period. After screening subjects were admitted to a trial site where they self-administered a single dose. Agitation was measured using the PEC score immediately pre-dose and repeatedly over a 6-hour period. Secondary analyses included the ACES and CGI-I (Clinical Global Impression of Improvement) scales. Subjects were monitored for an additional 1-2 days and returned a week later to complete the study. The mean total PEC scores at baseline were 17.8 for the BXCL501 dose groups (overall range 14-26), and 18.1 for the placebo group (overall range 14-25), representing patients with moderate to severe agitation. All subjects (100%) were able to self-administer dose and completed the study.

About Agitation
Agitation is a common and costly (approximately $40 Billion per year Health Care Burden) phenomenon associated with a number of psychiatric conditions including schizophrenia and bipolar disorder. Early identification and prompt intervention to relieve the symptoms of agitation are essential to avoid symptomatic escalation and emergence of aggression. Recent consensus guidelines emphasize the need for non-coercive management strategies to protect the therapeutic alliance between patients and their healthcare providers—an alliance that is critical for the effective management of chronic psychiatric conditions. Rapid symptom relief with a non-invasive approach to de-escalate agitation are necessary to avoid the costly and traumatic use of coercive techniques of physical restraint and seclusion, which require admission and prolonged hospitalization. It is estimated that approximately 19 million people are risk and 8.3 million in the U.S. suffer from agitation each year.

About the PEC (*P*ANSS or the Positive and Negative Syndrome Scale *E*xcitatory *C*omponent) Score for Agitation
The PEC score is a validated regulatory endpoint for measuring acute agitation in schizophrenia and bipolar patients. The PEC scale is used in clinical research to rate the severity of a patient's acute agitation. The PEC score comprises 5 items associated with agitation: poor impulse control, tension, hostility, uncooperativeness, and excitement; each scored 1 (minimum) to 7 (maximum). The PEC, the sum of these 5 subscales, thus ranges from 5 to 35.

About the ACES (Agitation Calmness Evaluation Scale)
ACES consists of a single item that rates overall agitation and sedation at the time of evaluation, where 1 indicates marked agitation; 2, moderate agitation; 3, mild agitation; 4, normal behavior; 5, mild calmness; 6, moderate calmness; 7, marked calmness; 8, deep sleep; and 9, unarousable.

About BXCL501:
BXCL501 is a potential first-in-class, proprietary sublingual thin film of dexmedetomidine, a selective alpha-2a receptor agonist for the treatment of acute agitation. BTI believes that BXCL501 directly targets a causal agitation mechanism and the Company has observed anti-agitation effects in multiple clinical studies across multiple neuropsychiatric indications. A Phase 1 pharmacokinetic (bioavailability) and safety study of BXCL501 yielded positive top-line data. It is now being evaluated for the acute treatment of agitation resulting from schizophrenia in a Phase 1b trial. The Company plans to unveil future development plans for BXCL501 in agitated dementia, opioid withdrawal symptoms and hyperactive delirium through 2019.

About BioXcel Therapeutics, Inc.:
BioXcel Therapeutics, Inc. is a clinical stage biopharmaceutical company focused on drug development that utilizes novel artificial intelligence approaches to identify and advance the next wave of medicines in neuroscience and immuno-oncology. BTI'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. BTI's two most advanced clinical development programs are BXCL501, a sublingual thin film formulation designed for acute treatment of agitation resulting from neuropsychiatric disorders, and BXCL701, an orally administered systemic innate immunity activator designed for treatment of a rare form of prostate cancer and for treatment of pancreatic cancer in combination with other immuno-oncology agents. For more information, please visit www.bioxceltherapeutics.com.

References

1. The Society of Critical Care Medicine – Critical Care Statistics. Retrieved from https://www.sccm.org/Communications/Critical-Care-Statistics
2. American Psychiatric Association – Practice Guidelines. Retrieved from https://psychiatryonline.org/guidelines
3. Substance Abuse and Mental Health Services Administration – Data and Dissemination. Retrieved from https://www.samhsa.gov/data/
4. National Institutes of Mental Health – Statistics. Retrieved from https://www.nimh.nih.gov/health/statistics/index.shtml

Forward-Looking Statements
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 Company's visibility in the financial community and the impact of inclusion in the Russell 3000® Index and related indices on the Company's clinical development initiatives for BXCL501 and 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 BTI's current expectations and various assumptions. BTI believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain.

BTI 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; 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; 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 period ended March 31, 2019 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 BTI 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 BTI’s views as of any date subsequent to the date of this press release.

Contact Information:
BioXcel Therapeutics, Inc.
www.bioxceltherapeutics.com
The Ruth Group
Janhavi Mohite
646-536-7026
jmohite@theruthgroup.com

Source: BioXcel Therapeutics, Inc.