BioXcel Therapeutics Announces Primary and Secondary Endpoints Met in Two Pivotal Phase 3 Trials of BXCL501 for the Acute Treatment of Agitation in Patients with Schizophrenia and Bipolar Disorder

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Highly statistically significant improvements in PEC score observed vs. placebo (p<0.0001) at two hours in the SERENITY trials for both doses tested

Statistically significant improvements in PEC score observed as early as 20 minutes after treatment

All exploratory endpoints demonstrated statistically significant and clinically meaningful reductions in agitation measures that were durable

BXCL501 was well tolerated with no serious adverse events

NDA submission to U.S. Food and Drug Administration planned for Q1 2021

Company to host conference call today at 8:30 a.m. ET

NEW HAVEN, Conn., July 20, 2020 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. (“BTI” or “Company”) (Nasdaq: BTAI), a clinical-stage biopharmaceutical company utilizing artificial intelligence to identify improved therapies in neuroscience and immuno-oncology, today announced that BXCL501, the Company’s proprietary sublingual thin film of dexmedetomidine, met the primary and secondary endpoints of SERENITY I and SERENITY II, demonstrating a robust treatment effect in the trials. Results demonstrated that BXCL501 was well tolerated, with rapid and durable reductions in agitation.

In patients with schizophrenia (SERENITY I) and a second study of bipolar disorder (SERENITY II), highly statistically significant and clinically meaningful reductions in the Positive and Negative Syndrome Scale, Excitatory Component (“PEC”) score at two hours, the primary endpoint, were reported for both high and low dose cohorts of BXCL501 compared to placebo (p<0.0001). Both studies also met the key secondary endpoint, demonstrating improvement in PEC scores beginning as early as 20 minutes in patients with bipolar disorder, at both dose levels, and as early as 20 minutes in patients with schizophrenia for the 180 mcg dose level. Exploratory efficacy endpoints confirmed the primary endpoint, with duration of response lasting at least four hours after treatment.

“These compelling Phase 3 results show that BXCL501, if approved, has the potential to become an important new treatment option for patients suffering from acute agitation,” commented Vimal Mehta, Ph.D., Chief Executive Officer of BTI. “We are extremely pleased that rapid and robust reductions in agitation were demonstrated in both patient populations despite differing neuropsychiatric diagnoses. We believe these results suggest that BXCL501 may have potential to treat agitation across a wide range of conditions. As we initiate steps toward regulatory submissions in these first two indications, we are also rapidly advancing the investigation of BXCL501 in additional disorders with significant unmet medical need including dementia, hyperactive delirium and opioid withdrawal symptoms.”

Summary of Topline Results

SERENITY I (Patients with Schizophrenia)

Effect at 120 minutes (Primary Endpoint)	**Placebo (n=126)**	**120 mcg (n=129)**	**180 mcg (n=126)**
Reduction in PEC Score vs. Baseline (LSM)	-4.8	-8.5 (p<0.0001)	-10.3 (p<0.0001)
Response Rate (% of Patients Achieving >40% Reduction in PEC Scores)	34%	67%	87%

SERENITY II (Patients with Bipolar Disorder*)

Effect at 120 minutes (Primary Endpoint)	**Placebo (n=126)**	**120 mcg (n=126)**	**180 mcg (n=126)**
Reduction in PEC Score	-5.0	-9.1 (p<0.0001)	-10.4 (p<0.0001)

vs. Baseline (LSM)			
Response Rate (% of Patients Achieving >40% Reduction in PEC Scores)	37%	69%	85%

*includes bipolar I and II disorder, with a diagnosis of depression, hypomania, mania, mixed episodes or unspecified

The secondary endpoint was highly statistically significant at 30 minutes, 45 minutes, 60 minutes, and 90 minutes in both studies. At 20 minutes, both doses were statistically significant in patients with bipolar disorder ($p<0.025$), and in patients with schizophrenia who received the higher 180 mcg dose.

Efficacy was further evaluated using two additional measures of agitation—the Agitation and Calmness Evaluation Scale (ACES), and Clinical Global Impression – Improvement Scale (CGI-I)—each of which showed statistically significant improvements for both doses of BXCL501 compared to placebo.

BXCL501 was well tolerated in both SERENITY trials. Overall, the most commonly reported adverse events from both trials were somnolence (22% for 180 mcg dose arms, 21% for 120 mcg dose arms and 6% for placebo arms; >75% of these events were classified as mild), dry mouth (4.4%, 7.5% and 1.2%, respectively), and dizziness (6.0%, 3.9%, and 0.8%, respectively). All adverse events were mild to moderate in severity, with none categorized as severe or requiring further intervention or monitoring. Few subjects discontinued the trials due to adverse events (SERENITY I: 0 for 180 mcg dose, 2 for 120 mcg dose and 0 for placebo arm; SERENITY II: 0, 1, and 0, respectively).

“I am impressed by the robust and consistent effects of BXCL501 across the SERENITY I and II studies, where it rapidly reduced agitation in patients with schizophrenia and bipolar disorder,” said Professor John Krystal, M.D., Chairman, Department of Psychiatry, Yale University School of Medicine. “Managing agitation has always been a major challenge for health care providers. We would welcome an oral treatment option that is safe, has a quick onset of action, and reduces agitation with a minimum of sedation.”

“In clinical studies, BXCL501’s mechanism of action in treating patients with agitation appeared to be independent of underlying neuropsychiatric disease conditions,” said Robert Risinger, M.D., Vice President, Clinical Development of BTI. “As a result, the Company believes that BXCL501 has significant potential to treat agitation associated with other disorders, and is actively advancing programs in dementia (TRANQUILITY), opioid withdrawal symptoms (RELEASE) and delirium (planned study). The Company is also exploring the potential of BXCL501 in other hyperarousable disease states, such as post-traumatic stress disorder, traumatic brain injury, alcohol withdrawal and as a treatment for phobias.”

ABOUT SERENITY I and SERENITY II

The SERENITY studies were randomized, double-blinded, placebo-controlled parallel group adaptive trials in a total of 759 patients, 18 to 75 years of age. SERENITY I (n=381) enrolled patients with agitation associated with schizophrenia or schizoaffective disorder, with arms randomized to receive BXCL501 at 120 micrograms, or 180 micrograms or matching placebo, respectively. SERENITY II (n=378) enrolled patients with agitation associated with bipolar disorders, in three treatment arms randomized to receive BXCL501 at 120 micrograms, 180 micrograms or placebo, respectively. The primary endpoint of the trials was the reduction in acute agitation measured by the Positive and Negative Syndrome Scale - Excitatory Component (“PEC”) change from baseline compared to placebo. The secondary endpoint was determination of the earliest time where an effect on agitation is apparent as measured by the change from baseline in PEC total score.

Conference Call

BTI will host a conference call and webcast today at 8:30 a.m. ET. To access the call, please dial 877-407-2985 (domestic) and 201-378-4915 (international). A live webcast of the call will be available on the Investors sections of the BTI website at www.bioxceltherapeutics.com. The replay will be available through August 3, 2020.

About Agitation in Neuropsychology

Agitation is a common and difficult to manage symptom associated with a number of psychiatric conditions, including schizophrenia and bipolar disorder. It is estimated that approximately 22 million people are at risk of agitation, and 13 million in the U.S. suffer from agitation each year, costing approximately $40 billion annually in treatment related expenses. Early identification and prompt intervention to relieve 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 health care providers—an alliance that is critical for the effective management of chronic psychiatric conditions. A non-invasive therapy that causes rapid symptom relief and de-escalates agitation may be necessary to avoid the costly and traumatic use of coercive techniques, like physical restraint and seclusion, which require admission and prolonged hospitalization.

About the PEC (PANSS-EC or the Positive and Negative Syndrome Scale-Excitatory Component) Score for Agitation

The PEC total score is a validated regulatory endpoint for measuring acute agitation in schizophrenia and bipolar patients. This scale is used in clinical research to quantify the severity of a patient’s acute agitation. The PEC rating evaluates 5 elements associated with agitation: poor impulse control, tension, hostility, uncooperativeness, and excitement; each scored 1 (minimum) to 7 (maximum). The PEC total score is the sum of these 5 elements and thus ranges from 5 to 35.

About BXCL501

BXCL501 is an investigational 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. BXCL501 has been granted Fast Track Designation by the U.S. Food and Drug

Administration for the acute treatment of agitation. BXCL501 is also being evaluated in a Phase 1b/2 trial (TRANQUILITY) for the treatment of agitation associated with dementia, and in a Phase 1b/2 study (RELEASE) for the treatment of opioid withdrawal symptoms.

BioXcel Therapeutics, Inc.

BioXcel Therapeutics, Inc. is a clinical stage biopharmaceutical company focused on drug development that utilizes artificial intelligence to identify improved therapies in neuroscience and immuno-oncology. BTI's drug re-innovation approach leverages existing approved drugs and/or clinically evaluated 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, an investigational sublingual thin film formulation in development for acute treatment of agitation resulting from neuropsychiatric disorders, and BXCL701, an investigational orally administered systemic innate immunity activator in development 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.

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 timing and data from clinical development initiatives and trials for BXCL501, the potential commercialization of BXCL501 and BTI’s corporate strategy. 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.

These forward-looking statements are based on management’s current expectations and beliefs. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause BTI’s actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: 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 BTI’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 March 31, 2020, 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* and Investors sections of our website at *www.bioxceltherapeutics.com*.

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 its 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.

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