BioXcel Therapeutics Announces Journal of the American Medical Association Publication of Data from SERENITY II Pivotal Phase 3 Trial Evaluating BXCL501 in Bipolar Disorders

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BXCL501 demonstrated statistically significant and clinically meaningful improvements in primary and key secondary efficacy measures compared with placebo

BXCL501 PDUFA Date is April 5, 2022 for acute treatment of agitation associated with schizophrenia and bipolar disorders

NEW HAVEN, Conn., Feb. 22, 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 the publication of results from its pivotal Phase 3 SERENITY II trial of BXCL501 (sublingual dexmedetomidine) for the acute treatment of agitation associated with bipolar disorder in the *Journal of the American Medical Association (JAMA).* BXCL501 is an investigational, proprietary, orally dissolving thin film formulation of dexmedetomidine, a selective alpha-2 receptor agonist for the treatment of agitation associated with neuropsychiatric disorders. The article, "Effect of Sublingual Dexmedetomidine vs Placebo on Acute Agitation Associated With Bipolar Disorder: A Randomized Clinical Trial" (Preskorn et al. 2022), was published online and is available here.

"This research is an important milestone in the development of a patient-centric treatment approach for agitation—a difficult-to-manage symptom associated with many psychiatric and medical conditions," said primary study author, Sheldon H. Preskorn, M.D., Professor, Department of Psychiatry and Behavioral Sciences, University of Kansas School of Medicine-Wichita. "These results demonstrate the potential of sublingual dexmedetomidine as a noninvasive, patient-administered approach for de-escalating a range of agitation episodes associated with bipolar disorder, supporting a collaborative treatment experience for patients and providers."

In the study, BXCL501 120 mcg and 180 mcg significantly reduced agitation compared with placebo as measured by change from baseline on the Positive and Negative Syndrome Scale-Excited Component (PEC) total score at two hours after treatment. On the key secondary endpoint, sublingual dexmedetomidine demonstrated statistically significant improvement in PEC scores compared with placebo beginning as early as 20 minutes after dosing for both treatment groups.

Key Findings

- For the primary endpoint, the mean (standard deviation) changes from baseline in PEC total score two hours after treatment were -10.4 (4.4) for sublingual dexmedetomidine 180 mcg and -9.0 (5.3) for 120 mcg, compared with -4.9 (4.7) for placebo.
- On the key secondary endpoint, statistically significant treatment effects were first evident 20 minutes after initial treatment for both doses (P = .007 for 180 mcg; P = .009 for 120 mcg) compared with placebo. Patients in both treatment groups showed greater improvement in the PEC total score than patients in the placebo group at all subsequent time points through 120 minutes after treatment.
- On prespecified exploratory endpoints, 90.5% and 77.0% of patients in the 180 mcg and 120 mcg BXCL501 treatment groups, respectively, experienced a treatment response at two hours, defined as at least 40% improvement from baseline on PEC score. In the placebo group, 46% were treatment responders.
- The incidence of adverse events (AEs) was 35.7% for sublingual dexmedetomidine 180 mcg, 34.9% for 120 mcg, and 17.5% for placebo. The most commonly reported AEs were somnolence, dry mouth, hypotension, and dizziness. No treatment-related serious or severe AEs were reported.

"We are pleased that *JAMA*'s publication of these data prominently validates BXCL501 as a potential treatment for the millions of patients experiencing agitation associated with bipolar disorders," said Frank D. Yocca, Ph.D., Chief Scientific Officer of BioXcel Therapeutics. "We look forward to our April 5, 2022 PDUFA date and potential FDA approval of BXCL501 for the acute treatment of agitation associated with bipolar disorders as well as schizophrenia. Building on the strength of these compelling data, we are also confidently progressing BXCL501 as a potential acute treatment for agitation associated with Alzheimer's disease."

About Bipolar Disorder and Schizophrenia-Related Agitation

Agitation is a common and difficult-to-manage symptom associated with multiple neuropsychiatric conditions, including bipolar disorders I and II and schizophrenia. An estimated 7.3 million people in the U.S. are diagnosed with schizophrenia or bipolar disorders.[1,2] For those who experience agitation, episodes can occur 10 to 17 times annually,[3] totaling approximately 25 million agitation episodes for these two patient populations – associated with a significant burden for patients, caregivers, and the healthcare system[3]. Early identification and prompt intervention to relieve agitation are essential to avoid symptomatic escalation and the emergence of aggression. Expert consensus best-practice guidelines have recommended that agitation should be treated by a combination of behavioral calming techniques, verbal de-escalation, and medications that are voluntarily accepted by patients without coercion, with the pharmacologic goal of "calming without excessive sedation." A non-invasive therapy that causes rapid and sustained symptom relief may be helpful to avoid the costly and traumatic use of coercive techniques, like physical restraint and seclusion, which may result in admission and prolonged hospitalization.

About SERENITY I and II

The SERENITY studies were randomized, double-blinded, placebo-controlled parallel group trials in a total of 760 patients, 18 to 75 years of age. SERENITY I (N=380) enrolled patients with agitation associated with schizophrenia or schizoaffective disorder, with arms randomized to receive BXCL501 at 120 micrograms, 180 micrograms, or matching placebo. SERENITY II (N=380) enrolled patients with agitation associated with bipolar disorders, in three treatment arms randomized to receive BXCL501 at 120 micrograms, 180 micrograms or placebo. 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.

About BXCL501

BXCL501 is an investigational, proprietary, orally dissolving thin film formulation of dexmedetomidine, a selective alpha-2 adrenergic receptor agonist for the treatment of agitation associated with neuropsychiatric disorders. BioXcel Therapeutics believes that BXCL501 potentially targets an important mediator of agitation, and the Company has observed anti-agitation results in multiple clinical studies across several neuropsychiatric disorders, including schizophrenia-related agitation (SERENITY I), bipolar disorder-related agitation (SERENITY II) and dementia-related agitation (TRANQUILITY). BXCL501 has been granted Breakthrough Therapy designation for the acute treatment of agitation associated with dementia and Fast Track designation for the acute treatment of agitation associated with schizophrenia, bipolar disorders, and dementia. The safety and efficacy of BXCL501 have not been established.

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 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 trials for BXCL501, the timing of potential commercial approval of BXCL501 for the acute treatment of schizophrenia and bipolar disorders I and II and the potential value of BXCL501 as a treatment option. When used herein, words including "anticipate," "will," "plan," "may," "continue," "intend," "designed," "goal" 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, BXCL502, 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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1. Wu EQ, Shi L, Birnbaum H, et al. Annual prevalence of diagnosed schizophrenia in the USA: a claims data analysis approach. Psychol Med. 2006;36(11):1535-1540.
2. Prevalence of bipolar disorder in adults. November 2017. https://www.hcp.med.harvard.edu/ncs/ftpdir/NCS-R_12-month_Prevalence_Estimates.pdf. Accessed June 24, 2021.
3. Data on file. BioXcel Therapeutics, Inc.