BioXcel Therapeutics Initiates Pivotal Phase 3 Program of BXCL501 for Acute Treatment of Agitation in Patients with Alzheimer's Disease

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Two Phase 3 studies to enroll a total of 300 patients in assisted living or residential facilities and nursing homes to evaluate the safety and efficacy of BXCL501

Studies designed to maximize BXCL501 opportunity to treat full spectrum of agitation, with an estimated 100 million agitation episodes in Alzheimer's patients occurring in the U.S. annually

No FDA approved therapies for treatment of agitation associated with Alzheimer's

NEW HAVEN, Conn., Dec. 15, 2021 (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 initiation of its pivotal Phase 3 program for BXCL501, the Company's proprietary, orally dissolving thin film formulation of dexmedetomidine, for the acute treatment of agitation in patients with Alzheimer's disease (AD). The program's two studies, TRANQUILITY II and TRANQUILITY III, are designed to evaluate the safety and efficacy of BXCL501 in adults 65 years and older in assisted living or residential facilities and nursing homes.

"We received FDA breakthrough therapy designation for BXCL501 in March 2021 based on our Phase 1b/2 TRANQUILITY study. Following multiple meetings with the FDA, we are pleased to announce the initiation of our Phase 3 program," said Vimal Mehta, Ph.D., CEO of BioXcel Therapeutics. "This marks an important advancement in potentially bringing this novel treatment to the more than 4 million patients, who experience agitation as one of AD's most devastating symptoms. We are leading the development path for this innovative therapy and are confident in BXCL501's potential to treat acute, as well as intermittent, forms of agitation."

The program expands the evaluation of patients in diverse medical settings across the range of dementia severity. It is designed to maximize the opportunity of BXCL501 for the treatment of the full spectrum of agitation associated with AD.

Pivotal Phase 3 Program Summary

- The program will consist of two randomized, placebo-controlled, adaptive, parallel group pivotal trials, TRANQUILITY II and TRANQUILITY III.
- Each study will enroll 150 dementia patients 65 years and older. Patients will self-administer 40 mcg or 60 mcg of BXCL501 or placebo whenever agitation episodes occur over a three-month period.
- TRANQUILITY II will enroll patients in assisted living or residential facilities requiring minimal assistance with activities of daily living. TRANQUILITY III will enroll patients in nursing homes with moderate to severe dementia requiring moderate or greater assistance with activities of daily living.
- The studies are designed to assess agitation as measured by the changes from baseline in the Positive and Negative Syndrome Scale-Excitatory Component (PEC) and Pittsburgh Agitation Scale (PAS) total scores. The primary efficacy endpoint for both studies will be change in PEC score from baseline measured at two hours after the initial dose and subsequent doses.
- Patients who complete TRANQUILITY II or TRANQUILITY III will be eligible to enroll in an open label, 52-week safety study designed to measure the safety and efficacy of BXCL501 in continued use.

About BXCL501
BXCL501 is an investigational, proprietary, orally dissolving thin film formulation of dexmedetomidine, a selective alpha-2a receptor agonist for the treatment of agitation associated with neuropsychiatric disorders. BioXcel Therapeutics believes that BXCL501 potentially targets a causal agitation mechanism, 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 has not been established.

About Alzheimer's Disease
Alzheimer's disease is the most prevalent type of dementia in the United States. By 2040, approximately 12 million Americans aged 65 years and over are expected to be impacted by the condition, double the approximately 6 million Americans impacted in 2020.[1,2] Of these patients, up to 70% experience agitation, with an estimated 100 million agitation episodes occurring in the United States every year.[3,4] There are no approved therapeutic options for the acute treatment of agitation related to dementia, including Alzheimer's disease.

About TRANQUILITY
The randomized, double-blind, placebo-controlled, ascending dose, adaptive Phase 1b/2 study was designed to evaluate the efficacy, pharmacokinetics, safety, and tolerability of BXCL501 in adults 65 years and older who exhibit acute agitation associated with all forms of dementia, including Alzheimer's disease. Following the completion of each dose cohort, a safety and tolerability review was performed to determine the next tested dose. The study was designed to assess agitation as measured by the changes from baseline in PAS and PEC total scores, as well as by improvements from baseline in the Mod-CMAI total score.

About the Positive and Negative Syndrome Scale-Excitatory Component Score (PEC or PANSS-EC)
The PEC total score is a validated 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 the Pittsburgh Agitation Scale (PAS)
PAS is a validated instrument used to monitor the severity of agitation associated with dementia. The PAS measures 4 behavior groups: aberrant vocalization, motor agitation, aggressiveness, and resisting to care. The groups are evaluated on a scale from 0 to 4, with 0 defined as no agitation present and 4 defined as the highest form of agitation. The PAS total score ranges from 0 to 16.

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 the TRANQUILITY II and TRANQUILITY III trials and the potential value of BXCL501 as a treatment option for agitation in patients with AD, and future financial and operational results. 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] Prevalence of bipolar disorder in adults. November 2017. Accessed June 24, 2021. https://www.hcp.med.harvard.edu/ncs/ftpdir/NCS-R_12-month_Prevalence_Estimates.pdf

[2] Alzheimer's Association

[3] Tractenberg, R Neuropsychiatry Clin Neuroscience 14:1 Winter 2002

[4] Estimate based on company market research