BioXcel Therapeutics Announces TRANQUILITY In-Care Pivotal Phase 3 Trial Plan With BXCL501 for Agitation Associated With Alzheimer's Dementia

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Company plans to initiate trial following recent meeting with FDA

No FDA-approved therapies for acute treatment of AAD are currently available

NEW HAVEN, Conn., April 10, 2024 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. (Nasdaq: BTAI), a biopharmaceutical company utilizing artificial intelligence to develop transformative medicines in neuroscience and immuno-oncology, today announced details regarding the planned design of its upcoming TRANQUILITY In-Care Phase 3 trial to evaluate BXCL501, the company's investigational proprietary, orally dissolving film formulation of dexmedetomidine, as a potential acute treatment for agitation associated with Alzheimer's dementia (AAD) in the care setting. The Company's plan to conduct this trial is based on feedback received from the U.S. Food and Drug Administration (FDA), following the recent receipt of minutes from the Type B/Breakthrough Therapy designation meeting held with the agency on February 20, 2024.

"The design of our upcoming TRANQUILITY In-Care trial largely mirrors TRANQUILITY II, which demonstrated positive efficacy and safety results with a 60 mcg dose of BXCL501," said Vincent O'Neill, M.D., Chief of Product Development and Medical Officer of BioXcel Therapeutics. "We have completed two recent meetings with the FDA on our TRANQUILITY program, and are pleased to have obtained clarity on the next steps for our AAD development path. This represents a major milestone since there is no U.S. regulatory precedent for episodic treatment of AAD. We are now intensely focused on advancing this important program."

TRANQUILITY In-Care Pivotal Phase 3 Trial Design Summary

- The TRANQUILITY In-Care trial is designed as a double blind, placebo-controlled study to evaluate the efficacy and safety of a 60 mcg dose of BXCL501 over a 12-week period.
- The trial is expected to enroll a total of approximately 150 patients 55 years and older across the spectrum of Alzheimer's disease severity with mild, moderate, and severe dementia with mini-mental state examination (MMSE) scores of 0 to 25 who reside in skilled nursing facilities, memory care units, or assisted living facilities.
- The trial is expected to enroll patients with episodic agitation, with patients self-administering 60 mcg of BXCL501 or placebo when agitation episodes occur over the trial period.
- The primary endpoint is expected to be a change from baseline in the Positive and Negative Syndrome Scale-Excitatory Component (PEC) total score at two hours post-first dose. This is the same endpoint used in previous TRANQUILITY trials and in studies that supported the FDA approval of IGALMI™ (dexmedetomidine) sublingual film.
- Continued efficacy evaluations are expected to be conducted through performing additional PEC and complementary efficacy measures, including the global impression of change in agitation.
- As part of the TRANQUILITY In-Care trial, the Company plans to include a feasibility cohort of 20 patients that would be evaluated in the home setting.

The Company expects to generate additional Phase 3 efficacy and safety data in the TRANQUILITY In-Care trial to expand the database beyond the 70 patients who have already been treated with 60 mcg of BXCL501 in TRANQUILITY I and II to date. The Company also plans to discuss the details of the requirement for long-term safety data at a future meeting with the FDA.

A slide presentation on the TRANQUILITY program is available on the Investors section of the Company's website: bioxceltherapeutics.com.

About IGALMI™(dexmedetomidine) sublingual film

INDICATION

IGALMI™ (dexmedetomidine) sublingual film is a prescription medicine, administered under the supervision of a health care provider, that is placed under the tongue or behind the lower lip and is used for the acute treatment of agitation associated with schizophrenia and bipolar disorder I or II in adults. The safety and effectiveness of IGALMI has not been studied beyond 24 hours from the first dose. It is not known if IGALMI is safe and effective in children.

IMPORTANT SAFETY INFORMATION

IGALMI can cause serious side effects, including:

- **Decreased blood pressure, low blood pressure upon standing, and slower than normal heart rate, which may be**

more likely in patients with low blood volume, diabetes, chronic high blood pressure, and older patients. IGALMI is taken under the supervision of a healthcare provider who will monitor vital signs (like blood pressure and heart rate) and alertness after IGALMI is administered to help prevent falling or fainting. Patients should be adequately hydrated and sit or lie down after taking IGALMI and instructed to tell their healthcare provider if they feel dizzy, lightheaded, or faint.

- **Heart rhythm changes (QT interval prolongation)**. IGALMI should not be given to patients with an abnormal heart rhythm, a history of an irregular heartbeat, slow heart rate, low potassium, low magnesium, or taking other drugs that could affect heart rhythm. Taking IGALMI with a history of abnormal heart rhythm can increase the risk of torsades de pointes and sudden death. Patients should be instructed to tell their healthcare provider immediately if they feel faint or have heart palpitations.
- **Sleepiness/drowsiness**. Patients should not perform activities requiring mental alertness, such as driving or operating hazardous machinery, for at least 8 hours after taking IGALMI.
- **Withdrawal reactions, tolerance, and decreased response/efficacy**. IGALMI was not studied for longer than 24 hours after the first dose. Physical dependence, withdrawal symptoms (e.g., nausea, vomiting, agitation), and decreased response to IGALMI may occur if IGALMI is used longer than 24 hours.

The most common side effects of IGALMI in clinical studies were sleepiness or drowsiness, a prickling or tingling sensation or numbness of the mouth, dizziness, dry mouth, low blood pressure, and low blood pressure upon standing.

These are not all the possible side effects of IGALMI. Patients should speak with their healthcare provider for medical advice about side effects.

Patients should tell their healthcare provider about their medical history, including if they suffer from any known heart problems, low potassium, low magnesium, low blood pressure, low heart rate, diabetes, high blood pressure, history of fainting, or liver impairment. They should also tell their healthcare provider if they are pregnant or breastfeeding or take any medicines, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Patients should especially tell their healthcare provider if they take any drugs that lower blood pressure, change heart rate, or take anesthetics, sedatives, hypnotics, and opioids.

Everyone is encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. You can also contact BioXcel Therapeutics, Inc. at 1-833-201- 1088 or medinfo@bioxceltherapeutics.com.

Please see full Prescribing Information at igalmi.com.

About BXCL501
In indications other than those approved by the U.S. Food and Drug Administration (FDA) as IGALMI™ (dexmedetomidine) sublingual film, BXCL501 is an investigational proprietary, orally dissolving film formulation of dexmedetomidine, a selective alpha-2 adrenergic receptor agonist. BioXcel Therapeutics believes that BXCL501 potentially targets an important mediator of agitation, and the Company has observed anti-agitation results in multiple clinical trials across several neuropsychiatric disorders. BXCL501 is under investigation by BioXcel Therapeutics for the acute treatment of agitation associated with dementia due to probable Alzheimer's disease and for the acute treatment of agitation associated with bipolar I or II disorder or schizophrenia in the at-home setting. The safety and efficacy of BXCL501 for these investigational uses have not been established. BXCL501 has been granted Breakthrough Therapy designation by the FDA 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.

About the Mini-Mental State Examination (MMSE)
The MMSE is the best-known and most frequently used short screening tool for providing an overall measure of cognitive impairment in clinical, research, and community settings. It is used for the detection of Alzheimer's disease and other dementias in people with mild cognitive impairment (MCI). The MMSE consists of a simple pen-and-paper test of cognitive function based on a total possible score of 30 points, and includes tests of orientation, concentration, attention, verbal memory, naming, and visuospatial skills.

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

The PEC total score is a validated endpoint for use 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 BioXcel Therapeutics, Inc.
BioXcel Therapeutics, Inc. (Nasdaq: BTAI) is a biopharmaceutical company utilizing artificial intelligence to develop transformative medicines in neuroscience. Its wholly owned subsidiary, OnkosXcel Therapeutics, is focused on the development of medicines in 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 indications. For more information, please visit bioxceltherapeutics.com.

Forward-Looking Statements
This press release includes "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. All statements contained in this press release other than statements of historical fact should be considered forward-looking statements, including, without limitation, statements regarding the planned trial design of the TRANQUILITY In-Care trial; expected discussions with the FDA; and the potential for the results from the Company's completed, ongoing and proposed clinical trials to support regulatory approvals for its product candidates in both the care-facility and at-home settings. When used herein, words including "anticipate," "believe," "can," "continue," "could," "designed," "estimate," "expect," "forecast," "goal," "intend," "may," "might," "plan," "possible," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements use these words or expressions. 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 and limited revenue generation; its incurrence of significant losses; its strategic reprioritization and related reduction in force may not achieve its intended outcome; its need for substantial additional funding and ability to raise capital when needed; its significant indebtedness, ability to comply with covenant obligations and potential payment obligations related to such indebtedness and other contractual obligations; the Company has identified conditions and events that raise substantial doubt about its ability to continue as a going concern; its limited experience in drug discovery and drug development; risks related to the TRANQUILITY program; risks related to the limited clinical data supporting potential safety or efficacy of BXCL501 for use in the at-home setting; its dependence on the success and commercialization of IGALMI, BXCL501, BXCL502, BXCL701 and BXCL702 and other product candidates; interim “top-line” and preliminary data from its clinical trials may change and result in material changes in the final data; its ability to receive regulatory approval from the FDA and comparable foreign authorities for its product candidates; clinical trials are expensive, time-consuming, difficult to design, difficult to conduct, and involve an uncertain income; its lack of experience in marketing and selling drug products; the risk that IGALMI or the Company’s product candidates may not be accepted by physicians or the medical community in general; the Company’s estimated number of episodes of agitation and its corresponding estimated total addressable market are subject to inherent challenges and uncertainties; the Company still faces extensive and ongoing regulatory requirements and obligations for IGALMI; 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 enroll patients in its clinical trials; undesirable side effects caused by the Company’s product candidates; its novel approach to the discovery and development of product candidates based on EvolverAI; the significant influence of and dependence on BioXcel LLC; its exposure to patent infringement lawsuits; its reliance on third parties; its ability to comply with the extensive regulations applicable to it; impacts from data breaches or cyber-attacks, if any; the Company is and may in the future be subject to legal proceedings, claims and investigations in or outside the ordinary course of business, which could be costly and time-consuming to defend and could result in unfavorable outcomes; risks related to unfavorable global political or economic events and conditions; risks associated with the increased scrutiny relating to environmental, social and governance (ESG) matters; risks associated with federal, state or foreign health care “fraud and abuse” laws; and its ability to commercialize its product candidates, as well as the important factors discussed under the caption “Risk Factors” in its Annual Report on Form 10-K for the fiscal year ended December 31, 2023, 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 the Investors section of the Company’s 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 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.

Website Disclosure
We may use our website as a distribution channel of material information about the Company. Financial and other important information regarding the Company is routinely posted on and accessible through the Investors & Media section of its website at www.bioxceltherapeutics.com. In addition, you may automatically receive email alerts and other information about the Company when you enroll your email address by visiting the “Email Alerts” option under the News / Events menu of the Investors & Media section of our website at www.bioxceltherapeutics.com.

Contact Information

Corporate
BioXcel Therapeutics Erik Kopp 1.203.494.7062
ekopp@bioxceltherapeutics.com

Investor Relations BioXcel Therapeutics Brennan Doyle 1.475.355.8462
bdoyle@bioxceltherapeutics.com

Media
Russo Partners
David Schull
1.858.717.2310
David.schull@russopartnersllc.com
Scott Stachowiak
1.646.942.5630
Scott.stachowiak@russopartnersllc.com

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