BioXcel Therapeutics Announces Positive Topline Results From TRANQUILITY II Phase 3 Trial of BXCL501 for Acute Treatment of Alzheimer's Disease-Related Agitation

June 29, 2023

Trial met primary endpoint with the 60 mcg dose, with BXCL501 demonstrating a statistically significant 39% greater reduction in PEC score from baseline compared to placebo at 2 hours (p=0.0112)

Met key secondary endpoint with statistically significant reduction (p=0.0185) in agitation symptoms versus placebo, as measured by PEC score change from baseline at 1 hour with 60 mcg dose; multiple secondary measures support efficacy

443 episodes for 149 patients were treated over 12 weeks across all doses; dosing with 60 mcg showed a similar reduction in agitation for first and all treated episodes at 1 and 2 hours, as measured by average change in PEC score

BXCL501 was well tolerated with no drug-related serious adverse events over trial duration

Company intends to engage with FDA in H2 2023 on a potential path to sNDA submission

BioXcel Therapeutics to host conference call today at 8:00 a.m. ET

NEW HAVEN, Conn., June 29, 2023 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. (Nasdaq: BTAI), a biopharmaceutical company utilizing artificial intelligence approaches to develop transformative medicines in neuroscience and immuno-oncology, today announced positive topline results for TRANQUILITY II, a Phase 3 trial of BXCL501, the Company's proprietary, orally dissolving film formulation of dexmedetomidine under investigation for the acute treatment of Alzheimer's disease-related agitation.

The Phase 3 trial met its primary efficacy endpoint with the 60 mcg dose; a statistically significant and clinically meaningful 7.5 point reduction from baseline in Positive and Negative Syndrome Scale-Excitatory Component (PEC) total score was observed at 2 hours versus 5.4 with placebo (p=0.0112). The 60 mcg dose also met the first key secondary endpoint of reducing agitation symptoms at 1 hour during the first episode of agitation (p=0.0185) but did not meet the other key secondary endpoint of change from baseline in PEC score at 30 minutes.

Efficacy for this dose was supported by a number of secondary measures, including CGI-I and ACES. Most patients (76%) responded to the first 60 mcg dose and were determined to be "Very Much" or "Much Improved" (CGI-I of 1 or 2) compared to 50% with placebo. The primary endpoint was not met for the 40 mcg dose, with a 5.7 point reduction from baseline in PEC score.

BXCL501 continued to show a PEC reduction over repeated dosing. A total of 443 episodes were dosed over the 12-week trial period, including 294 episodes occurring after the first treatment across all dose groups. Dosing with 60 mcg showed a reduction in PEC total score from pre-dose versus placebo at 1 hour (p=0.011) and 2 hours (p=0.0044) for all episodes of agitation.

"We believe these results represent a significant milestone for BioXcel Therapeutics and a potential important step forward in our goal to helping those impacted by Alzheimer's disease," said Vimal Mehta, CEO of BioXcel Therapeutics. "Today, there are approximately 100 million Alzheimer's-related agitation episodes in the U.S. annually, and there are no episodic treatment options for these patients. We believe that our data from TRANQUILITY II show that BXCL501 has the potential to treat acute episodes of agitation in patients with mild to moderate Alzheimer's disease, if approved. This is particularly critical as the prevalence of this disease is expected to nearly double over the next 15 to 20 years. We are excited at the prospect of continuing to expand BXCL501's market potential."

BXCL501 was well tolerated, with a side effect profile substantially consistent with prior trials of BXCL501 and the current label for IGALMI™. The 60 mcg dose had previously been evaluated in different patient populations and in healthy volunteers. Data from TRANQUILITY II add to this safety database and show that the majority of safety events occurring within 24 hours of dosing in this population were mild or moderate in severity and consistent with the current IGALMI™ label. In addition, dosing for subsequent episodes did not result in a meaningful increase in the number of adverse events and no treatment-related serious adverse events were observed over the 12-week study period.

For all 443 episodes over the 12-week period, there were no syncope or falls related to trial drug. All falls except one with placebo were outside the 24-hour treatment window (5 falls in the 40 mcg arm, 7 falls in the 60 mcg arm, and 5 falls in the placebo arm).

"I believe that the results from the TRANQUILITY II trial are an exciting development for potentially addressing Alzheimer's disease-related agitation," said George Grossberg, M.D., Professor and Director Division of Geriatric Psychiatry in the Department of Psychiatry & Behavioral Neuroscience at St. Louis University School of Medicine. "In this trial, BXCL501 showed a desirable onset of action and a meaningful reduction in agitation at 2 hours with the 60 mcg dose, and was well tolerated in this patient population. I believe it has potential to be a new treatment option for a condition that not only impacts patients but also caregivers and families."

TRANQUILITY II Topline Results

Efficacy Results at 2 Hours (Primary Endpoint)

	BXCL501 60 mcg n=50	**BXCL501 40 mcg n=48**	**Placebo n=51**

Reduction in PEC Total Score from Baseline LSM (SE)	7.5 (0.6)	5.7 (0.6)	5.4 (0.6)
p-value (vs. placebo)	0.0112*	0.7648	

*Statistical significance achieved at 0.025

Adverse Events of Special Interest Reported Within 24 Hours of First Dose**

Adverse Event	Severity	BXCL501 60 mcg n=50 (%)	BXCL501 40 mcg n=48 (%)	Placebo n=51 (%)
Somnolence*	Mild Moderate	8 (16.0) 1 (2.0)	6 (12.5) 2 (4.2)	2 (3.9) 0
Lethargy	Mild Moderate	2 (4.0) 1 (2.0)	1 (2.1) 1 (2.1)	1 (2.0) 0
Hypotension	Mild Moderate	7 (14.0) 1 (2.0)	4 (8.3) 0	2 (3.9) 0
Bradycardia	Mild Moderate	3 (6.0) 1 (2.0)	0 1 (2.1)	0 0
Orthostatic Hypotension	Mild Moderate	2 (4.0) 2 (4.0)	2 (4.2) 1 (2.1)	1 (2.0) 0

*Verbatim; drowsy or feeling sleepy

** The adverse events of special interest (AESI) are defined as those related to mechanism of action of the drug. Those that are listed were observed within 24 hours after the first dose and occur with a frequency of at least 2% and greater than with placebo. Subjects are counted once at highest severity for each preferred term

“We are extremely pleased with the positive topline results of this trial in elderly patients with Alzheimer’s disease-related agitation,” said Robert Risinger, M.D., Chief Medical Officer, Neuroscience of BioXcel Therapeutics. “The favorable safety data, along with the consistent efficacy observed for the 60 mcg dose, underscores BXCL501’s potential in mitigating a condition that impacts millions of patients and their families annually. In addition to our positive topline results with TRANQUILITY II, we have a robust safety database of more than 1,200 subjects across a range of ages, multiple neuropsychiatric conditions, and doses. Additionally, BXCL501 has been granted a Breakthrough Therapy Designation for the acute treatment of dementia-related agitation based on TRANQUILITY I data. We believe this body of evidence lays the foundation to potentially bring a differentiated acute agitation treatment option for patients with Alzheimer’s disease.”

The Company plans to develop a path to potential sNDA submission for the acute treatment of agitation associated with Alzheimer’s disease in H2 2023, subject to further discussions with the FDA.

Conference Call

BioXcel Therapeutics will host a conference call and webcast on June 29, 2023 at 8:00 a.m. ET to discuss the Phase 3 TRANQUILITY II trial results. To access the call, please dial 877-407-5795 (domestic) or 201-689-8722 (international). A link to a live webcast and accompanying presentation materials will be available on the Investors section of the corporate website, bioxceltherapeutics.com, and a replay will be available through September 29, 2023.

BioXcel Therapeutics may use its 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 sections of its website at bioxceltherapeutics.com. In addition, you may sign up to automatically receive email alerts and other information about the Company by visiting the “Email Alerts” option under the News/Events section of the Investors & Media website section and submitting your email address. You can also review our public filings on the SEC's website at www.sec.gov, including the Current Report on Form 8-K filed with the SEC on June 29, 2023 for additional important information relating to the TRANQUILITY II trial.

About TRANQUILITY II

TRANQUILITY II, a randomized, placebo-controlled, parallel group trial, evaluated the safety and efficacy of BXCL501 for the acute treatment of Alzheimer’s-related agitation in adults 65 years and older in assisted living facilities (ALFs) and residential care settings who required minimal assistance with activities of daily living. The trial dosed 149 patients with mild to moderate dementia. Randomized patients self-administered 40 mcg or 60 mcg of BXCL501 or placebo for agitation episodes that occurred over a 12-week period. The primary endpoint was the change from pre-dose in PEC total score at 2 hours post-dose for the first treated episode of agitation. The key secondary efficacy endpoints were PEC change from pre-dose at 1 hour post-dose of study treatment for the first treated episode of agitation, and PEC change from pre-dose at 30 minutes post-dose of study treatment for the first treated episode of agitation.

For additional information regarding the TRANQUILITY II Phase 3 trial, including data integrity and protocol adherence issues at one of the trial sites, see the Company’s Current Report on Form 8-K filed with the SEC on June 29, 2023, which should be read in conjunction with this press release.

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 the Agitation Calmness Evaluation Scale (ACES)

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 the Clinical Global Impressions – Improvement Scale (CGI-I)

The CGI-I scale is a widely used rating scale to assess overall improvement or change in a patient's condition. It provides a subjective evaluation of the patient's global improvement relative to their baseline or previous state. The scale consists of categories ranging from "Very much improved" to "Very much worse," allowing healthcare professionals or researchers to rate the patient's progress based on their clinical judgment.

About BXCL501

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 studies across several neuropsychiatric disorders. BXCL501 is under investigation for the acute treatment of agitation associated with bipolar I or II disorder or schizophrenia in the at-home setting, for the acute treatment of Alzheimer's-related agitation, and as an adjunctive treatment for Major Depressive Disorder. The safety and efficacy of BXCL501 for these investigational uses have not been established. 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.

About BioXcel Therapeutics, Inc.

BioXcel Therapeutics, Inc. is a 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 indications. The Company's commercial product, IGALMI™ (developed as BXCL501), is a proprietary, sublingual film formulation of dexmedetomidine approved for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder in adults. The safety and effectiveness of IGALMI have not been established beyond 24 hours from the first dose. For more information, please visit igalmi.com and also see the IGALMI full Prescribing Information. BXCL501 is under evaluation for at-home use for the acute treatment of agitation in bipolar and schizophrenia patients, for acute treatment of agitation associated with Alzheimer's disease, and as an adjunctive treatment for major depressive disorder. The safety and efficacy of BXCL501 for these uses have not been established. The Company is also developing BXCL502 as a potential therapy for chronic agitation in dementia. Under its subsidiary, OnkosXcel Therapeutics, the Company is developing BXCL701, an investigational, oral systemic innate immune activator for the treatment of aggressive forms of prostate cancer and other solid and liquid tumors. The safety and efficacy of BXCL502 and BXCL701 have not been established. 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 (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). 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 Company's expected timing of, trial design and data results from, future clinical trials and future regulatory approvals of BXCL501, in particular for treatment of dementia, potential safety and tolerability features of BXCL501, the potential addressable market for BXCL501 and the potential benefits from treatment with BXCL501. 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 ability to receive regulatory approval for its product candidates and the possibility that the FDA does not conclude that its product candidates satisfy the regulatory requirements for approval; dependence on third-party clinical investigators who may not comply with good clinical practice or other regulatory requirement; the outcomes of its internal and third-party investigations into one of the principal investigators on the TRANQUILITY II trial; 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 IGALMI™, BXCL501, BXCL502 and BXCL701 and other product candidates; its lack of experience in marketing and selling drug products; 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; 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, 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. 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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