BioXcel Therapeutics Announces Update on NIDA-funded Trial of BXCL501 (sublingual dexmedetomidine) for Potential Treatment of Opioid Use Disorder (OUD)

November 6, 2023

Columbia University-led trial expected to add fourth site to target completion of 4-arm, 160-patient trial in 2024

Fentanyl adulterated or associated with xylazine (FAAX) designated an emerging threat by the White House Office of National Drug Control Policy[1]

Company to seek FDA feedback on potential registrational paths

NEW HAVEN, Conn., Nov. 06, 2023 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. (Nasdaq: BTAI), a biopharmaceutical company utilizing artificial intelligence to develop transformative medicines in neuroscience, today announced an update on the National Institute on Drug Abuse (NIDA)-funded trial evaluating BXCL501 (sublingual dexmedetomidine) as a potential treatment for opioid use disorder (OUD).

BioXcel Therapeutics is supplying BXCL501 for an ongoing 4-arm, 160-patient trial that is enrolling patients who have been predominantly exposed to fentanyl and/or predominantly exposed to fentanyl adulterated or associated with xylazine (FAAX), which has been designated an emerging threat by the White House Office of National Drug Control Policy[1]. NIDA has requested Columbia University, the trial coordinator, to add a fourth site to target trial completion in 2024. After this time, BioXcel Therapeutics plans to seek FDA feedback on potential registrational paths.*

According to NIDA, xylazine has been linked to an increasing number of overdose deaths nationwide in the evolving drug addiction and overdose crisis. Studies show people exposed to xylazine often knowingly or unknowingly used it in combination with other drugs, particularly illicit fentanyl.[2] Recently, the Biden administration requested $46 billion in its fiscal 2024 National Drug Control Budget[3] to address the opioid epidemic, while opioid settlements reached between U.S. state and local governments and the 14 major pharmaceutical opioid manufacturers, distributors, and retailers have aggregated between $51 billion and nearly $55 billion.[4]

“We have long known that the locus coeruleus drives various opioid withdrawal symptoms [5] but have lacked access to a sublingual formulation of dexmedetomidine, one of the most potent and selective alpha 2-adrenergic receptor agonists available, as a treatment option,” said Dr. Sandra Comer, Principal Investigator of the trial and Professor of Neurobiology in the Department of Psychiatry at Columbia University. “With BXCL501, we are excited about the potential to treat patients who are physically dependent on illicit and prescription opioids. We believe dexmedetomidine might be particularly helpful in treating withdrawal symptoms in patients who are dependent on fentanyl and/or fentanyl adulterated with xylazine.”

Between June 2020 and January 2021, Columbia University enrolled patients in the Company’s RELEASE trial — a multicenter, randomized, double-blind, placebo-controlled, ascending-dose Phase 1b/2 trial designed to evaluate the safety, pharmacokinetics, tolerability, and efficacy of BXCL501 administered twice daily for seven days — in patients experiencing opioid withdrawal symptoms. In March 2021, BioXcel Therapeutics announced RELEASE topline results. BXCL501 was generally well tolerated, with no severe or serious adverse events reported across all doses evaluated (30 mcg, 60 mcg, 90 mcg, 120 mcg, 180 mcg, and 240 mcg). After further post-hoc analysis, a peer-review article published in the *American Journal of Drug and Alcohol Abuse* in January 2023 [6] reported that the 240 mcg BID dose (480 mcg per day) was well tolerated, demonstrated statistically significant reduction in both Clinical Opiate Withdrawal Scale (COWS) and Subjective Opiate Withdrawal Scale (SOWS), and demonstrated a greater completion of treatment among enrolled patients, 87% of whom had been exposed to fentanyl. In August 2022, the Company announced an NIH NIDA grant to Columbia University to support further studies of BXCL501 for the treatment of OUD.

“While BXCL501 has already demonstrated statistical significance in patients exposed to fentanyl, this current study has a high proportion of patients exposed to FAAX and is comparing 180 mcg and 240 mcg BID doses to both placebo and the standard of care, lofexidine,” said Robert Risinger, M.D., Chief Medical Officer, Neuroscience of BioXcel Therapeutics. “BXCL501 is one of the only potential treatments being studied in this patient population and represents an important potential option to help address the growing OUD crisis.”

The BXCL501 OUD trial is supported by the National Institute on Drug Abuse of the National Institutes of Health (NIH) under award number UG3DA056247.

*In 2017, the U.S. federal government determined that a public health emergency under the Public Health Service Act for the opioid crisis existed, and this determination was recently renewed for 90 days in September 2023, although such public health emergency is independent from any public health emergency determined under the Federal Food, Drug, and Cosmetic Act. A separate determination under the act has not been issued and would be a prerequisite for FDA to declare that circumstances exist justifying emergency use of drugs to address the public health emergency, which must occur before FDA is authorized to issue emergency use authorizations for OUD drugs. The Company may consider advocating for such determination under the Federal Food, Drug and Cosmetic Act, as well as a declaration from the government that drugs targeting OUD are eligible for the emergency use authorization path to market, though they are not currently permitted under the law to be authorized pursuant to this pathway today.

Government-Supported Investigator-Initiated Trial Programs for BXCL501 and Commercialization Opportunities
BioXcel Therapeutics has retained all rights to the commercialization of BXCL501 in all potential indications evaluated in clinical trials supported by the U.S. government. In addition to OUD as an indication, BioXcel Therapeutics has been awarded key opportunities for the development of BXCL501 in post-traumatic stress disorder and alcohol use disorder. These are being funded through cooperative agreements with the U.S. Department of Defense Congressionally Directed Medical Research Program and NIDA. Clinical and regulatory responsibilities are being led by clinical researchers and regulatory staff at Columbia University New York State Psychiatric Institute, the Veterans Affairs Connecticut Healthcare System, Yale University Medical School, RTI International, and NIDA.

About BXCL501
In indications other than those approved by the FDA as IGALMI™, 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 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 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. (Nasdaq: BTAI) is a biopharmaceutical company utilizing artificial intelligence to develop transformative medicines in neuroscience. 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 (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: expected timing of, trial design and data results from, clinical trials of BXCL501, the potential addressable market for BXCL501, potential registrational paths and potential advocating activities relating to BXCL501, the potential for BXCL501 to treat opioid withdrawal symptoms and potential benefits of such treatment. The words "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; risks associated with the strategic reprioritization; its limited experience in drug discovery and drug development; its dependence on the success and commercialization of IGALMI™, BXCL501, BXCL502, BXCL701 and BXCL702 and other product candidates; 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; undesirable side effects caused by the Company's product candidates; its exposure to patent infringement lawsuits; its reliance on third parties; its ability to comply with the extensive regulations applicable to it; 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 June 30, 2023, 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.

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
T: 858-717-2310
David.schull@russopartnersllc.com
Scott Stachowiak
T: 646-942-5630
Scott.stachowiak@russopartnersllc.com

Source: BioXcel Therapeutics, Inc.

BT BIOXCEL THERAPEUTICS is a registered trademark of BioXcel Therapeutics, Inc.
All other trademarks are the properties of their respective owners.
Copyright © 2023, BioXcel Therapeutics, Inc. All rights reserved.

References

1. Whitehouse.gov. Biden-Harris Administration Designates Fentanyl Combined with Xylazine as an Emerging Threat to the United States. Accessed November 1, 2023. Accessed November 1, 2023. https://www.whitehouse.gov/ondcp/briefing-room/2023/04/12/biden-harris-administration-designates-fentanyl-combined-with-xylazine-as-an-emerging-threat-to-the-united-states/
2. nida.nih.gov. Research Topics. Accessed November 2, 2023. https://nida.nih.gov/research-topics/xylazine
3. Whitehouse.gov. National Drug Control Budget FY2024 Funding Highlights March 2023. Accessed November 1, 2023. https://www.whitehouse.gov/wp-content/uploads/2023/03/FY-2024-Budget-Highlights.pdf
4. Opioidsettlementtracker.com. Global Settlement Tracker. Accessed November 1, 2023. https://www.opioidsettlementtracker.com/globalsettlementtracker
5. Rasmussen K 1991. Afferent effects on locus coeruleus in opiate withdrawal. Prog Brain Res. 1991;88:207-16. doi: 10.1016/s0079-6123(08)63810-8. PMID: 1839935.
6. Jones JD, Rajachandran L, Yocca F, Risinger R, De Vivo M, Sabados J, Levin FR, Comer SD. Sublingual dexmedetomidine (BXCL501) reduces opioid withdrawal symptoms: findings from a multi-site, phase 1b/2, randomized, double-blind, placebo-controlled trial. Am J Drug Alcohol Abuse. 2023 Jan 2;49(1):109-122. doi: 10.1080/00952990.2022.2144743. Epub 2023 Jan 11. PMID: 36630319.