BioXcel Therapeutics Announces Positive Phase 2 Topline Results from Columbia University-Led Study of BXCL501 for Treatment of Opioid Withdrawal

March 5, 2026

BXCL501 demonstrated clinical benefits and favorable tolerability profile for treatment of opioid withdrawal symptoms

Results from this NIDA-funded study support potential future development of BXCL501 in opioid withdrawal

Opioid use disorder is a global health crisis, affecting approximately 5.9 million adults in the U.S.

NEW HAVEN, Conn., March 05, 2026 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. (Nasdaq: BTAI), a biopharmaceutical company built on artificial intelligence ("AI") to develop transformative medicines in neuroscience, today announced positive topline results from a Phase 2 investigator-sponsored trial (IST) evaluating BXCL501 for the treatment of opioid withdrawal symptoms in adults with opioid use disorder (OUD) undergoing a methadone taper.

The study suggested that BXCL501 may be as effective as or superior to lofexidine (Lucemyra®) for reducing the symptoms of opioid withdrawal during methadone taper, while having a more convenient dosing regimen and demonstrating a favorable tolerability profile. In this study, BXCL501 had similar or lower overall rates of cardiovascular (CV) effects than lofexidine. Specifically, the most common CV adverse event for Lucemyra, orthostatic hypotension, was significantly lower for the 180 µg twice daily (BID) BXCL501 dose group (18% vs 50% lofexidine, $p<0.05$) and remained lower in the highest 240 µg BID BXCL501 dose group (37%) over the seven-day dosing period. There were no reports of sedation or somnolence in the BXCL501 treatment arms (5% reported sedation in the lofexidine arm). These results support potential future development of BXCL501 in opioid withdrawal.

These findings build on the earlier Company-sponsored Phase 1b/2 study, RELEASE,[1] which established the tolerability profile of selected BXCL501 doses in opioid-dependent patients and extend those results into a clinically distinct setting that included a methadone taper and an active comparator.

The results are consistent with the mechanism of action of BXCL501 (alpha 2-adrenergic receptor agonism), as locus coeruleus drives various opioid withdrawal symptoms.[2] These results strengthen the growing body of evidence supporting BXCL501 across multiple potential indications, reinforcing its potential as a "pipeline within a product." These findings build on positive results from Phase 3 pivotal studies evaluating BXCL501 for the treatment of acute agitation associated with bipolar disorder and schizophrenia, as well as Alzheimer's disease.

For this National Institute on Drug Abuse (NIDA)-funded study, BioXcel Therapeutics supplied BXCL501. This study was planned as a 4-arm trial: BXCL501 180 µg BID or 240 µg BID, placebo, and lofexidine 0.54 mg QID as a positive control. It enrolled participants who were predominantly exposed to fentanyl and included a high proportion of participants exposed to fentanyl adulterated or associated with xylazine (FAAX), which has been designated as an emerging threat by the White House Office of National Drug Control Policy.[3] The trial was completed after 80 patients were enrolled.

Key takeaways from the study include:

- BXCL501 240 µg BID reduced opioid withdrawal symptoms compared to placebo during a seven-day methadone taper, as measured by the Short Opiate Withdrawal Scale-Gossop (SOWS-Gossop).
  - After receiving BXCL501 240 µg, patients experienced a greater than 30% reduction in SOWS-Gossop scores, with peak symptom improvement observed on days 3 and 4.
  - The reduction in withdrawal symptoms with BXCL501 numerically exceeded that observed with lofexidine 0.54 mg administered four times daily.
- BXCL501 demonstrated a favorable tolerability profile, with rates of key adverse events (including dizziness, orthostatic hypotension, bradycardia and insomnia) comparable to or lower than those reported for lofexidine in the Lucemyra® (lofexidine) FDA label.

"As we continue to face a worldwide crisis encompassing a large patient population suffering from opioid use disorder, these results showcase an encouraging therapeutic milestone demonstrating the significant potential of BXCL501 as a therapy for meaningfully reducing opioid withdrawal symptoms," said Dr. Sandra Comer, Principal Investigator of the study and Professor of Neurobiology in the Department of Psychiatry at Columbia University. "Opioid withdrawal remains a significant burden on the healthcare system and patients, and despite available therapies, there is still a substantial unmet need for safe and more effective treatment options that can help patients successfully transition to other medications such as buprenorphine or naltrexone for long-term benefits."

Notably, OUD remains a critical global health crisis, with an estimated 36 to 61 million people worldwide living with opioid dependence.[4] Approximately 85% of chronic opioid users experience at least one withdrawal episode every six months, suggesting that 30 to 50 million individuals globally may require withdrawal management each year. In the United States alone, approximately 5.9 million people have diagnosed OUD, and about 8.9 million report annual opioid misuse.[5] Despite this substantial need, only about 25% of individuals with a substance use disorder receive specialized treatment, highlighting a significant treatment gap.[6] Currently approved options for opioid withdrawal management are limited, and tolerability challenges may affect adherence, underscoring the potential importance of BXCL501's differentiated profile as a non-opioid, orally dissolving thin film

formulation of dexmedetomidine administered twice daily. Another potential advantage of BXCL501 is that it may be particularly well-suited for treating withdrawal from opioids adulterated with xylazine.

About BioXcel Therapeutics, Inc.

BioXcel Therapeutics, Inc. (Nasdaq: BTAI) is a biopharmaceutical company built on artificial intelligence ("AI") 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.

About BXCL501

Outside of its approved indication by the U.S. Food and Drug Administration as IGALMI® (dexmedetomidine) sublingual film, BXCL501 is an investigational proprietary, orally dissolving film formulation of dexmedetomidine, a selective alpha-2 adrenergic receptor agonist. BXCL501 is under investigation by BioXcel Therapeutics for the acute treatment of agitation associated with Alzheimer's dementia 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.

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 related to: potential future development of BXCL501 in opioid withdrawal; BXCL501's potential as a "pipeline within a product"; the potential of BXCL501 to serve as a safe and effective treatment option that can help patients successfully transition to other medications. 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; its incurrence of significant losses; its need for substantial additional funding and ability to raise capital when needed; the impact of the reprioritization; 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; its dependence on the success and commercialization of IGALMI®, BXCL501, BXCL502, BXCL701 and BXCL702 and other product candidates; the number of episodes of agitation and the size of the Company's total addressable market may be overestimated, and approval that the Company may obtain may be based on a narrower definition of the patient population; 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 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 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 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; 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, 2024, 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 and the Investors section of the Company's website at. 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/Investors
Russo Partners
Nic Johnson
nic.johnson@russopartnersllc.com
1.303.482.6405

Media
Russo Partners
David Schull
david.schull@russopartnersllc.com
1.858.717.2310

Source: BioXcel Therapeutics, Inc.

References

1. Jones et al., Am J Drug Alcohol Abuse. 2023 49(1):109–122
2. Ivanov and Aston-Jones, Journal of Neurophysiology 2001 85:6, 2388-2397
3. https://clinicaltrials.gov/study/NCT05712707
4. https://www.unodc.org/res/wdr2022/MS/WDR22_Booklet_1.pdf
5. https://drugabusestatistics.org/
6. https://www.cdc.gov/mmwr/volumes/73/wr/mm7325a1.htm