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BioXcel Therapeutics Announces Results of Phase 1b/2 Study of BXCL501 for the Treatment of Opioid Withdrawal Symptoms

Primary safety endpoint achieved in first study of BXCL501 dosed twice-daily over seven days

RELEASE results demonstrated numerically improved retention rates in multiple BXCL501 dose cohorts

Data from multiple dosing regimen in RELEASE supports investigation across additional indications and treatment settings

NEW HAVEN, Conn., March 31, 2021 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. ("BioXcel" or the "Company") (NASDAQ: BTAI), a clinical-stage biopharmaceutical company utilizing artificial intelligence approaches to develop transformative medicines in neuroscience and immuno-oncology, today announced topline results from its Phase 1b/2 proof-of-concept RELEASE study of BXCL501, the Company's proprietary, orally dissolving thin film formulation of dexmedetomidine, for the treatment of opioid withdrawal symptoms.

The study met its primary safety endpoint across multiple doses given twice-daily over seven days. BXCL501 was generally well tolerated, with no severe or serious adverse events reported, and dose dependent exposures were observed across all doses evaluated (30 mcg, 60 mcg, 90 mcg, 120 mcg, 180 mcg and 240 mcg). See table below with focus on cardio-vascular and nervous system treatment emergent adverse events.

System Organ Class Preferred Term	BXCL501 30 mcg (N=17) n (%)	BXCL501 60 mcg (N=17) n (%)	BXCL501 90 mcg (N=21) n (%)	BXCL501 120 mcg (N=19) n (%)	BXCL501 180 mcg (N=21) n (%)	BXCL501 240 mcg (N=15) n (%)	Placebo (N=25) n (%)
Cardiac disorders	0	0	0	0	0	1 (6.7)	0
Bradycardia	0	0	0	0	0	1 (6.7)	0
Vascular disorders	0	1 (5.9)	0	0	2 (9.5)	6 (40.0)	0
Hypotension	0	1 (5.9)	0	0	0	5 (33.3)	0
Orthostatic hypotension	0	0	0	0	2 (9.5)	4 (26.7)	0

Nervous system disorders	0	0	0	0	3 (14.3)	7 (46.7)	0
Dizziness	0	0	0	0	1 (4.8)	0	0
Presyncope	0	0	0	0	0	1 (6.7)	0
Somnolence	0	0	0	0	2 (9.5)	7 (46.7)	0

Treatment Emergent Adverse Events ("TEAEs") are adverse events with an onset date (and ti
Subjects are counted once within each system organ class and preferred term.
Includes number of any TEAEs, and number (%) of subjects with any TEAEs.
BXCL501 doses were administered BID (twice a day).

With respect to retention, a secondary endpoint, the study showed that patients in multiple dose cohorts treated with BXCL501 had numerical improvements in retention rates, a key goal of opioid withdrawal treatment. The 120 mcg and 180 mcg dose groups showed 42% and 52% rates of retention at Day 6 of BXCL501 treatment, respectively, versus 24% for placebo, though observations were not statistically significant. The results also showed that of the 87% of patients who had fentanyl in their systems upon entry, greater than 50% remained fentanyl positive following the morphine stabilization phase of 5 days. Consequently, withdrawal symptoms were not equivalent across various dose cohorts indicating morphine did not normalize withdrawal symptoms. Improvements were not observed in the severity of opiate withdrawal as measured by the Short Opiate Withdrawal Scale of Gossop (“SOWS-Gossop”) or the Clinical Opiate Withdrawal Scale (“COWS”). The Company believes that the high fentanyl prevalence and lack of normalization observed in study subjects could have confounded these results and made them difficult to interpret.

“We’re very pleased with the tolerability of BXCL501 observed across multiple doses, twice-a-day and for consecutive treatment days in this study, which we believe provides valuable insights as we explore additional indications and treatment settings that require multiple dosing regimens,” commented Reina Benabou, M.D., Ph.D., Senior Vice President & Chief Development Officer. “Treating opioid withdrawal is a significant national challenge, complicated by the more recent high rates of fentanyl addiction, which is significantly more potent and more prevalent than other opioids. We’re encouraged that the RELEASE study helped us to identify a dose range that was generally well tolerated and resulted in numerical improvements in retention in this patient population. We’ll continue to analyze these results in collaboration with our advisors regarding potential next steps for this important indication.”

“With more than 81,000 drug overdose deaths in the U.S. last year, there is an urgent need for improved strategies to help transition patients off opioids. Over the past five years, the epidemic has grown more challenging due to the widespread emergence of counterfeit fentanyl,” said Tom Kosten, M.D., Waggoner Professor in Psychiatry, Pharmacology, Neuroscience and Immunology at Baylor College of Medicine. “The results from the RELEASE study, which identified dosing regimens for BXCL501 that were well tolerated, showed that more patients receiving BXCL501 were able to complete treatment, suggesting that BXCL501 may have potential as a non-opioid based treatment option to address this unmet need.”

About RELEASE

The multicenter, randomized, double-blind, placebo-controlled, ascending dose Phase 1b/2

study was designed to evaluate the safety, pharmacokinetics, tolerability, and efficacy of escalating doses of BXCL501 versus placebo, following discontinuation of morphine maintenance in patients (n=125) with opioid use disorder who are physically dependent on opioids. Throughout the 7-day treatment phase, BXCL501 was evaluated in sequential, ascending dose cohorts and patients received BXCL501 at either the 30 mcg, 60 mcg, 90 mcg, 120 mcg, 180 mcg and 240 mcg or placebo, administered twice daily, approximately 12 hours apart. 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 patients' symptoms of acute opioid withdrawal, following the morphine maintenance phase with the Clinical Opiate Withdrawal Scale ("COWS") and the Short Opiate Withdrawal Scale of Gossop ("SOWS-Gossop").

About Opioid Drug Withdrawal

According to the Centers for Disease Control and Prevention ("CDC"), the misuse of and addiction to opioids is a serious national crisis and is the leading cause of death in the U.S. for those under 50 years old. Between 1999-2019, almost 450,000 people died from an overdose involving an opioid, with approximately 36,000 deaths occurring in 2019 alone involving synthetic opioids, including fentanyl. The surge in fentanyl availability began in 2013. Synthetic opioid-involved death rates increased by over 15% from 2018 to 2019 and accounted for nearly 73% of all opioid-involved deaths in 2019. The rate of overdose deaths involving synthetic opioids were more than 11 times higher in 2019 than in 2013. The CDC estimates the total "economic burden" of prescription opioid misuse alone in the U.S. is $78.5 billion a year, including the costs of healthcare, lost productivity, addiction treatment and criminal justice involvement. Opioid withdrawal is a condition characterized by symptoms such as anxiety, agitation, sleep problems, muscle aches, runny nose, sweating, nausea, vomiting, diarrhea, and drug craving — that occur after stopping or reducing the use of opioids in anyone with physical dependence on opioids.

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 and opioid withdrawal symptoms. BioXcel 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. BXCL501 has been granted Breakthrough Therapy designation for the acute treatment of agitation in dementia and Fast Track designation for the acute treatment of agitation in schizophrenia, bipolar disorders, and dementia. BXCL501 has been studied in two Phase 3 trials (SERENITY I and II) for the acute treatment of schizophrenia related agitation and bipolar disorder related agitation, respectively, a Phase 1b/2 trial (TRANQUILITY) for the acute treatment of dementia related agitation, as well as a Phase 1b/2 trial (RELEASE) for the treatment of opioid withdrawal symptoms. This product candidate is also being evaluated in a Phase 2 trial (PLACIDITY) for the treatment of delirium related agitation.

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. BioXcel'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's two most advanced clinical development programs are BXCL501, an investigational, proprietary, orally dissolving thin film formulation of dexmedetomidine for the treatment of agitation and opioid withdrawal symptoms, 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 potential for BXCL501 to treat opioid withdrawal symptoms, the possible impact of the presence of fentanyl on treatment with BXCL501 and the Company's future strategy for BXCL501 for the treatment of opioid withdrawal symptoms and other indications. When used herein, words including "anticipate," "being," "will," "plan," "may," "continue," 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 BioXcel's current expectations and various assumptions. BioXcel believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain.

BioXcel 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 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 BioXcel'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 Annual Report on Form 10-K for the year ended December 31, 2020, 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 our 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 BioXcel 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 BioXcel's views as of any date subsequent to the date of this press release.

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