BioXcel Therapeutics Reports Positive Topline Exploratory Efficacy Data from SERENITY At-Home Pivotal Phase 3 Safety Trial for Agitation Associated with Bipolar Disorders or Schizophrenia

September 10, 2025

BXCL501 demonstrated a significant mean reduction in mCGI-S score from baseline compared to placebo at 2 hours across 2,433 treated episodes (p<.05)

Complete resolution of agitation was significantly higher with BXCL501 compared to placebo across agitation episode severity (p<.0001)

BXCL501 showed a similar reduction in agitation symptoms over both the duration of the trial and number of treated episodes, demonstrating continued effects and consistent benefit with repeat dosing of BXCL501

Based on the large body of evidence and positive FDA feedback, Company plans to submit a sNDA in Q1 2026 for expanded usage of IGALMI® in the outpatient setting

Company to host virtual KOL call with Dr. Leslie Citrome on SERENITY At-Home program at 2 p.m. today

NEW HAVEN, Conn., Sept. 10, 2025 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. (Nasdaq: BTAI), a biopharmaceutical company utilizing artificial intelligence to develop transformative medicines in neuroscience, today announced positive topline exploratory efficacy data from the SERENITY At-Home Pivotal Phase 3 safety trial, which demonstrated BXCL501 had continued effects and consistent benefit with repeat dosing. The trial in the home setting evaluated 120 mcg dose of BXCL501, the Company's proprietary, sublingual film formulation of dexmedetomidine, IGALMI®, for treatment of agitation associated with bipolar disorders or schizophrenia.

BioXcel previously reported positive topline safety results, the primary objective of the trial, on August 27, 2025 and is reporting additional findings today. While the trial was not powered for efficacy assessments, continued effects and consistent benefits with repeat dosing seen in the trial further support the potential of BXCL501 for use in the outpatient setting. The data from this successful trial will form the basis of the sNDA submission for label expansion of IGALMI® in the at-home setting planned for the first quarter of 2026.

"The SERENITY At-Home results mark a pivotal step in advancing the potential for outpatient use of BXCL501 for the acute treatment of agitation in bipolar disorders and schizophrenia," said Vimal Mehta, Ph.D., CEO of BioXcel Therapeutics. "These positive results, along with the safety and tolerability data previously announced, reinforce BXCL501's potential in the at-home setting where there is substantial unmet need with no FDA-approved options currently available. We remain committed to redefining the treatment paradigm for these patients and families in the outpatient setting, which we believe represents a large addressable market and a catalyst for long-term growth and value creation."

Leslie Citrome, M.D., M.P.H., Clinical Professor of Psychiatry and Behavioral Sciences at New York Medical College, added, "These findings, in a pragmatic trial, are very encouraging for patients living with bipolar disorder or schizophrenia and their families. They open the door for patients and their caregivers to better manage agitation outside of the emergency department, reducing burden on families and the healthcare system while fostering patient-centered care."

The SERENITY At-Home trial is a Pivotal Phase 3, double-blind, placebo-controlled, 12-week clinical trial designed to evaluate the safety of BXCL501 (120 mcg dose) for the acute treatment of agitation associated with bipolar disorders or schizophrenia in an at-home setting. The trial also included an exploratory objective of assessing the continued efficacy of BXCL501 in the treatment of episodes of agitation.

SERENITY At-Home Topline Summary

- Summary of Agitation Episodes
  - A total of 246 patients randomized
  - Data collected on 2,628 agitation episodes in 215 patients over a 12-week period
    - Treated 2,437 episodes in 208 patients
    - 168 patients (81%) completed the full 12-week trial
    - Average of 11.7 agitation episodes recorded per treated patient
    - Reported agitation episodes were classified as mild (664), moderate (1,369) or severe (395)
- All patients were able to successfully self-administer the film
- Distribution of enrolled patients was 45% bipolar disorders and 55% schizophrenia
- Protocol allowed for concomitant interventions to self-regulate or manage agitation episodes

SERENITY AT-Home Topline Exploratory Efficacy Results

The efficacy of IGALMI® has already been established in the institutional setting in the SERENITY I and II trials that led to the approval by FDA (see label below) in April 2022. In addition to the primary objective of evaluating the safety of BXCL501, the SERENITY At-Home trial also had an exploratory objective of assessing continued efficacy of BXCL501 with repeat dosing. The trial was not powered for these assessments. The positive results demonstrated continued effects and consistent benefits with repeat dosing of BXCL501, reinforcing the potential of BXCL501 in the outpatient setting.

Effect Across Total Number of Agitation Episodes

Across 2,433 treated episodes in the trial, BXCL501 demonstrated a significant mean reduction in the modified Clinical Global Impression–Severity (mCGI-S) score from baseline compared to placebo at 2 hours (p<.05).

Effect Across Severity of Agitation Episodes

Patients experienced a complete resolution of agitation symptoms measured by mCGI-S at significantly higher rates with BXCL501 compared to placebo across severity of agitation episodes, with an overall resolution of 50% in the BXCL501 arm, compared to 33% on placebo (p <.0001). Severe agitation episodes fully resolved (no agitation) in 61% of episodes in the BXCL501 arm, compared to 18% on placebo (p <.0001). Moderate agitation episodes fully resolved in 43% of cases for patients in the BXCL501 arm, compared to 34% on placebo (p <.0005). Mild agitation episodes fully resolved in 60% of cases for patients in the BXCL501, compared to 40% on placebo (p <.0001). In sum, complete resolution of agitation was significantly higher with BXCL501 compared to placebo regardless of agitation episode severity.

Effect Across Number of Treated Agitation Episodes

The mean reduction in agitation symptoms experienced by patients following administration of BXCL501 was maintained throughout repeated dosing in the trial. There was a mean reduction in mCGI-S score of 1.2 following the first 12 doses and a mean reduction of 1.4 following 13 or more doses of BXCL501. This underscores the potential of BXCL501 to continue to provide benefit across repeated dosing.

Efficacy Across Duration of the Trial

The reduction in agitation symptoms experienced by patients following administration of BXCL501 was also maintained throughout the trial's duration. Evaluating the 12-week trial period on a time-based scale, agitation episodes treated with BXCL501 during weeks 1-4, 5-8 and 9-12 all had a mean reduction in mCGI-S score of 1.3. This underscores the potential of BXCL501 to maintain a sustained benefit across longer treatment durations.

IGALMI® is currently FDA-approved and marketed for the acute treatment of agitation associated with bipolar I or II disorder or schizophrenia in medically supervised settings. IGALMI® is available in 2 dose strengths, 120 mcg and 180 mcg. To support the potential label expansion for at-home use, an important component of the regulatory package will be data from the SERENITY At-Home Pivotal Phase 3 trial. The trial design and protocol were previously agreed to with FDA.

BXCL501 was granted Fast Track Designation for the acute treatment of agitation associated with bipolar disorders or schizophrenia in December 2018. There are no FDA-approved therapies for the acute treatment of agitation in the at-home setting.

At-Home Agitation Market Insights[1-4]

- The Company believes the total addressable market is significantly higher (57-77M agitation episodes annually) than previously anticipated (23M agitation episodes annually).
- The previous estimate of 23M annual episodes was based on historic claims data, reflecting approximately 1.2 episode per patient per month. The claims data likely underestimate the actual episode frequency due to the lack of approved treatment options. We believe the total addressable market is significantly higher than previously reported.
- Market research and published survey data indicate that episodes may occur 3-4 times a month on average, with the majority of these episodes being moderate or severe.
- Data from more than 2,600 episodes of agitation recorded in the SERENITY At-Home Pivotal Phase 3 trial are in line with these higher frequency estimates.
- Physicians believe a significant unmet need is the lack of an effective and fast acting treatment at-home.
- Physicians underdiagnose and undertreat these episodes in a community setting, with only a third of patients receiving prescription drugs, which are off-label and often suboptimal, for their agitation symptoms.
- Patients are the primary stakeholder for the treatment of their agitation episodes.
    - Patients feel that they lack control over their thoughts and actions during agitation episodes.
    - In a market survey, patients indicated they would take BXCL501 for 80% of their agitation episodes.
    - 90% of those patients indicated they would take BXCL501 when they feel an episode coming on or when an episode begins.

The Serenity At-Home Pivotal Phase 3 Safety Trial Topline Results Presentation has been updated which is on the Investors section of the corporate website, bioxceltherapeutics.com.

The results of the SERENITY At Home trial will be discussed during a live webcast and Q&A session with KOL Leslie Citrome, M.D., M.P.H., Clinical Professor of Psychiatry and Behavioral Sciences at New York Medical College. To access the webcast, please use the following link: https://event.webcasts.com/starthere.jsp?ei=1734890&tp_key=71fab56f2e, or dial in at 877-407-5795 / +1 201-689-8722. A link to the webcast and accompanying presentation materials will also be available on the Investors section of the corporate website, bioxceltherapeutics.com, and a replay will be available for approximately 90 days.

Additional data and results will be presented at upcoming medical meetings and conferences.

About the SERENITY At-Home Pivotal Phase 3 Trial
The trial was designed to study 200 patients with a history of agitation episodes despite being on stable treatment for their underlying bipolar or schizophrenia residing at home either alone or with caregivers/informants. Patients were required to self-administer 120 mcg of BXCL501 (the approved dose under medical supervision) or placebo when they experienced agitation episodes over the 12-week trial period, and their safety data (adverse events) was collected during the trial. In addition, patients or caregivers/informants completed a modified global impression of severity (mCGIs) two hours after dosing as an exploratory endpoint to assess their experience in the outpatient setting.

About Modified Clinical Global Impression – Severity Scale (mCGI-S)
The mCGI-S was used as an assessment of exploratory efficacy in the Serenity At-Home trial. The original clinician rated CGI-S scale describes an 8-point rating of agitation symptoms where zero means there was no assessment performed and scores of 1-7 rate increasing severities of the symptoms being assessed. For ease of implementation by the patient and informant in the home setting this scale was modified in conjunction with FDA. The modified CGI-S is a 4-point scale where 0 is no agitation, and scores of 1-3 describe increasing severities of agitation (mild, moderate, or severe).

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.

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 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 related to: the Company's planned advancement of its SERENITY program; potential market opportunity for BXCL501; release of data from the SERENITY At-Home trial; the submission of an sNDA to the FDA; the supply of IGALMI® through existing distribution channels; the potential for the results from the Company's completed, ongoing and proposed clinical trials to support regulatory approvals for its product candidates and change the treatment paradigm for agitation. 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 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.

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