BioXcel Therapeutics Announces SERENITY At-Home Pivotal Phase 3 Safety Trial Met its Primary Endpoint in Support of sNDA Submission for Label Expansion of IGALMI®

August 27, 2025

BXCL501 achieved SERENITY At-Home's primary endpoint of being well tolerated in the at-home treatment of agitation episodes in patients with bipolar disorders or schizophrenia

No discontinuations for tolerability in the BXCL501 arm

While not the primary objective of the SERENITY At-Home trial, the preliminary results demonstrate continued effects and consistent benefit with repeat dosing across the course of the trial

Following previously disclosed positive FDA feedback, BioXcel plans to submit a sNDA in Q1 2026 for expanded usage of BXCL501 in the outpatient setting without the supervision of a healthcare provider

More than 2400 episodes of agitation were treated in the SERENITY At-Home trial suggesting a significantly larger potential market opportunity

Company to host conference call at 8 a.m. EDT today

NEW HAVEN, Conn., Aug. 27, 2025 (GLOBE NEWSWIRE) -- BioXcel Therapeutics, Inc. (Nasdaq: BTAI), a biopharmaceutical company utilizing artificial intelligence to develop transformative medicines in neuroscience, today announced that the SERENITY At-Home Pivotal Phase 3 trial evaluating the safety of BXCL501, the Company's proprietary, sublingual film formulation of dexmedetomidine, as an acute treatment for agitation associated with bipolar disorders or schizophrenia in the at-home setting, met its primary endpoint. The data from this successful study 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 are transformative in our journey toward outpatient use of BXCL501 for the acute treatment of agitation associated with bipolar disorders or schizophrenia," said Vimal Mehta, Ph.D., CEO of BioXcel Therapeutics. "By meeting its primary endpoint, the SERENITY At-Home Pivotal Phase 3 trial reinforces BXCL501's potential to be safely used at home like it is already used in the previously FDA approved institutional setting. The unmet medical need in the at-home setting is significant with no FDA approved treatments. We are committed to changing the treatment paradigm as we prepare for our planned sNDA submission intended to provide patients with access to IGALMI® in the home setting. We believe the total addressable market is significantly larger than previously reported."

"The management of agitation associated with bipolar disorder and schizophrenia in the home setting is an important clinical challenge where we currently have few optimal options," said Dr. John Krystal, M.D., the Robert L. McNeil, Jr. Professor of Translational Research and Chair of the Department of Psychiatry at Yale School of Medicine. "Timely intervention has the potential to mitigate patient distress, decrease emergency room visits, and enhance overall patient safety while reducing healthcare costs, and I am pleased that this promising data could pave the way for a potential first approval of BXCL501 for at-home treatment."

The SERENITY At-Home Pivotal Phase 3 trial is a double-blind, placebo-controlled 12 week trial designed to evaluate the safety of a 120 mcg dose of BXCL501 for the acute treatment of agitation associated with bipolar disorders or schizophrenia in the at-home setting.

SERENITY At-Home Topline Summary

- Summary of agitation episodes:
  - A total of 246 patients randomized
  - Data collected 2628 agitation episodes in 215 patients
  - Treated 2437 episodes in 208 patients
    - 168 patients (81%) completed the full 12-week trial
  - Average of 11.7 agitation episodes recorded per treated patient
- All patients were able to successfully self-administer the film
- Distribution of enrolled patients was 45% bipolar disorders and 55% schizophrenia

SERENITY AT-Home Primary Endpoint Data

The 120 mcg dose of BXCL501 was well-tolerated in patients with episodes of agitation in the outpatient setting and met the primary objective. This tolerability outcome was observed across repeat dosing and through the duration of the trial.

- No discontinuations due to tolerability in the BXCL501 arm
- Adverse event profile consistent with approved IGALMI® label and multiple clinical trials in the institutional setting
  - No drug-related serious adverse events (SAEs), syncopes or falls reported
  - No new or unexpected treatment emergent adverse events (TEAEs)
  - No severe TEAEs associated with BXCL501 treatment and most TEAEs were mild

- No trend of more frequent AEs over time or with repeat dosing
- Tolerability remained consistent throughout the repeat dosing in the trial

BXCL501 120 mcg Tolerability Profile Consistent with IGALMI® Label

Treatment-Emergent Adverse Events [2]	Serenity I & II (IGALMI® Label[1])		Serenity At-Home Adverse Event by Dose (Episode)[1]			
	Single Dose		First Dose		All Doses (2437 episodes)	
	IGALMI® N=255 n (%)	Placebo N=252 n (%)	BXCL501 N=102 n (%)	Placebo N=106 n (%)	BXCL501 N=1160 n (%)	Placebo N=1277 n (%)
Somnolence [3]	56 (22%)	16 (6%)	23 (22.5%)	18 (17%)	161 (13.9%)	103 (8.1%)
Oral Paresthesia/Hypoesthesia	14 (6%)	2 (1%)	2 (2.0%)	1 (0.9%)	6 (0.5%)	1 (0.1%)
Dizziness	10 (4 %)	2 (1%)	5 (4.9%)	1 (0.9%)	19 (1.6%)	2 (0.2%)
Dry mouth	19 (7%)	3 (1%)	7 (6.9%)	1 (0.9%)	56 (4.8%)	24 (1.9%)
Nausea	6 (2%)	4 (2%)	1 (1.0%)	0(0%)	6 (0.5%)	1 (0.1%)
Headache	12 (5%)	12 (5%)	0 (0%)	2 (1.9%)	4 (0.3%)	4 (0.3%)

[1] SERENITY I and II evaluated a single agitation episode in each patient. SERENITY AT-Home evaluated a total of 2437 episodes in 208 patients. Adverse events are presented on an episode basis. Only AEs observed in Serenity At-Home Pivotal Phase 3 trial are listed

[2] AEs within 24 hours following dosing

[3] Includes fatigue

BXCL501 Tolerability Profile Consistent with Repeat Dosing[1]

Treatment-Emergent Adverse Event [2]	Doses 1-3		Doses 4 to 12		Doses 13 and beyond	
	BXCL501 N=266 n (%)	PLACEBO N=274 n (%)	BXCL501 N=398 n (%)	PLACEBO N=485 n (%)	BXCL501 N= 496 n (%)	PLACEBO N=518 n (%)
Somnolence [3]	58 (22.0%)	43 (16.0%)	61 (15.3%)	52 (10.8%)	42 (8.5%)	8 (1.5%)
Oral Paresthesia/Hypoesthesia	4 (1.5%)	1 (0.4%)	2 (0.5%)	0 (0%)	0 (0%)	0 (0%)
Dizziness	10 (3.8%)	1 (0.4%)	7 (1.8%)	1 (0.2%)	2 (0.4%)	0 (0%)
Dry mouth	14 (5.3%)	2 (0.7%)	29 (7.3%)	2 (0.4%)	13 (2.6%)	20 (3.9%)
Nausea	1 (0.4%)	1 (0.4%)	3 (0.8%)	0 (0%)	2 (0.4%)	0 (0%)
Headache	3 (1.1%)	2 (0.7%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)

[1] Adverse events are presented on an episode basis

[2] AEs within 24 hours following dosing

[3] Includes fatigue

BXCL501 Tolerability Profile Consistent over the Trial Duration[1]

Treatment-Emergent Adverse Event[2]	Weeks 1 to 4		Weeks 5 to 8		Weeks 9 to 12	
	BXCL501 N=454 n (%)	PLACEBO N=474 n (%)	BXCL501 N=369 n (%)	PLACEBO N=433 n (%)	BXCL501 N=337 n (%)	PLACEBO N=370 n (%)
Somnolence[3]	74 (16.4%)	53 (11.2%)	47 (12.7%)	29 (6.7%)	36 (10.7%)	19 (5.2%)
Oral Paresthesia/Hypoesthesia	6 (1.3%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dizziness	13 (2.9)	2 (0.4%)	3 (0.8%)	0 (0%)	3 (0.9%)	0 (0%)
Dry mouth	25 (5.5%)	2 (0.4%)	20 (5.4%)	10 (2.3%)	11 (3.3%)	12 (3.3%)
Nausea	3 (0.7%)	1 (0.2%)	2 (0.5%)	0 (0%)	1 (0.3%)	0 (0%)

[1]Adverse events are presented for agitation episodes in the weeks indicated

[2]AEs within 24 hours following dosing

[3] Includes fatigue

SERENITY At-Home Preliminary Exploratory Data

The efficacy of IGALMI® has already been established in the institutional setting in the SERENITY I and II trials that led to FDA approval (see label

below). The available topline data for the exploratory endpoints from more than 2400 episodes in SERENITY At-Home demonstrates that treatment with BXCL501 regularly reduced symptoms of agitation throughout the trial. A greater percentage of patients experiencing mild, moderate, or severe agitation had full resolution of symptoms in the BXCL501 arm compared with placebo. The initial results demonstrate continued effects and consistent benefit with repeat dosing across the course of the trial.

Complete analyses of the full data set is ongoing, and results will be shared in the near future.

“We are pleased with the positive results and consistent tolerability profile demonstrated for BXCL501 in more than 1100 self-administered treated episodes in the at-home setting," Matt Mandel, M.D., Vice President of Clinical Development at BioXcel Therapeutics, stated. “With efficacy already established for the 120mcg dose of IGALMI®, demonstrating evidence of benefit to patients with repeat dosing in the outpatient setting is highly encouraging. We believe the totality of the evidence, combined with the favorable tolerability, supports our planned regulatory submission and positions BXCL501 to potentially become the first at-home treatment for this critical unmet need affecting patients and their families.”

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 part of the regulatory package will be data from this SERENITY At-Home Pivotal Phase 3 trial, which is a double-blind, placebo-controlled 12-week study designed to evaluate the safety of a 120 mcg dose of BXCL501 for the acute treatment of agitation associated with bipolar disorders or schizophrenia in the at-home setting. 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 previous estimate of 23 million annual episodes was based on historic claims data, reflecting approximately 1.2 episode per patient per month. The claims data likely underestimate the true 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 2600 episodes of agitation recorded in the SERENITY At-Home Pivotal Phase 3 trial are in line with these higher frequency estimates.
- Based on these higher frequency estimates, we believe patients experience an estimated 57 million to 77 million agitation episodes in the at home setting annually in the United States.
- 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.

Analyses of the full Phase 3 dataset from the SERENITY At-Home Pivotal Phase 3 trial are ongoing, and additional data and results will be presented at upcoming medical meetings and conferences.

Conference Call

BioXcel Therapeutics will host a conference call and webcast at 8 a.m. EDT today to discuss the SERENITY At-Home trial results. To access the webcast, please use the following link https://ir.bioxceltherapeutics.com/news-events/ir-events, 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 through November 26, 2025.

About the SERENITY At-Home 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 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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Source: BioXcel Therapeutics, Inc.

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