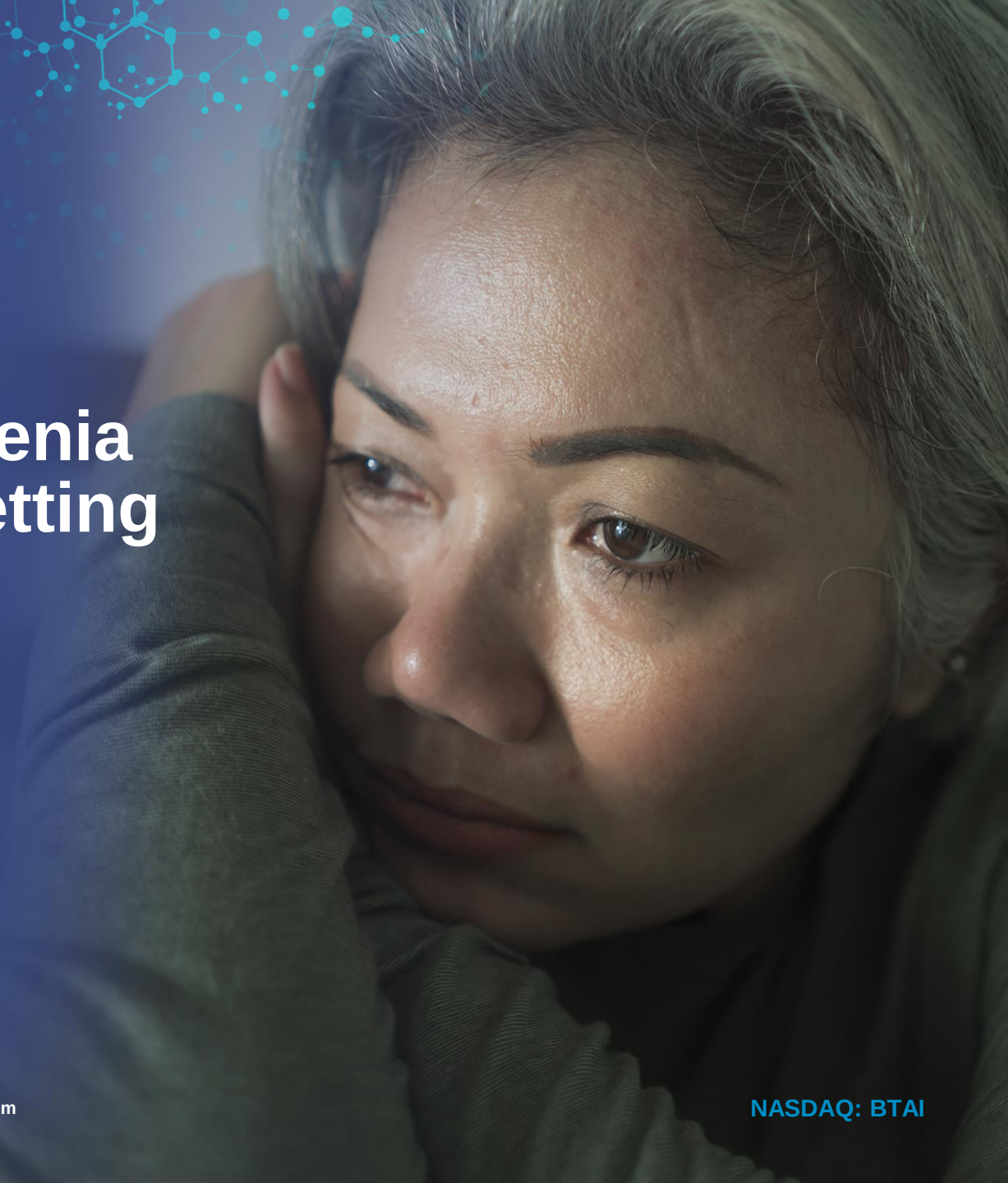
# Bipolar Disorder/Schizophrenia Agitation in the At-Home Setting

## SERENITY III Part 1 Summary & Key Market Insights

**May 25, 2023**



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This presentation includes "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995.Forward-looking statements in this presentation include but are not limited to: statements regarding the Company's expected timing of, trial design and data results from, future clinical trials of BXCL501, in particular for the SERENITY III Part 2 trial, potential. safety and tolerability features of BXCL501, the potential addressable market for BXCL501 and the potential benefits from treatment with BXCL501. 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 Therapeutics' current expectations and various assumptions. BioXcel Therapeutics believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain.

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# Contents

# Patients' Perspective of Agitation

Patients report feeling out of control with their thoughts and actions, with a sense of helplessness. Most of these episodes happen outside an institutional setting.

> It feels like there's something inside of me telling me **there's something wrong**, and I can't sit still, and I feel like my body's about to jump out of my skin. It's just really annoying, and **you get short-tempered** because of it and angry and snappy at people. **It's hard to describe** because you can't get it to go away, and it's just there, and **you're stuck with it**, and **there's nothing you can do** to make it go away.
>
> *(Q1, R10, PT, SCZ)*

Question 1: Take a moment to describe what it is like to experience an episode of agitation associated with schizophrenia or bipolar disorder. How do you (or your loved one) feel during these times, both physically and emotionally?
Source: InVibe July 2022

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# ~39 Million Annual Episodes of Agitation Associated With Bipolar Disorders or Schizophrenia Occur Annually in U.S.[1-3]

## An estimated 23 million episodes (~60%) occur outside of a medical institution

- **Patients report feeling out of control and helpless** when agitation episodes occur at home. [4]
- **Episodes may occur several times per month**, with the majority escalating to moderate or severe.[4]
- **Physicians underrecognize and undertreat these episodes in a community setting**, with only a third of patients receiving prescription drugs, off-label and often suboptimal, for their agitation symptoms.[4]
- **Nearly one quarter of agitation episodes can be sensed by patients prior to onset**.[4]
- Surveyed patients indicated they would take BXCL501 for **80% of their agitation episodes.**[4]
  - 90% of patients indicated they would take BXCL501 when they feel an episode coming on[4]

1 Data on file. BioXcel Therapeutics, Inc. New Haven, CT December 2020. 2. Wu EQ, Shi L, Birnbaum H, et al. Annual prevalence of diagnosed schizophrenia in the USA: a claims data analysis approach. Psychol Med. 2006;36(11):1535-1540. 3. National Institute of Mental Health. Prevalence of bipolar disorder in adults. November 2017. Accessed December 16, 2022. https://www.nimh.nih.gov/health/statistics/bipolar-disorder.
4 InVibe Feb 2023

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# Promising Topline Results: SERENITY III Part 1

## BXCL501 for At-Home Use in Acute Treatment of Agitation in Bipolar Disorders or Schizophrenia

- **Clinically meaningful efficacy results observed with 60mcg dose**
  - Half of lowest approved IGALMI™ dose, 120 mcg
- **Majority of patients (52%) were PEC responders**
  - Proportionally consistent dose-response with two approved IGALMI™ doses
- **Well tolerated with no reported serious adverse events (SAEs)**
  - Lower incidence of AEs observed compared to studies evaluating approved IGALMI™ doses for at-home use
- **SERENITY III Part 2 advancing**
  - Primary objective is safety, secondary is efficacy
    - Alignment obtained with FDA for 60 mcg and repeat 60 mcg dose, if required
  - Adaptive trial design using 60 mcg or greater doses such as 80 mcg at home
    - 80mcg demonstrated statistical significance in prior Phase 1b trial
  - Rigorous PK/PD modeling [60 – 120 mcg] started to select optimal dose and regimen
- **Protocol amendment for adaptive dosing in progress**

# SERENITY III

## Trial Design

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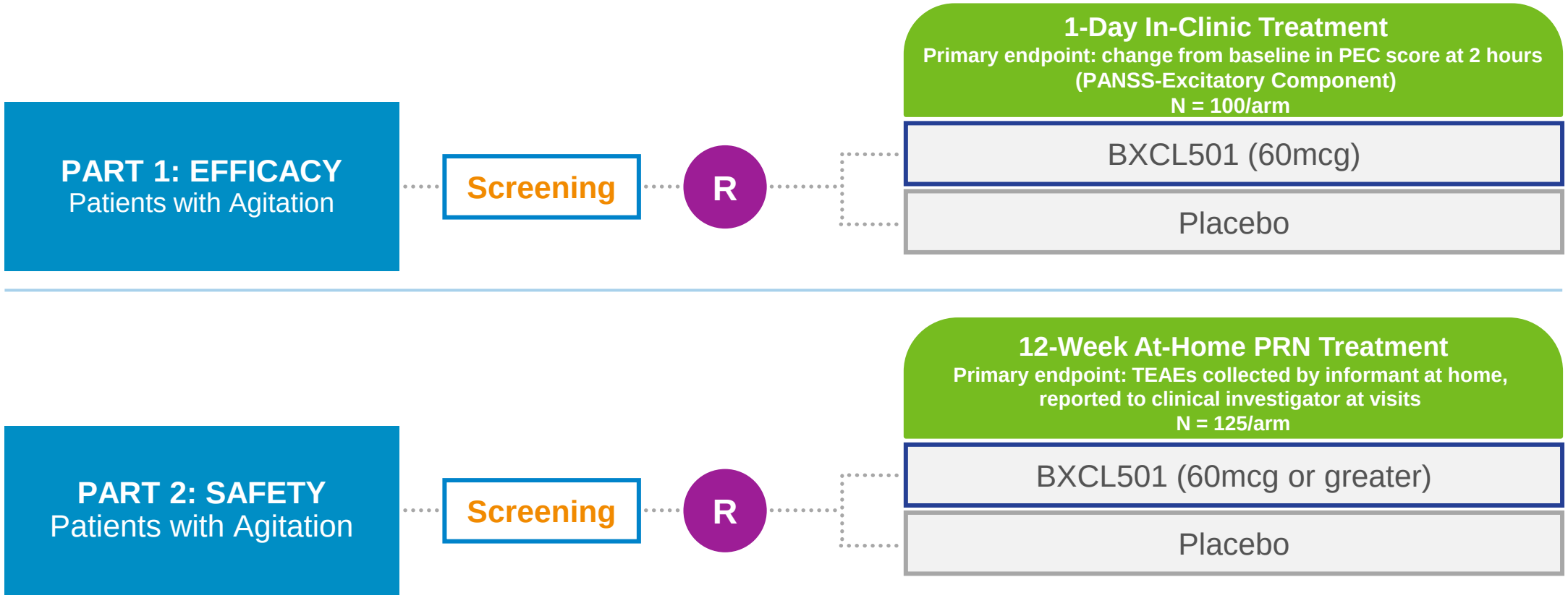
# SERENITY III

## At-home Use of BXCL501 for Acute Treatment of Bipolar Disorders or Schizophrenia-related Agitation

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# BXCL501 At-Home Intervention

The potential advantage for BXCL501 in the at-home setting is the ability for patients to intervene with their agitation episodes much earlier in escalation.

BXCL501 CLINICAL DEVELOPMENT

**23M EPISODES**

AT HOME SETTING

SERENITY III PART 1

PRE-AGITATION | AGITATION INITIATION | MILD | MODERATE | SEVERE

OPTIMAL INTERVENTION

SERENITY III PART 2

HOSPITAL SETTING

**16M EPISODES**


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# Exclusion/Inclusion Criteria: Part 1

## Inclusion Criteria included:

- Male and female patients ages 18 - 75 years with bipolar I or II disorder, schizophrenia, schizoaffective, or schizophreniform disorder
- Total score of ≥ 14 on the PEC and a score of ≥4 on at least 1 of the 5 items at baseline

## Exclusion Criteria included:

- Agitation caused by acute intoxication
- Use of benzodiazepines, hypnotic, or antipsychotic in the 4 hours prior to study treatment
- Patients at significant risk of suicide
- Those with an unstable or serious medical or neurological condition
- Previously received BXCL501 in a clinical trial or IGALMI via prescription

# SERENITY III Part 1

Topline Safety and Efficacy Results

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# Demographics and Baseline Characteristics

| | 60mcg BXCL501 (N = 101) | Placebo (N = 100) | Overall (N = 201) |
|---|---|---|---|
| Age, years , Mean (SD) | 47.8 (13.1) | 44.4 (12.5) | 46.1 (12.9) |
| Female, n (%) | 44 (43.6) | 43 (43) | 87 (43.3) |
| Race, n (%) | | | |
| White | 29 (28.7) | 36 (36) | 65 (32.3) |
| Black or African American | 69 (68.3) | 57 (57.0) | 126 (62.7) |
| Ethnicity, n (%) | | | |
| Hispanic or Latino | 17 (16.8) | 21 (21.0) | 38 (18.9) |
| Primary diagnosis, n (%) | | | |
| Schizophrenia | 72 (71.2) | 57 (57.0) | 129 (64.1) |
| Bipolar Disorder | 29 (28.7) | 43 (43.0) | 72 (35.8) |
| Time Since Diagnosis, years, Mean (SD) | 21.7 (12.2) | 17.7 (11.6) | 19.7 (12.1) |
| Baseline PEC | 17.1 | 17.0 | |

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# Adverse Events Reported In SERENITY III Part 1 and in SERENITY I and II

| Adverse Event | SERENITY III Part 1 | | SERENITY I and II | | |
|---|---|---|---|---|---|
| | BXCL501 60mcg N = 101 | Placebo N = 100 | IGALMI™ 120mcg[3] N = 255 | IGALMI™ 180mcg[3] N = 252 | Placebo N = 252[3] |
| Somnolence[1] | 13 (13) | 7 (7) | 56 (22) | 57 (23) | 16 (6) |
| Oral paresthesia or oral hypoesthesia | 6 (6) | 4 (4) | 14 (5) | 18 (7) | 2 (1) |
| Dizziness | 3 (3) | 1 (1) | 10 (4) | 15 (6) | 2 (1) |
| Hypotension | 1 (1) | 0 | 14 (5) | 13 (5) | 0 |
| Orthostatic hypotension | 1 (1) | 0 | 7 (3) | 13 (5) | 1 (0) |
| Dry mouth | 5 (5) | 3 (3) | 19 (7) | 11 (4) | 3 (1) |
| Nausea | 2 (2) | 1 (1) | 6 (2) | 7 (3) | 4 (2) |
| Bradycardia | 0 | 0 | 5 (2) | 5 (2) | 0 |
| Abdominal discomfort[2] | 0 | 0 | 0 (0) | 6 (2) | 1 (0) |

No SAEs. All AEs reported of mild to moderate severity, none were severe

1 Somnolence includes the terms feeling drowsy, feeling sleepy, fatigue and sluggishness
2 Abdominal discomfort includes dyspepsia, gastroesophageal reflux disease
3 IGALMI™ (dexmedetomidine) USPI, July 2022
No SAEs observed
The adverse events (AEs) listed correspond to those in the label for IGALMI. No other AEs were observed that would fulfill the criteria for inclusion in the AE table (at least 2% and greater than with placebo).

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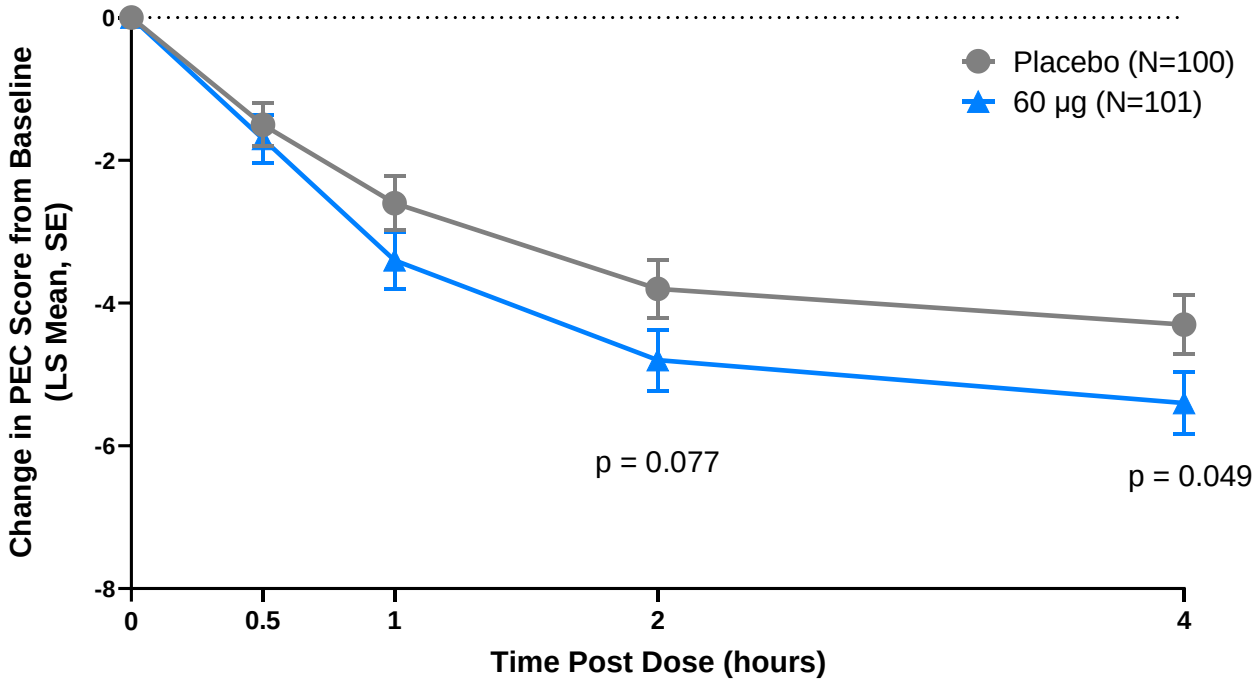
# SERENITY III Part 1: Results Over Time

## Change From Baseline PANSS Excitatory Component (PEC) Total Score Over Time

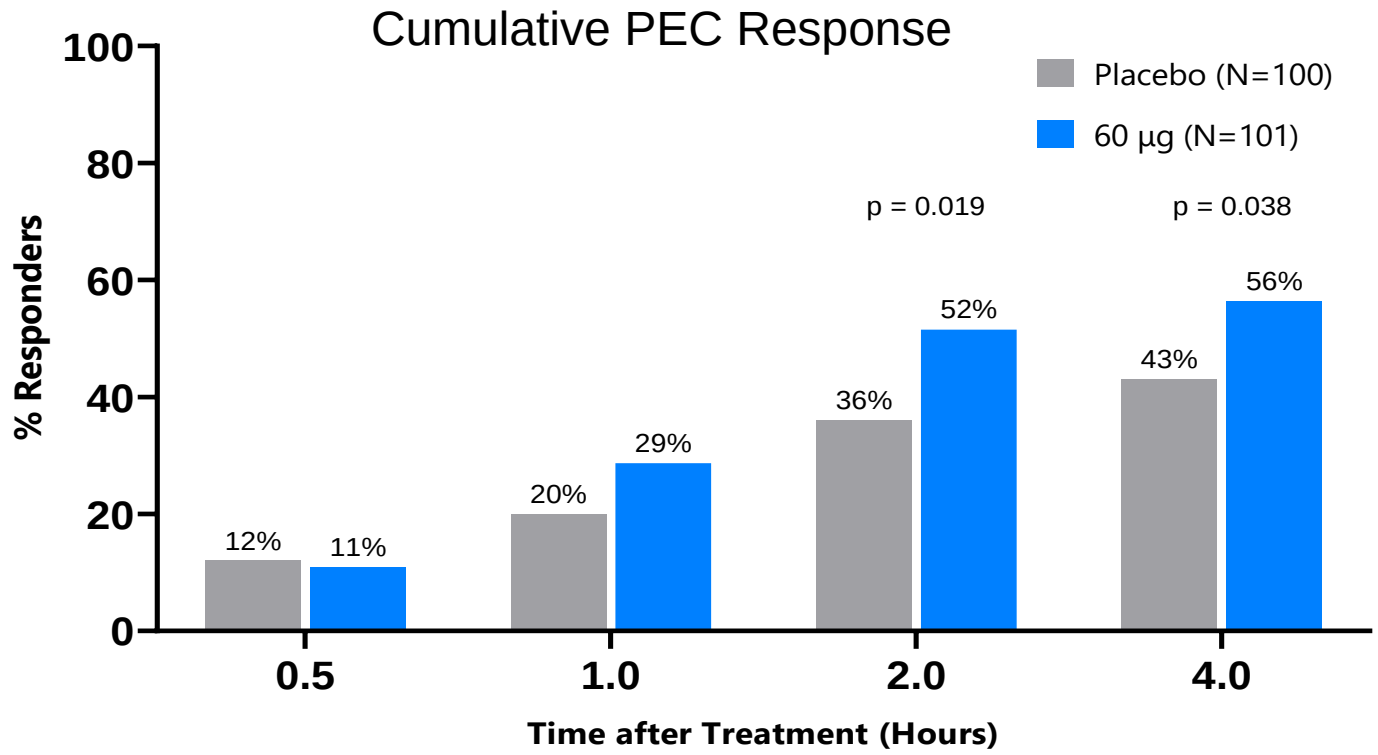



| Endpoint | Placebo N = 100 | BXCL501 60mcg N = 101 |
|---|---|---|
| Change from Baseline (LS Mean (SE)) | -3.8 (0.4) 2 hours<br>-4.3 (0.4) 4 hours | -4.8 (0.4) (p = 0.077)<br>-5.4 (0.4) (p = 0.049) |
| Response Rate[1] | 36% | 52% (p = 0.019) |

[1]Responder: patients who had a ≥ 40% reduction from baseline PEC total score by 2 hours

# Meaningful Clinical Response by 2 Hours

## Significantly Greater Proportion Improved by PEC and CGI-I




- Starting at 1 hour, greater proportion respond; 52% achieve response at or before 2 hours
- Significantly greater proportion judged as improved by CGI-I at 2 hrs (39% vs 26% placebo, p = 0.0389)

PEC Responders: proportion achieving a ≥ 40% improvement from baseline PEC total score
CGI-I Response: achieve CGI-I score of 1 or 2 (“very much improved” or “much improved”)

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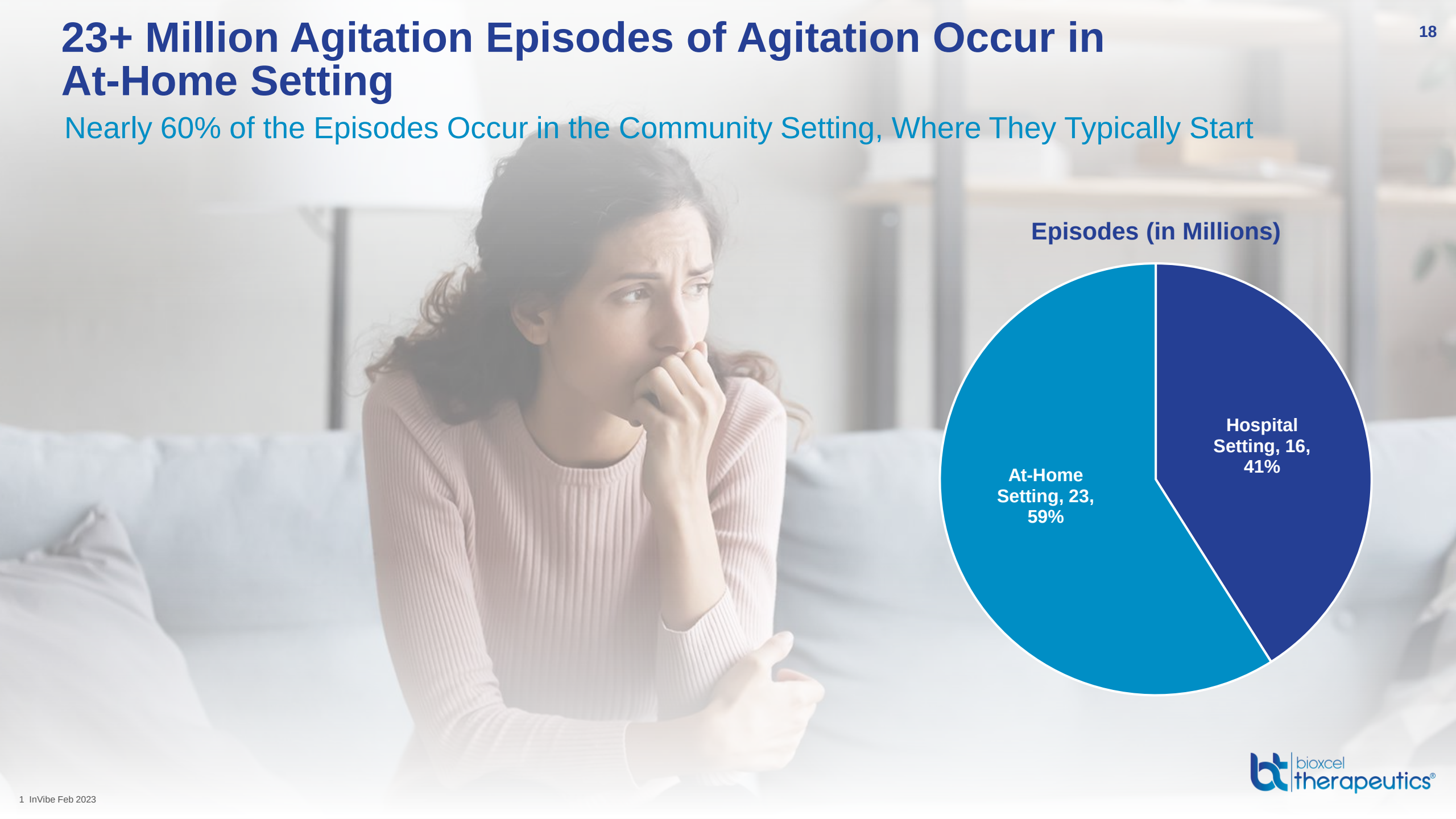
# Clinical Summary

- **Group mean change from baseline in PEC total score was not significant at 2 hours** (p = 0.077)
  - Separated from placebo at 4 hours (p = 0.049)
- **PEC separated at 4 hours**
  - Consistent with low dose requiring a longer period to respond
- **Simple majority respond to this single dose**
  - Nominally significant proportional response to 60mcg dose at 1, 2, and 4 hrs vs. placebo
  - 52% achieved response by 2 hours, defined as ≥ 40% improvement from baseline PEC total score
- **Clinically meaningful response at 2 hours**
  - CGI responders by 2 hours vs. placebo (p = 0.0389)
- **Safety results for 60mcg dose were comparable to placebo**
  - Potentially greater safety margin compared to that observed in studies evaluating approved IGALMI™ doses of 120 and 180mcg
- **Data support testing as a treatment option for agitation episodes at home, outside medical supervision**

# Key Market Insights

# 23+ Million Agitation Episodes of Agitation Occur in At-Home Setting

## Nearly 60% of the Episodes Occur in the Community Setting, Where They Typically Start





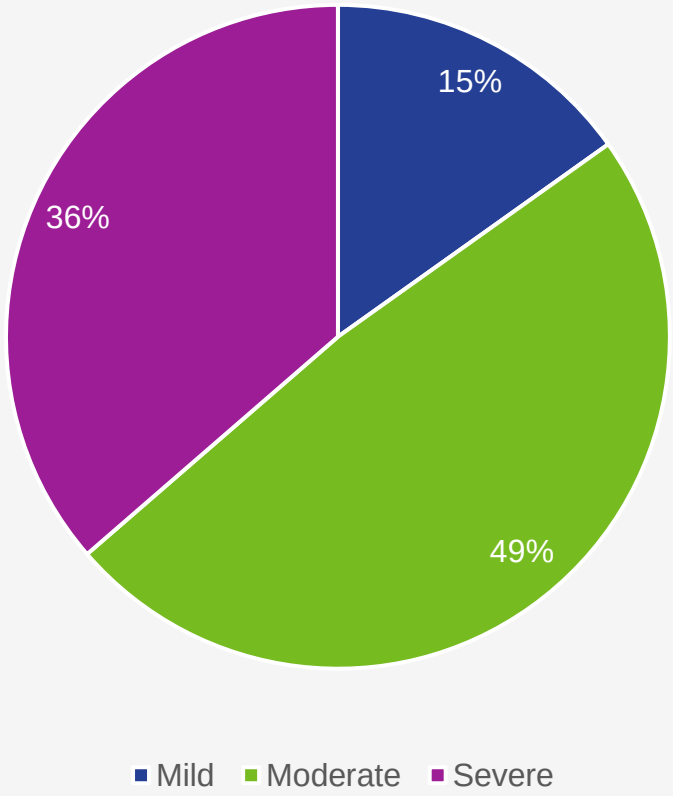

1 InVibe Feb 2023

# Episode Frequency

## Patients report an average of 3 episodes per month, with the majority moderate to severe

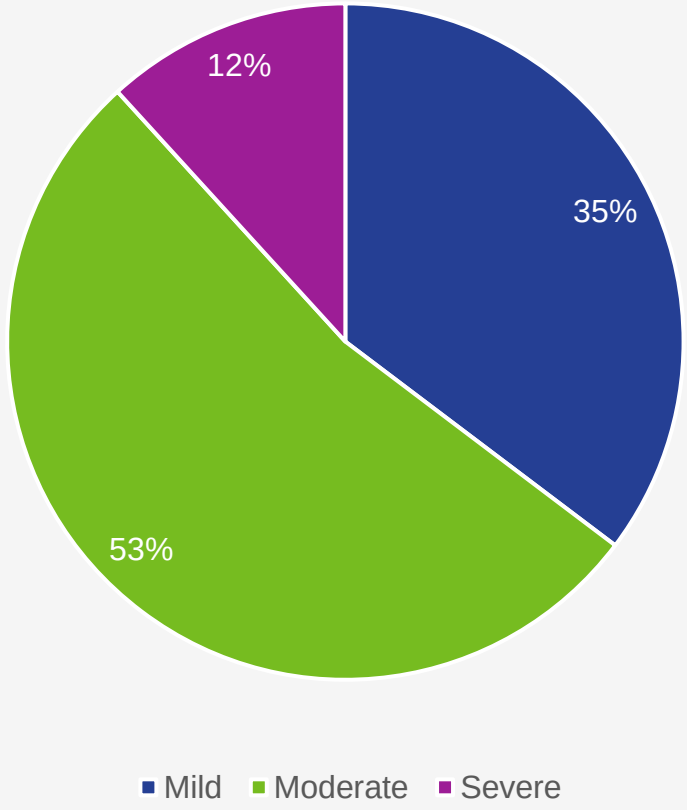
### Categorization of Episodes (Schizophrenia PTs/ CGs)

*(Avg. # of Episodes, n=20)*




### Categorization of Episodes (BPD PTs/ CGs)

*(Avg. # of Episodes, n=60)*




Q4: In the past month, about how many agitation episodes [IF PATIENT SHOW “have you” IF CG SHOW “has your loved one”] experienced?
Q5. Of the [XX] agitation episodes you experienced in the past month, how many would you categorize as mild, moderate, or severe?
Source: InVibe Feb 2023

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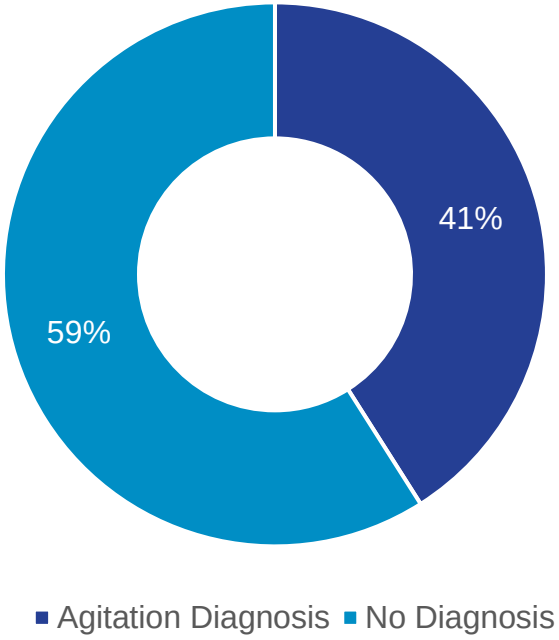
# HCP Underrecognition and Undertreatment of Agitation

## According to patient market research, only 41% receive a diagnosis for agitation and only 35% receive a treatment specifically for agitation

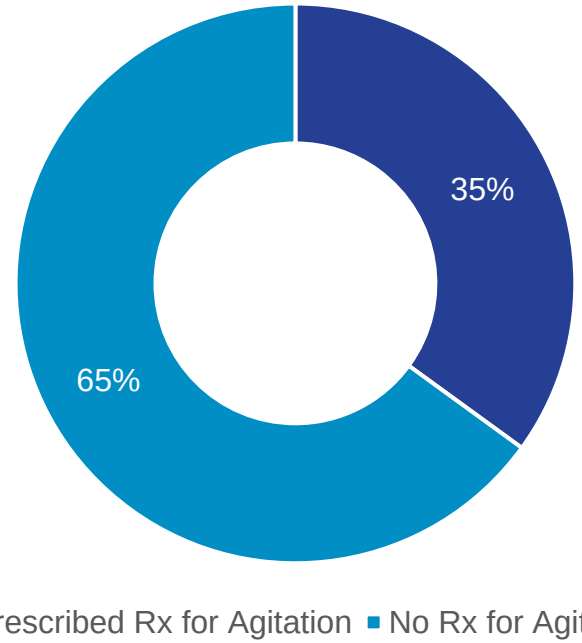
### Agitation Diagnosis

*(% of Total PT/CGs, n=80)*




### Prescribed a Treatment for Agitation

*(% of Total PT/CGs, n=80)*




Q1. Have you ever been diagnosed with agitation specifically? This can be a related but separate diagnosis to other mental health conditions
Q2. Have you ever been prescribed a treatment specifically for agitation episodes?
Q3. What was the treatment you were prescribed for agitation episodes?
Source: InVibe Feb 2023

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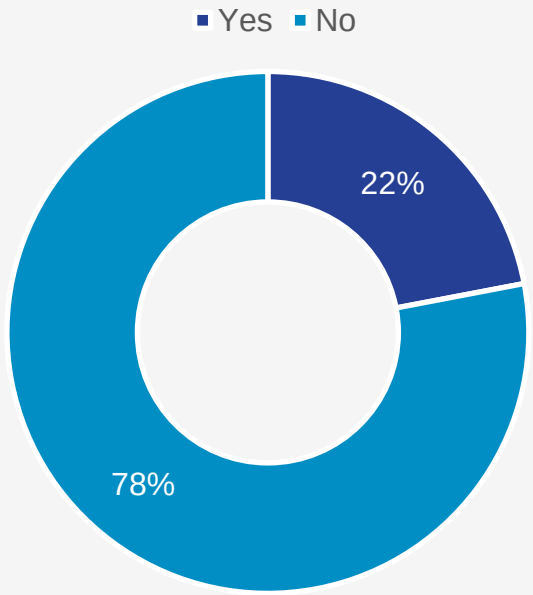
# Episode Anticipation

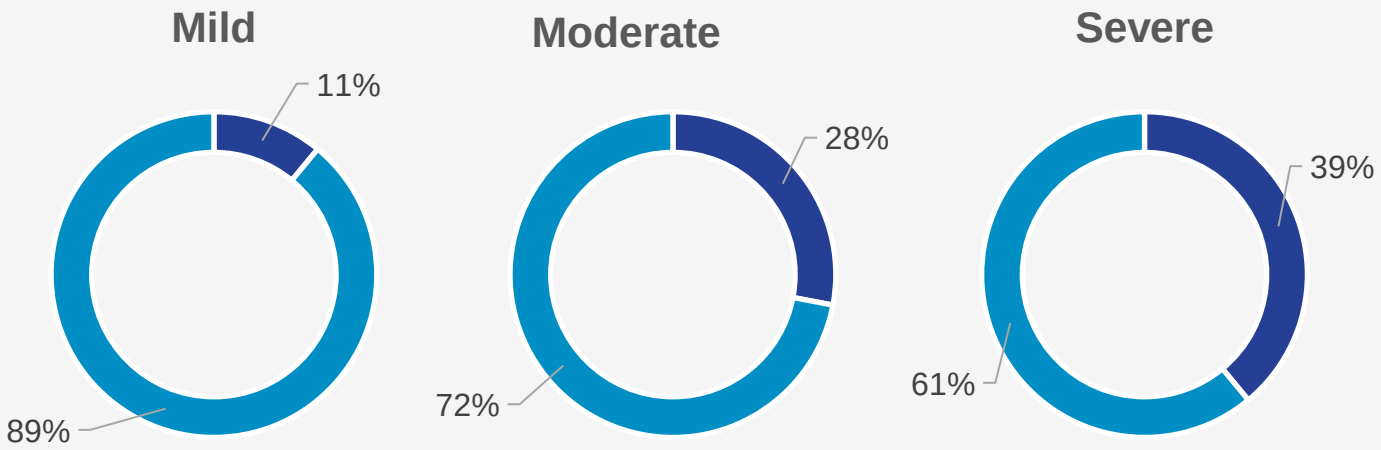
## Almost a quarter of all patients have a prodrome, or anticipation, preceding an agitation episode which increases with agitation severity




*Caregivers and patients were equally likely to have advance knowledge of an episode (22% for both groups)*

### Advance Knowledge of Agitation Episodes

*(% of Episodes, n=240*)*



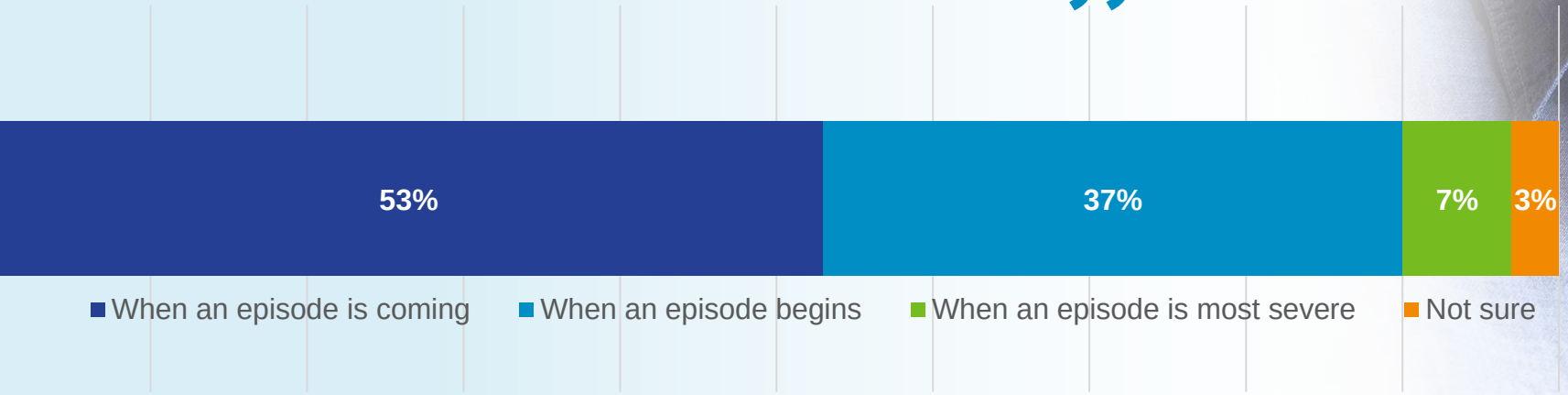

* These data are compiled from 3 episodes described by each patient (N=80 pts/cgs *3 = 240)

Source: InVibe Feb 2023

# BXCL501 Patient Usage

## More than half of patients surveyed would like to take BXCL501 when they know an episode is coming during the prodromal phase, and another 37% would take it at episodic onset.

> I would love to be able to have it available **when I knew an episode was coming**…That would be such a benefit for me.
>
> *(VR4, R8, PT, BPD, age 57)*




Source: InVibe Feb 2023

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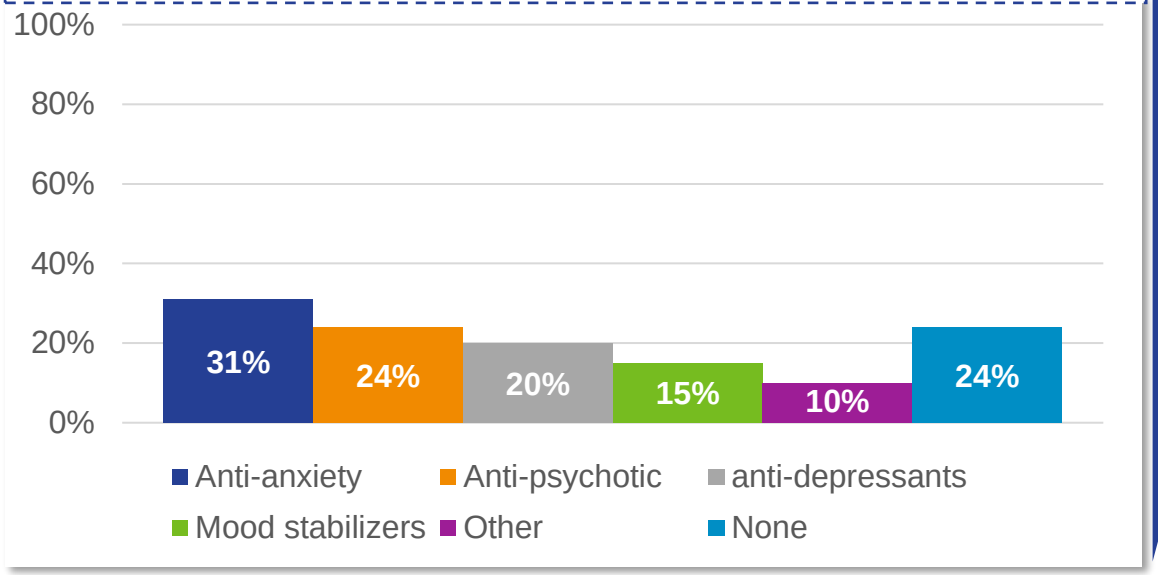
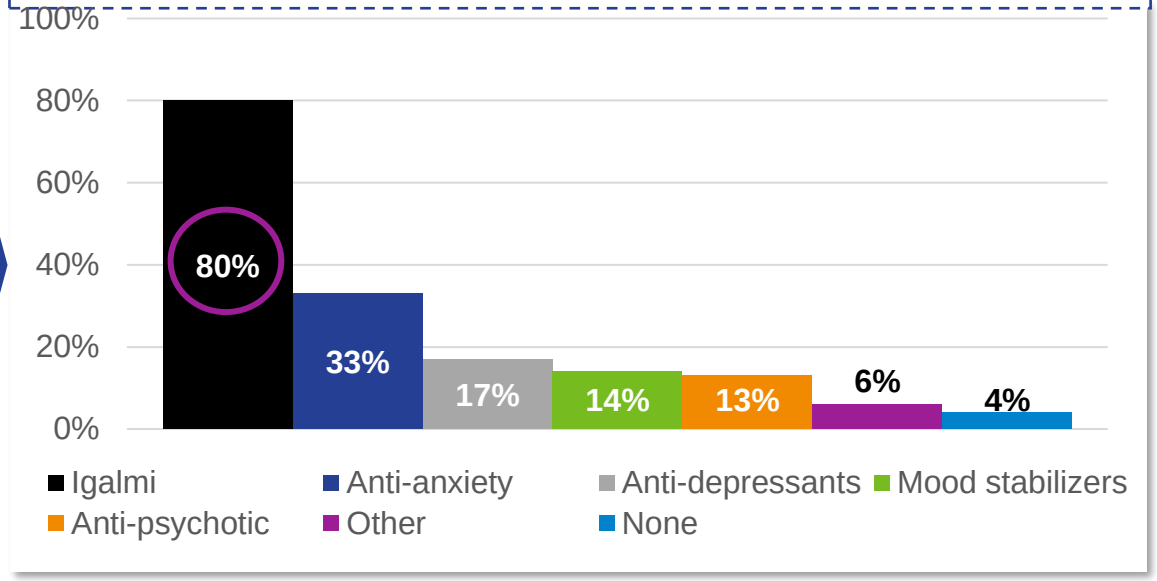
# Anticipated Use of BXCL501 id Approved for At-Home Market

When shown a target product profile, patients said they would use BXCL501 for 80% of their episodes and for those on therapy it would be largely additive.

**Medications Used to Treat Agitation Episodes (Current Market)**
*(% of Episodes, n=240)*




**Self-Reported Anticipated Use for BXCL501 (Future Market in % Episodes Treated)**
*(% of Episodes, n=240)*




Q7/8/9. Thinking about Episode 1/2/3, what prescription treatment(s) did you **specifically take** to treat this episode? *Please do not include medications taken regularly your underlying mental health condition. Please select all that apply*..
Q22. You previously indicated that you used the following medications to manage your last 3 agitation episodes. Now please imagine that Igalmi was also available for you to use. Please indicate what treatment you would have chosen to treat the last 3 episodes if Igalmi were also available to you. We have provided your previous below for reference.

Source: InVibe Feb 2023

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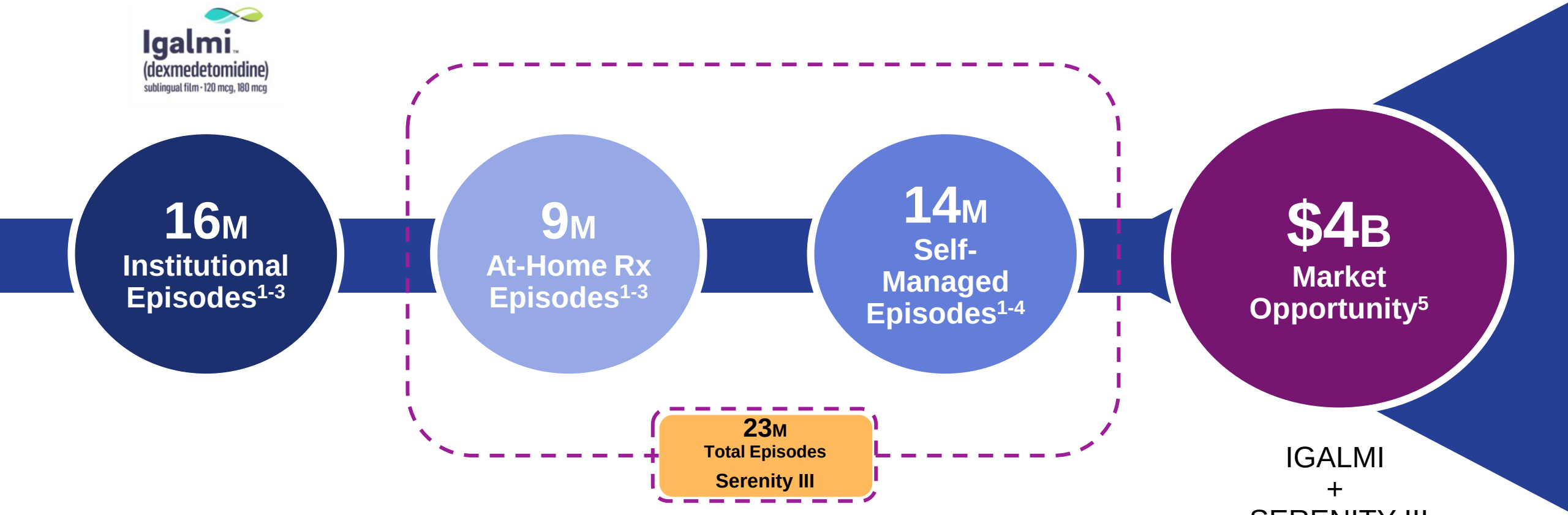
# Considerable Potential Market Size

## Potential At-Home Indication for Bipolar Disorders & Schizophrenia Could Add an Incremental 23M Agitation Episodes to Addressable Market Opportunity

Igalmi™ (dexmedetomidine) sublingual film · 120 mcg, 180 mcg




IGALMI
+
SERENITY III

Source: 1. Wu, 2006, NAMI 2. NIMH- Prevalence of bipolar disorder in adults. November 2017. Accessed June 24, 2021. https://www.hcp.med.harvard.edu/ncs/ftpdir/NCS-R_12-month_Prevalence_Estimates.pdf 3. Data on File 4. inVibe Patient Agitation Market Research, July 2022 (n=57) 5. 39M episodes @ $105/episode

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# Conclusion

- Clinically meaningful efficacy results observed with half (60mcg) of the approved dose of IGALMI™
- Greater than 50% PEC response rate attained; responder rate proportionally consistent with dose response when compared to rates seen in SERENITY I and II
- BXCL501 was well tolerated and demonstrated favorable safety results supporting potential for at-home use
- SERENITY III Part 2 planned as an adaptive trial design with 60mcg and 80mcg to potentially address agitation spectrum for patients at home

# TRANQUILITY Program

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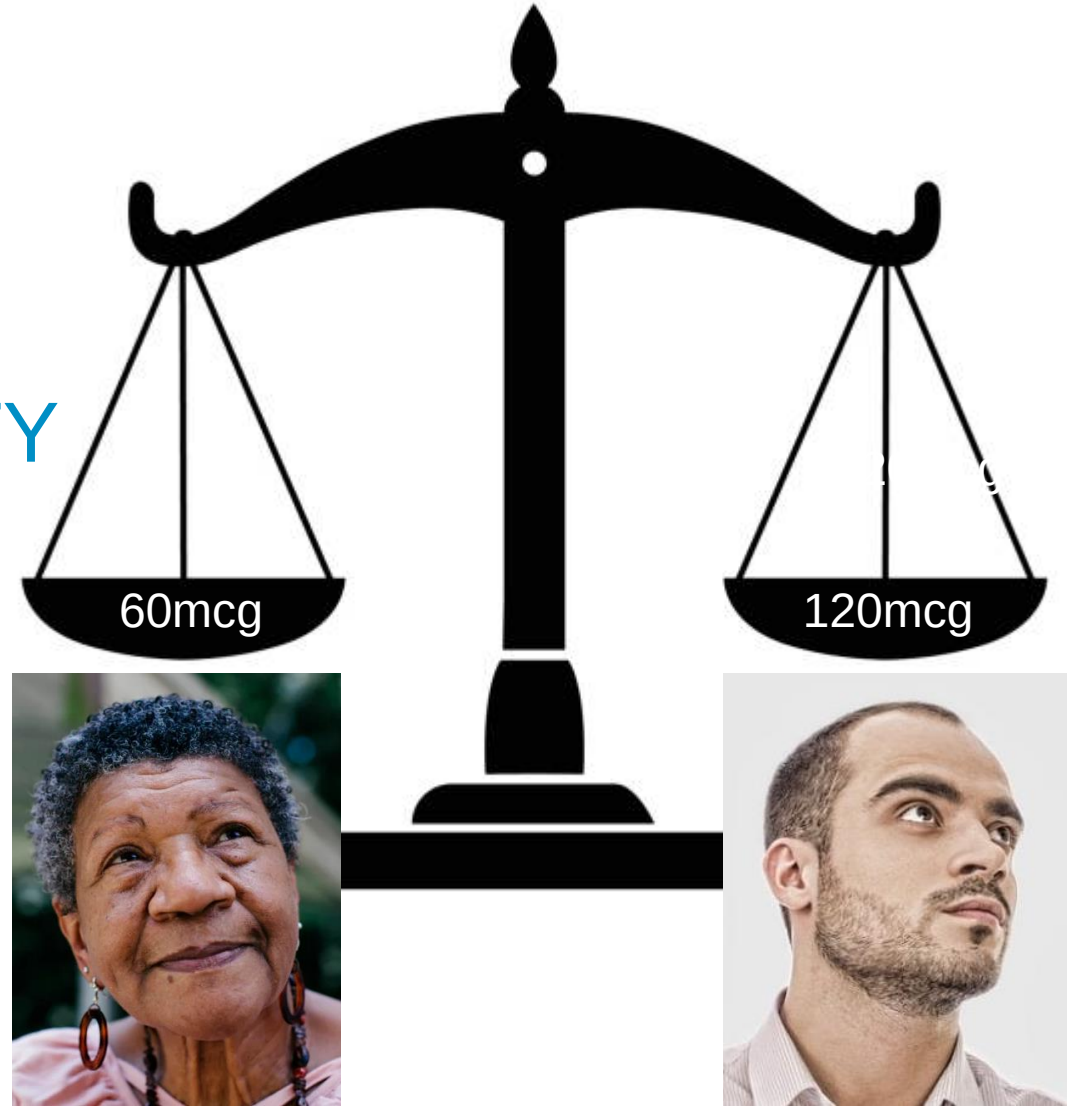
# TRANQUILITY II Evaluating 40 and 60 mcg Doses

## Elderly patients: 60mcg produces exposure of ~120mcg

TRANQUILITY

- Elderly




SERENITY

- Adults

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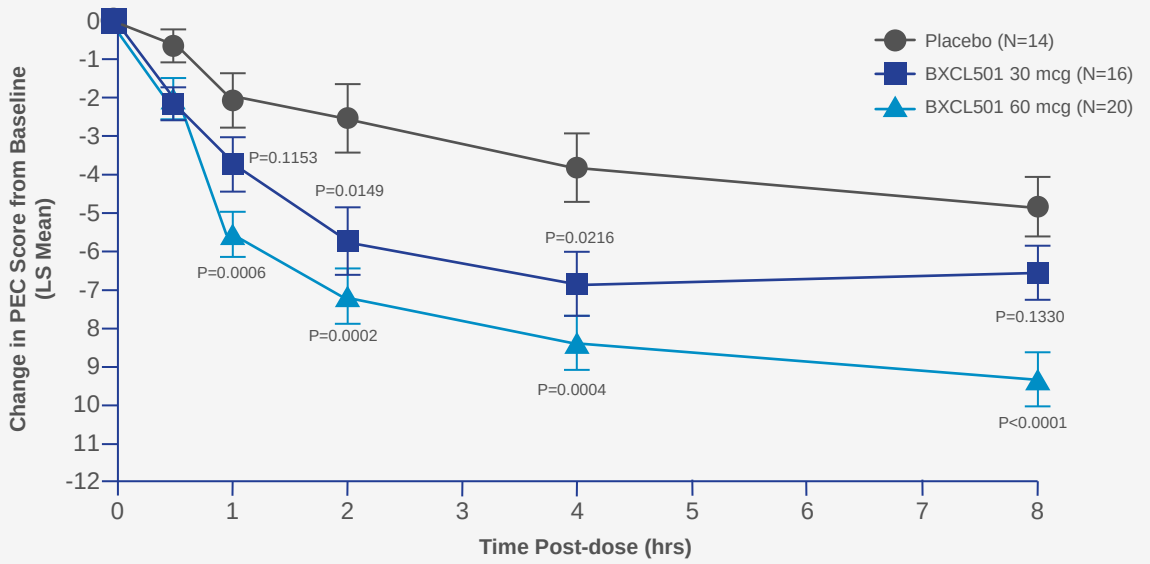
# TRANQUILITY I Trial

## Clinically Meaningful, Rapid, and Durable Response Observed with 30 or 60mcg doses

### Change in PEC Score from Baseline

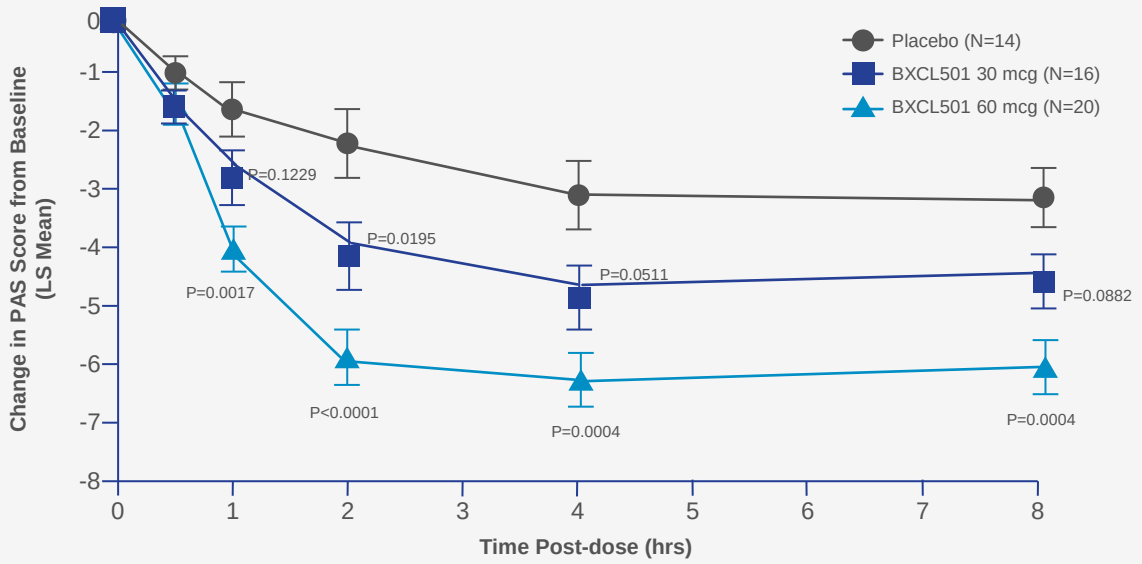



P values at 0.5 hrs are 0.0295 for BXCL501 30 mcg and 0.0568 for BCXL501 60 mcg

| | Placebo | BXCL501 30 mcg | BXCL501 60 mcg |
|---|---|---|---|
| Change from Baseline at 120 mins (LS Mean) | -2.5 | -5.7 | -7.1 |
| Response ° | 0% | 31% | 70% |

PANSS-Excitatory Component (PEC) is a 5 items scale: Excitement, Hostility, Tension, Uncooperativeness, Poor Impulse Control, rated 1-Absent to 7-Extreme
ITT analysis, Least Square Means ± SEM
° Proportion achieving ≥ 40% PEC reduction

### Change in PAS Score from Baseline




P values at 0.5 hrs are 0.3.162 for BXCL501 30 mcg and 0.2631 for BCXL501 60 mcg

| | Placebo | BXCL501 30 mcg | BXCL501 60 mcg |
|---|---|---|---|
| Change from Baseline at 120 mins (LS Mean) | -2.2 | -4.1 | -5.9 |

Pittsburgh Agitation Scale (PAS) measures 4 behavior groups: aberrant vocalization, motor agitation, aggressiveness, and resisting to care rated 0- no agitation present to 4 – highest form of agitation.
ITT analysis, Least Square Means ± SEM

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# Thank you!