



Acute Treatment of Agitation in Alzheimer's Disease

TRANQUILITY II Summary

June 29, 2023

Forward-Looking Statements

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 and future regulatory approvals of BXCL501, in particular for the treatment of dementia, 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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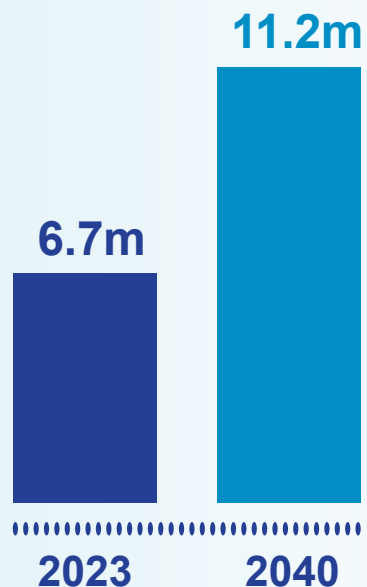
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For additional information regarding the TRANQUILITY II Phase 3 trial, see the Company's Current Report on Form 8-K filed on June 29, 2023, which should be read in conjunction with this presentation.

Alzheimer's Disease-Related Agitation Market

Agitation is reported in 40-60% of patients with Alzheimer's Disease (AD), the prevalence of which is expected to grow substantially over the next two decades.

~100M
agitation episodes
per year
in the U.S.²



U.S. adults
65+ with AD to
**Nearly
Double
by 2040¹**



Alzheimer's Disease-Related Agitation: Debilitating for Families and Caregivers

- AD-related agitation typically worsens over time¹
- As underlying disease progresses, the number and severity of agitation episodes increase in tandem²
 - Often places significant burden and despair on caregivers at home^{1,2}
- Agitation was cited as a top driver in deciding to move a patient from home setting to residential care facility²
- No FDA-approved therapeutic options for an as-needed (PRN) acute treatment of agitation in AD patients³
- When presented a target product profile for BXCL501 in Alzheimer's dementia agitation, over 70% of caregivers were very interested in the treatment for their loved one²
- Over 80% of AD drugs delivered through retail channels⁴
- BXCL501 expected to be dispensed through retail channels as are other products in Alzheimer's dementia, if approved



1 Alzheimer's Association. 2023 Alzheimer's Disease Facts and Figures. Alzheimer's Dement 2023;19(4). DOI 10.1002/alz.13016.
2 Data on File InVibe Patient and Caregiver Research (n=75) December 2022
3 Joint Meeting of the Psychopharmacologic and the Peripheral and Central Nervous System Drugs Advisory Committee Meeting April 14th, 2023
4 Symphony METYS, 2023

Positive Topline Results: TRANQUILITY II Phase 3 Trial

- Statistically significant improvement in PEC score observed with BXCL501 60 mcg vs. placebo for first episode at 2 hours ($p= 0.0112$)
 - The earliest statistically significant separation from placebo occurred at 1 hour ($p=0.0185$) with 60 mcg
 - Results were not statistically significant for 40 mcg
- Clinically meaningful response supported by CGI-Improvement at 1 and 2 hours, and calming effects by ACES scale with 60 mcg
- 443 episodes for 149 patients were treated over 12 weeks; dosing with 60 mcg showed a similar reduction in agitation for first and all treated episodes at 1 and 2 hours, as measured by average change in PEC score
- BXCL501 was well tolerated with no serious adverse events related to dosing
 - Repeat dosing adverse events were consistent with those of first dose
 - No syncope or falls observed within 24 hours of dosing with 40 or 60 mcg
- Consistent with TRANQUILITY I, exposure levels observed were higher than those observed in younger bipolar/schizophrenia patients

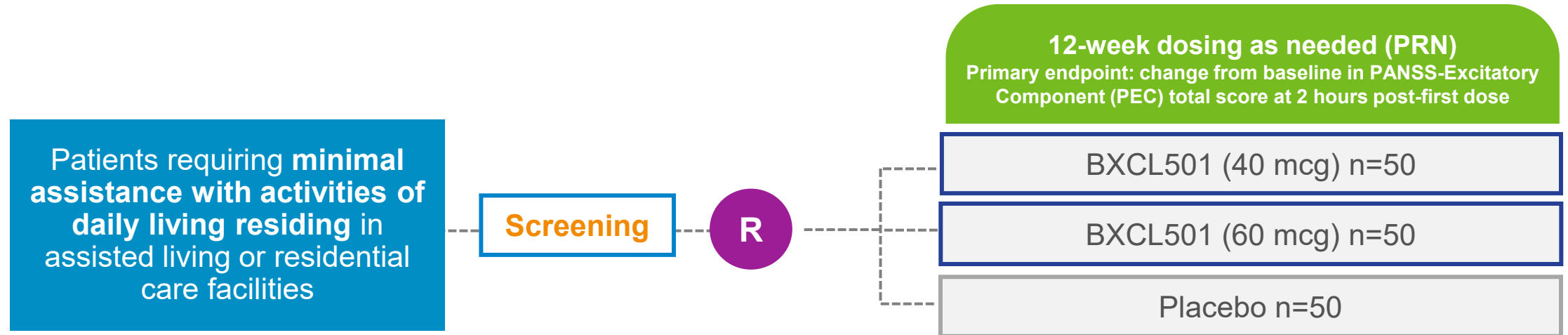
TRANQUILITY II

- Trial Design
- Topline Results



TRANQUILITY II Trial Design

BXCL501 for acute treatment of agitation in mild to moderate AD



Randomized: BXCL501 (40 mcg) n=48, BXCL501 (60 mcg) n=50, Placebo n=53
Dosed: BXCL501 (40 mcg) n=48, BXCL501 (60 mcg) n=50, Placebo n=51

Select Inclusion/Exclusion Criteria

Inclusion Criteria included:

- Male and female subjects 65 years and older
- All subjects must have a diagnosis of probable Alzheimer's disease based on NIAAA criteria (2018). If criteria are unavailable, then the diagnosis will be based on the 2011 NIA-AA criteria.*
- Subjects exhibit behaviors congruent with International Psychogeriatric Association criterion for agitation representing a change from subject's usual behavior
- Subjects who have a score of 15 to 23 on the Mini-Mental State Exam (MMSE) at screening and at pre-dose and require minimal assistance with activities of daily living (e.g., bathing, dressing, and toileting)

Exclusion Criteria included:

- Subjects with dementia or other memory impairment not due to probable AD, or any other specific non-Alzheimer's-type dementia
- Subjects whose agitation is attributed to any condition other than dementia i.e. pain as determined by investigator
- Subjects with serious, unstable, or uncontrolled medical illnesses such as cardiac, respiratory, or renal

A total score ≥ 14 on the PEC was required to receive dosing in the trial.

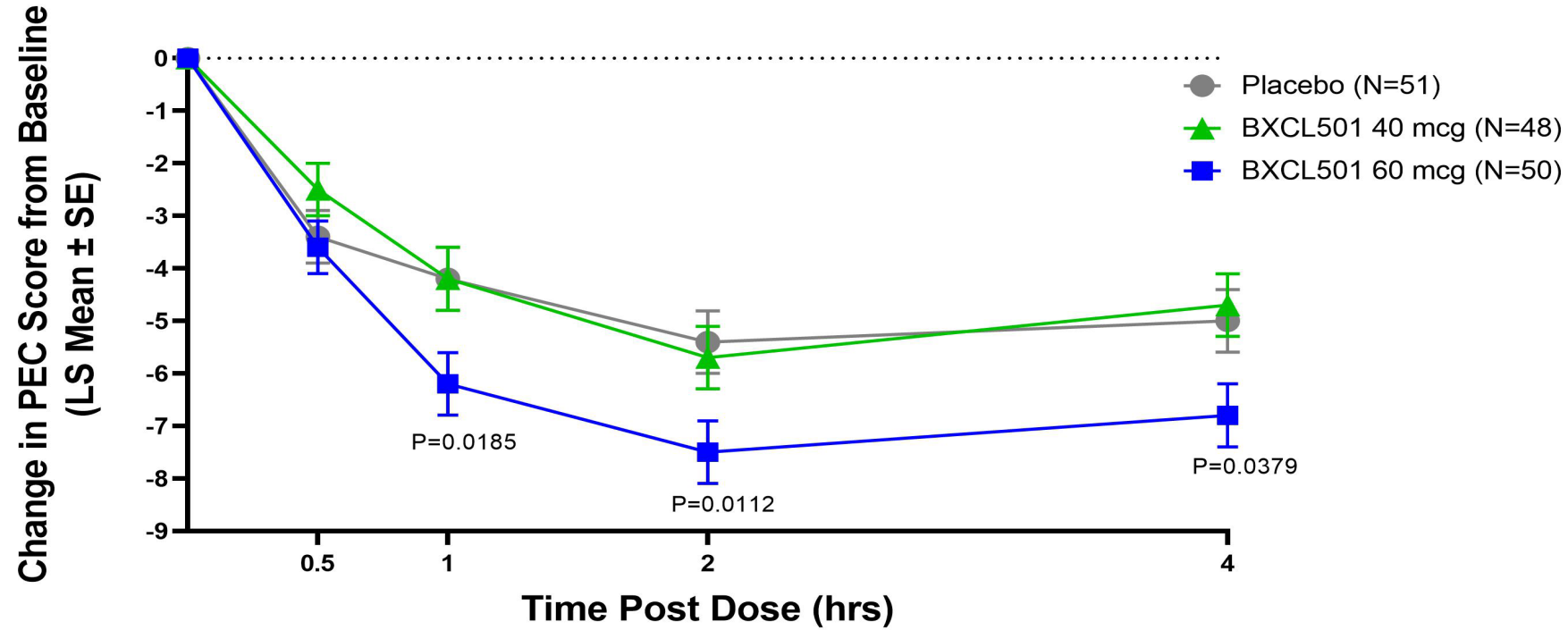
* A maximum of 15 non-ambulatory subjects representing ~10% of the total number of subjects enrolled.

Baseline Demographics and Disease Characteristics

	BXCL501 60 mcg (N=50)	BXCL501 40 mcg (N=48)	Placebo (N=51)	Overall (N=149)
Mean age (SD) Min, Max	79.5 (8.1) 65, 95	79.4 (6.4) 65, 92	80 (7.5) 65, 94	79.6 (7.4) 65, 95
Female (%)	30 (60.0)	27 (56.3)	33 (64.7)	90 (60.4)
Race (% white/non-white)	86.0/14.0	72.9/27.1	76.5/23.5	78.5/21.5
Mean BMI (SD)	24.5 (5.2)	27.6 (10.6)	25.9 (5.8)	26.0 (7.6)
Mean MMSE (SD)	19.2 (2.2)	19.0 (2.3)	19.0 (2.6)	19.0 (2.4)
Mean PEC (SD)	18.0 (2.2)	17.3 (2.3)	17.5 (2.6)	17.6 (2.4)
Anti-psychotic use	50.0%	56.3%	56.9%	54.4%

Demographics are based on the safety population

Change From Baseline in PEC Total Score Compared to Placebo for the First Episode of Agitation



PEC = The Positive and Negative Syndrome Scale - Excited Component Scale; LS = least square; SD = standard deviation; SE = standard error

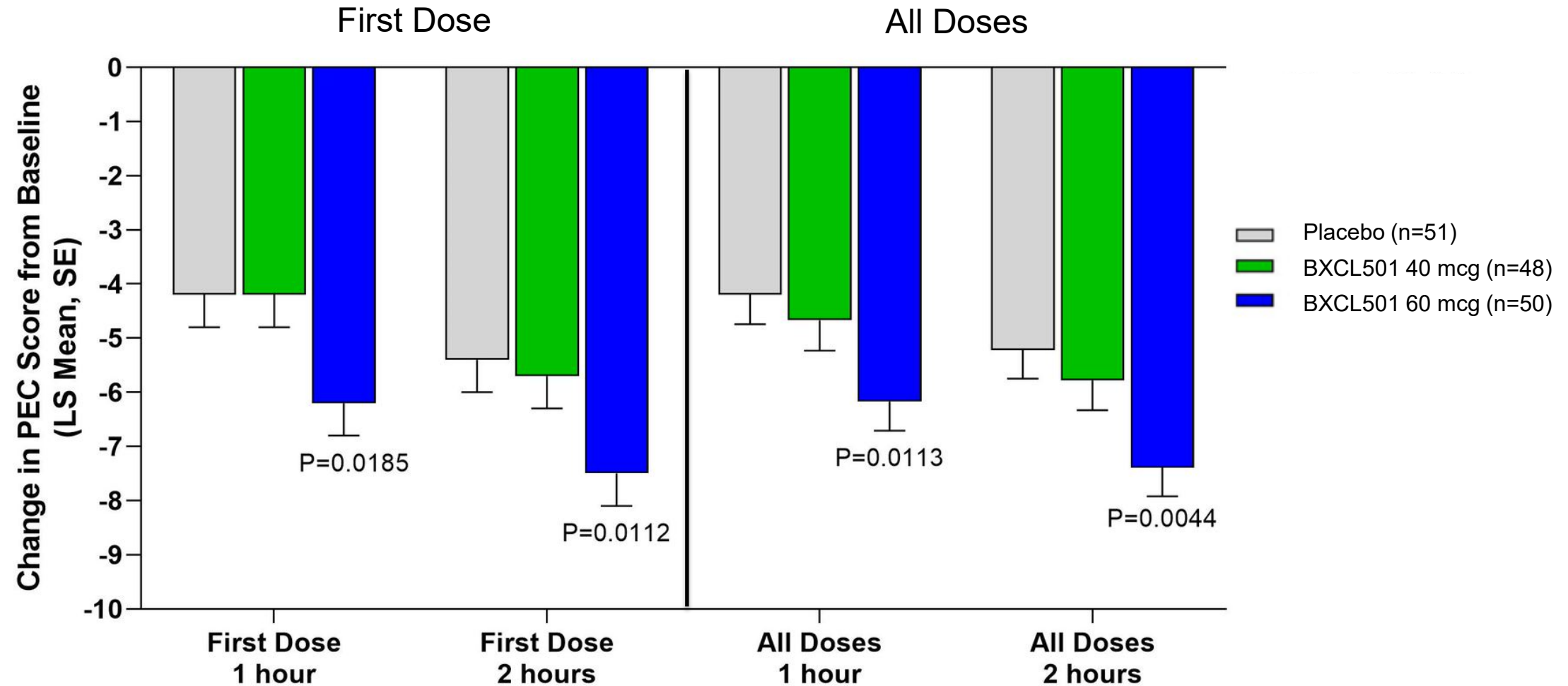
Mean (SD) baseline PEC scores in the Placebo, BXCL501 40 mcg, and BXCL501 60 mcg groups were: 17.5 (2.62), 17.3 (2.26), and 18.0 (2.18), respectively.

ENDPOINT	BXCL501 60 mcg (N=50)	BXCL501 40 mcg (N=48)	PLACEBO (N=51)
Change from baseline [LS Mean (SE)] @ 1 hour	-6.2 (0.6) p = 0.0185	- 4.2 (0.6) p = 0.9590	- 4.2 (0.6)
Change from baseline [LS Mean (SE)] @ 2 hours	-7.5 (0.6) p = 0.0112	- 5.7 (0.6) p = 0.7648	- 5.4 (0.6)
Change from baseline [LS Mean (SE)] @ 4 hours	-6.8 (0.6) p = 0.0379	- 4.7 (0.6) p = 0.7100	-5.0 (0.6)

The trial met its primary endpoint for the 60 mcg dose with statistically significant (p=0.0112) reduction in agitation at 2 hours.

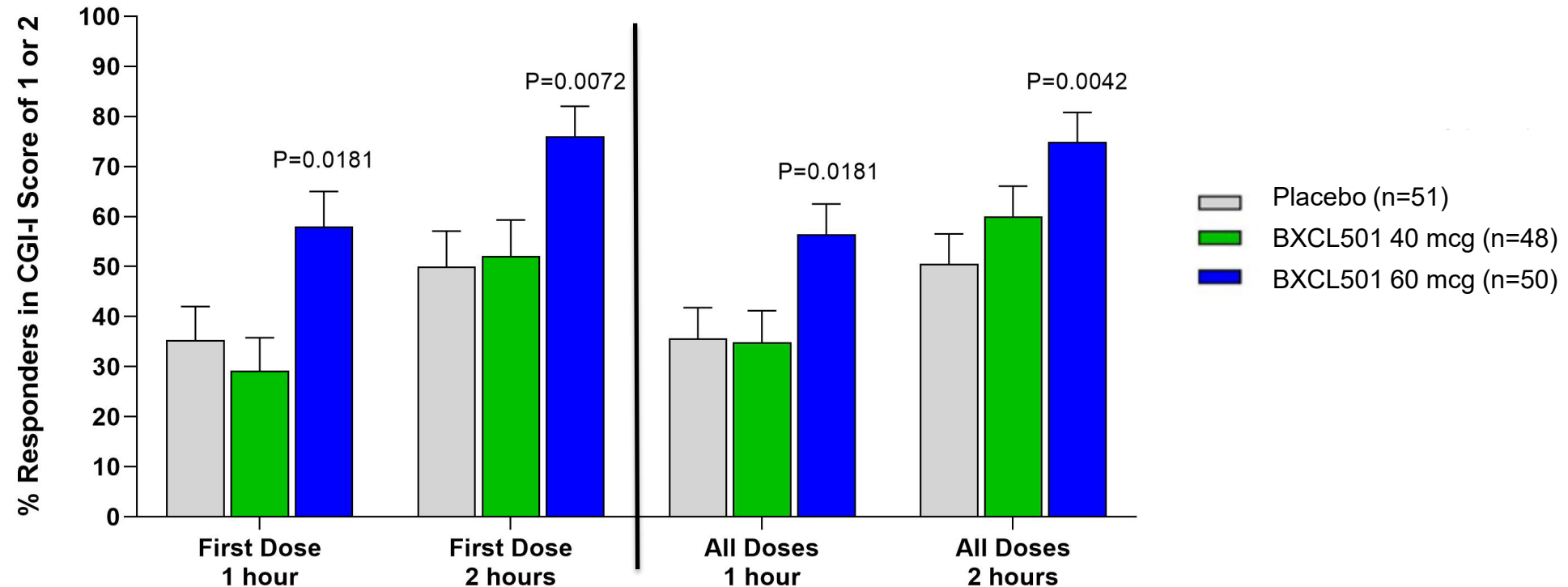
Response as Measured by PEC for First and All Treated Episodes

Significant change from baseline in PANSS Excitatory Component (PEC) total score for first dose and all doses



P-values for repeated doses are nominal.
Average change from pre-dose in the PEC score presented.
Full data results on repeated doses are forthcoming.

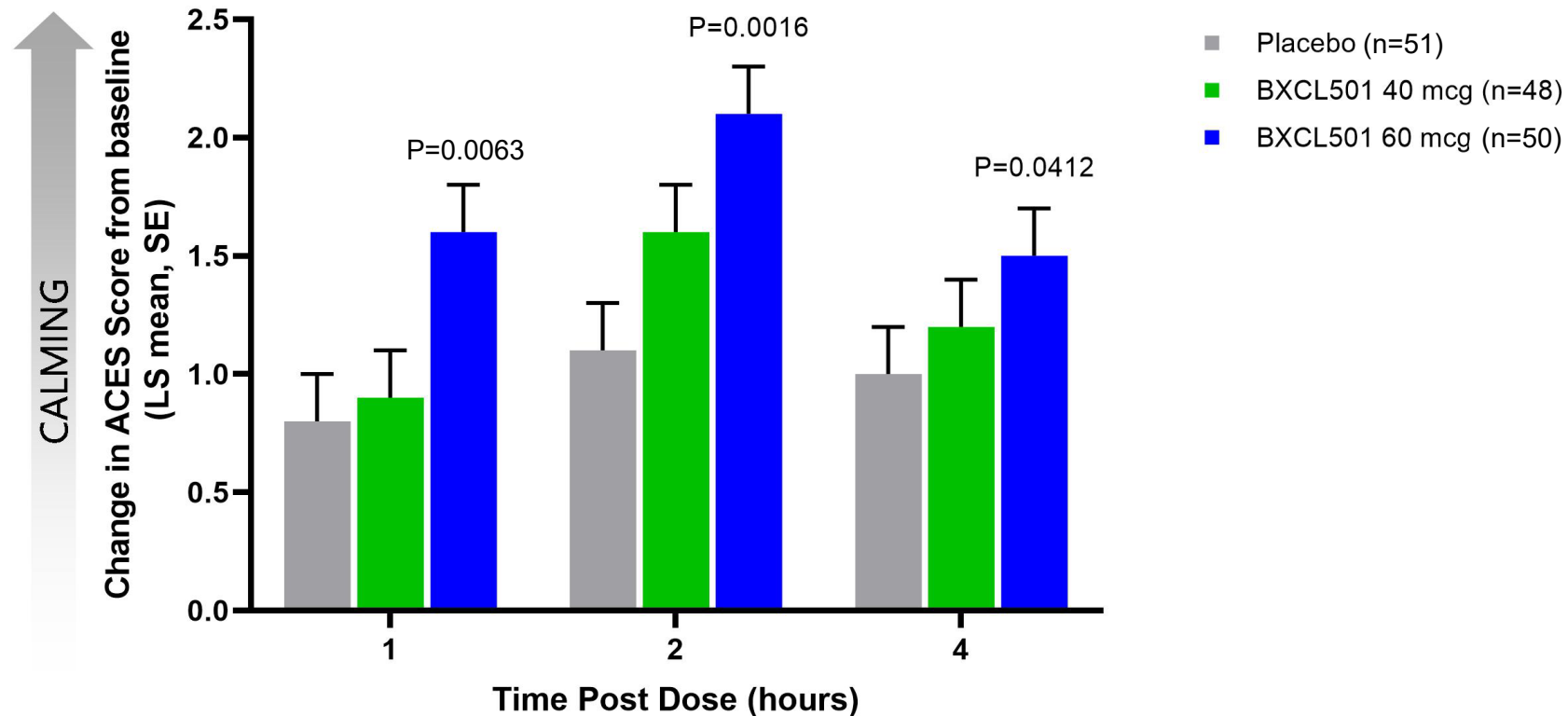
Response as Measured by CGI-Improvement for First and All Treated Episodes



The Clinical Global Impression Scale - Improvement (CGI-I) is a 7 point scale. Ratings of (1) Very Much or (2) Much Improved were considered Responders. The data in this chart are the percentage of patients who achieved a CGI-I score of 1 or 2 through 2 hours after the first dose and after all doses. P-values compare BXCL501 and Placebo.

P-values are nominal. The percentage of all treated agitation episodes with a CGI- Score of 1 or 2 through 2 hours are presented for ALL Doses.

Calming Effects as Measured by Agitation Calmness Evaluation Scale (ACES)



ACES = Agitation-Calmness Evaluation Scale; LS = least square; SD = standard deviation; SE = standard error

Mean (SD) baseline ACES scores in the Placebo, BXCL501 40 mcg, and BXCL501 60 mcg groups were: 2.4 (0.54), 2.4 (0.54), and 2.2 (0.57), respectively.

The ACES consists of a single item that rates overall agitation and calming where 1 indicates marked agitation; 2, moderate agitation; 3, mild agitation; 4, normal behavior; 5, mild calmness; 6, moderate calmness; 7, marked calmness; 8, deep sleep; and 9, unarousable. P values are nominal.

Dosing Frequency

The number of doses received for treatment of agitation over the 12-week treatment period

- 443 episodes for 149 patients were treated over 12 weeks; dosing with 60 mcg showed a similar reduction in agitation for first and all treated episodes at 1 and 2 hours, as measured by average change in PEC score
- Summary of Episodes
 - More than 90% received 5 or fewer doses
 - 42% of patients received one dose
 - 5.4% received >10 treatments, up to 28 treatments
- All subjects were able to successfully self-administer the sublingual film



BXCL501 Was Well Tolerated

Treatment-emergent adverse events of special interest (AESI) occurring within 24 hours after first dose and over entire trial period

		AEs within 24 hours of first dose			AEs during 12-week trial (443 doses)		
Adverse Event	Severity	BXCL501 60 mcg n=50 (%)	BXCL501 40 mcg n=48 (%)	Placebo n=51 (%)	BXCL501 60 mcg n=50 (%)	BXCL501 40 mcg n=48 (%)	Placebo n=51 (%)
Somnolence*	Mild	8 (16.0)	6 (12.5)	2 (3.9)	8 (16.0)	9 (18.8)	2 (3.9)
	Moderate	1 (2.0)	2 (4.2)	0	3 (6.0)	2 (4.2)	0
Lethargy	Mild	2 (4.0)	1 (2.1)	1 (2.0)	4 (8.0)	1 (2.1)	1 (2.0)
	Moderate	1 (2.0)	1 (2.1)	0	1 (2.0)	1 (2.1)	0
Hypotension	Mild	7(14.0)	4 (8.3)	2 (3.9)	7(14.0)	8(16.7)	2 (3.9)
	Moderate	1 (2.0)	0	0	4 (8.0)	0	1 (2.0)
Bradycardia	Mild	3 (6.0)	0	0	4 (8.0)	3 (6.3)	1 (2.0)
	Moderate	1 (2.0)	1 (2.1)	0	2 (4.0)	1 (2.1)	0
Orthostatic Hypotension	Mild	2 (4.0)	2 (4.2)	1 (2.0)	5 (10.0)	8 (16.7)	2 (3.9)
	Moderate	2 (4.0)	1 (2.1)	0	2 (4.0)	2 (4.2)	0

*Somnolence was primarily mild and no subject was unarousable

The adverse events of special interest (AESI) are defined as those related to mechanism of action of the drug. Those that are listed were observed within 24 hours after the first dose and occur with a frequency of at least 2% and greater than with placebo. Subjects are counted once at highest severity for each preferred term.

Adverse Events: Falls, Deaths, and Discontinuations

- Over the 12-week trial, all falls were determined to be unrelated to treatment and occurred in between agitation episodes
 - 5 falls occurred in the 40 mcg arm, 7 in the 60 mcg arm, and 5 in the placebo arm
 - No falls occurred within 24 hours of dosing the 40 mcg or 60 mcg doses
 - 1 fall occurred within 24 hours of dosing in the placebo arm
- Three deaths, one in each treatment arm, occurred more than 1 month after last dose of trial treatment and were not determined to be related to treatment
- Over the 12-week trial 13 patients (9%) discontinued due to an adverse event; only 2 patients (0, 60 mcg; 1, 40 mcg; 1, PBO) discontinued within 24 hours of dosing
 - Overall, 34% of patients discontinued the trial
 - 42%, 21%, and 40% discontinued at 60 mcg, 40 mcg, and PBO, respectively



Summary



- Primary and a key secondary endpoint of reduction in agitation symptoms at 2 hours and 1 hour met at 60 mcg dose
- Clinically meaningful improvement in agitation at 60 mcg dose by CGI-I and ACES
- Dosing with 60 mcg showed a similar reduction in agitation for first and all treated episodes
- Well tolerated, with no treatment-related serious adverse events throughout trial and AEs consistent with MOA of BXCL501

Next Steps: Acute Treatment of Agitation in Alzheimer's Disease



- Engage with FDA in H2 2023 on a potential path to sNDA submission
- TRANQUILITY II data to support ongoing clinical development program
 - TRANQUILITY III and other potential studies
- Present results of TRANQUILITY I and TRANQUILITY II at upcoming medical congresses

TRANQUILITY Program Overview

TRANQUILITY I NCT04251910	TRANQUILITY II NCT05271552	TRANQUILITY III NCT05665088	LONG-TERM SAFETY
Phase 1b/2	Phase 3	Phase 3	
Efficacy, pharmacokinetics, safety, and tolerability of BXCL501 vs. placebo	Efficacy, safety, and tolerability of BXCL501 vs. placebo in patients with mild to moderate AD	Efficacy, safety, and tolerability of BXCL501 vs. placebo in patients with moderate to severe AD	Long-term safety and tolerability of BXCL501 in patients with mild, moderate, or severe AD
Adaptive, randomized, double-blind, placebo-controlled, ascending dose-finding trial in residential care facilities	12-week, 1:1:1 randomized, 3-arm, double-blind, placebo-controlled trial in residential care facilities	12-week, 1:1:1 randomized, 3-arm, double-blind, placebo-controlled trial (with ability to re-dose) in residential care facilities	52-week, open-label trial including residential care facilities
Completed	Completed	Enrolling	Planned

Thank you!

