



Topline Results

Phase 3 RECOVER trial of
brilaroxazine in schizophrenia

October 30, 2023

Forward Looking Statements

This presentation contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's RECOVER Phase 3 trial and timing of topline data, the Company's expectations regarding the anticipated clinical profile of its product candidates, including statements regarding anticipated efficacy or safety profile, and those relating to the Company's expectations, intentions or beliefs regarding matters including product development and clinical trial plans, clinical and regulatory timelines, trial results, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth and financing opportunities and other statements that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions. These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or the Company's financial performance and involve known and unknown risks, uncertainties, and other factors, including the potential impact of the COVID19 pandemic and the potential impact of sustained social distancing efforts, on the Company's operations, clinical development and clinical trial plans and timelines, which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's most recent Annual Report on Form 10-K for the fiscal year ended December 31, 2022, and the Company's other filings from time to time with the Securities and Exchange Commission. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this presentation. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

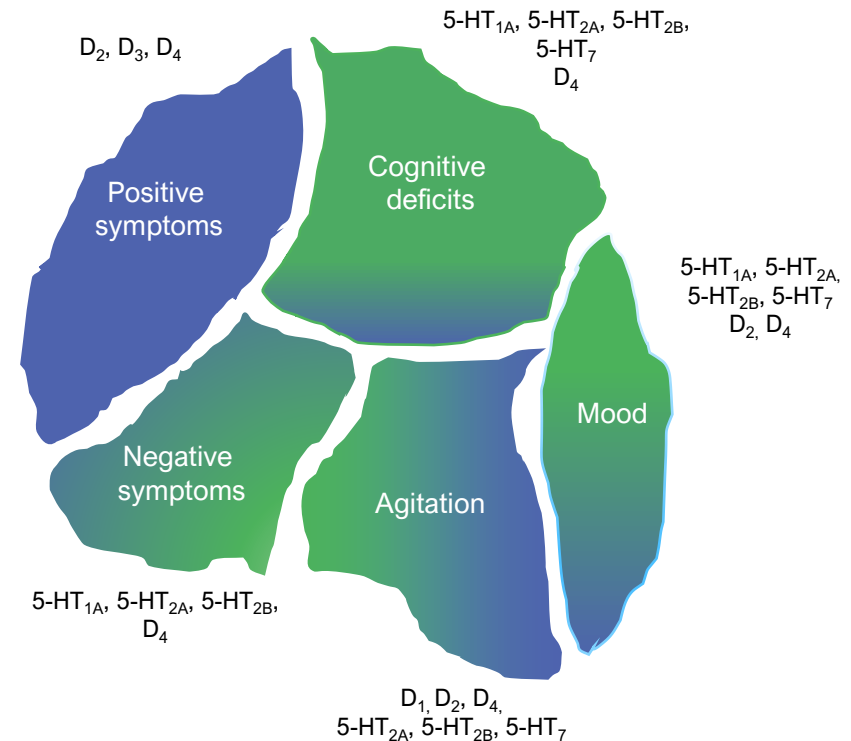
Topline Results of
brilaroxazine Phase 3
RECOVER trial in
schizophrenia

**Successfully met
primary efficacy and
safety endpoints and key
secondary endpoints**

Schizophrenia: Common Psychiatric Condition With Multiple Symptom Domains

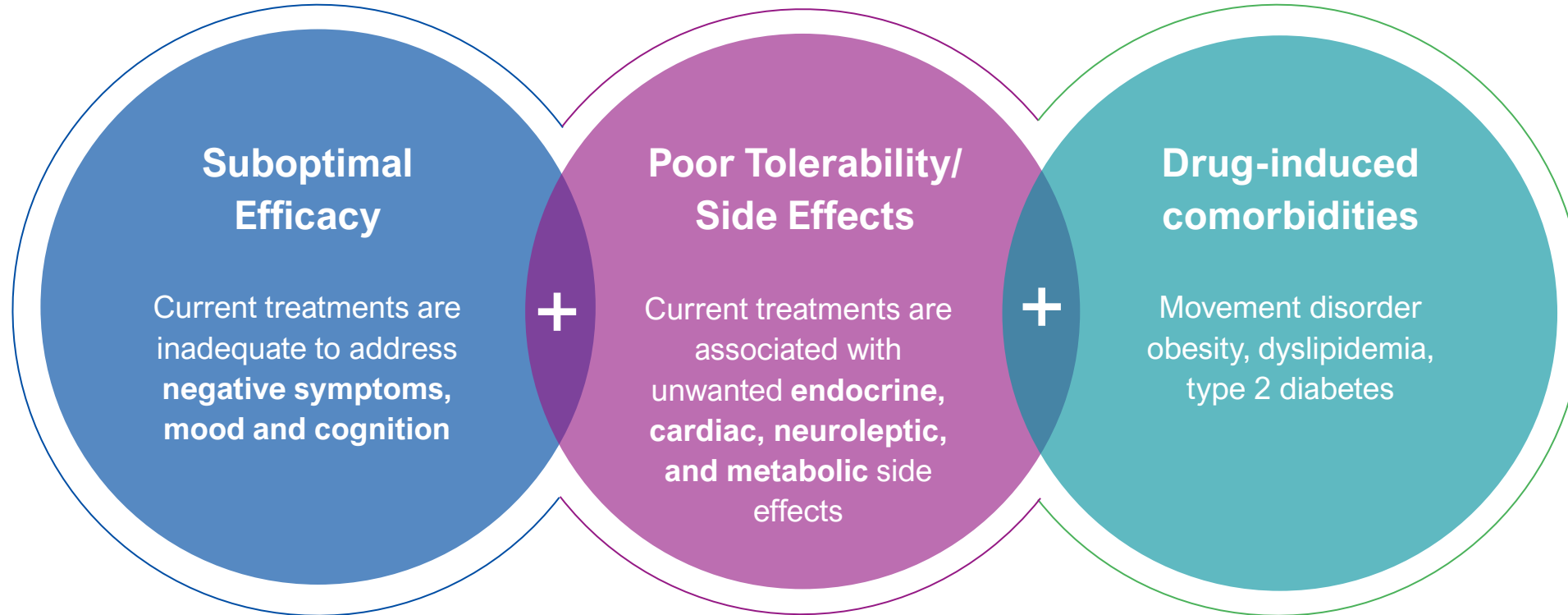
Primarily driven by dysfunctional serotonin and dopamine signaling

- Affects ~1.1% of the world's population
 - ~3.5 million people in the US
 - ~24 million globally
- Leading cause of disability worldwide, with onset in late-teens and early-adulthood
- Requires lifelong treatment
- Up to 30% of patients are treatment refractory
- Neuroinflammation is implicated as a major contributing factor to schizophrenia



No Current Therapies Address All Needs Of Patients With Schizophrenia

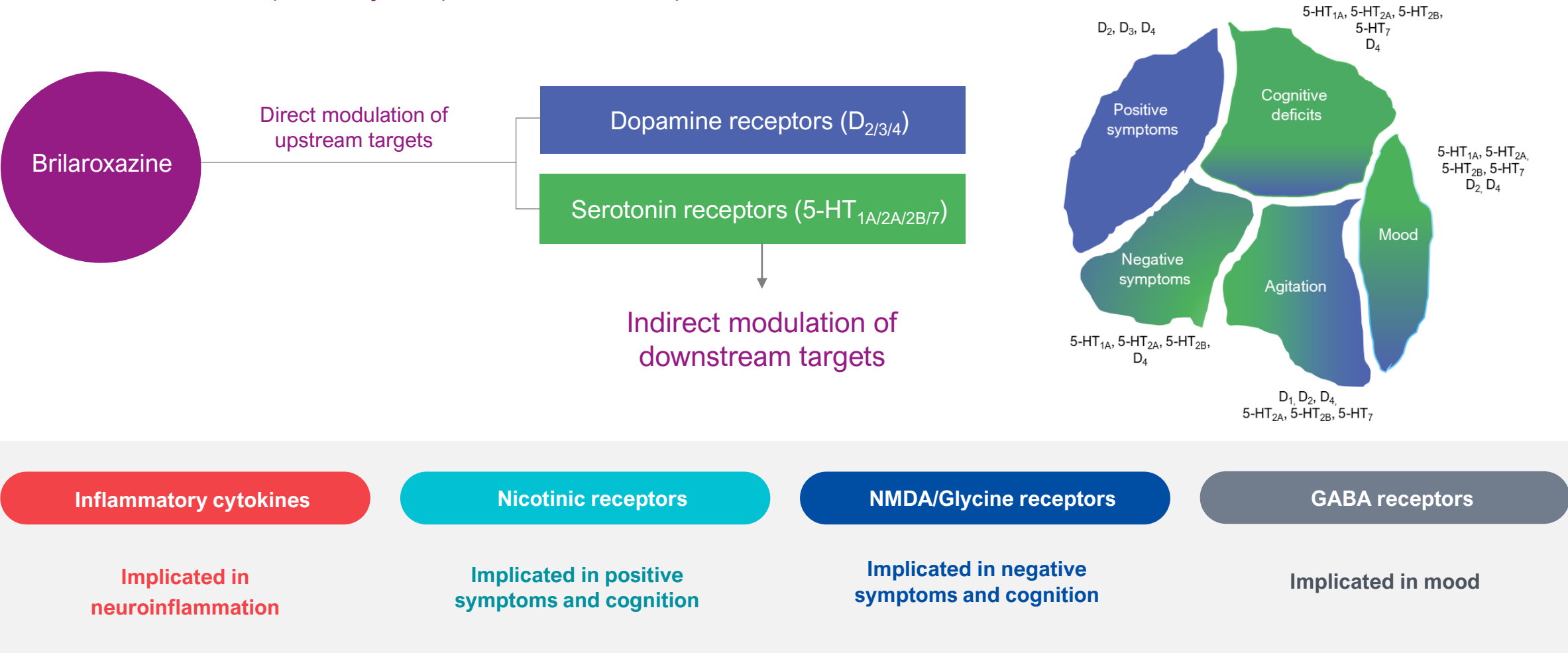
Suboptimal efficacy and side effects of current treatments continue to limit long-term use for this chronic condition



Leading to high discontinuation rates and non-compliance

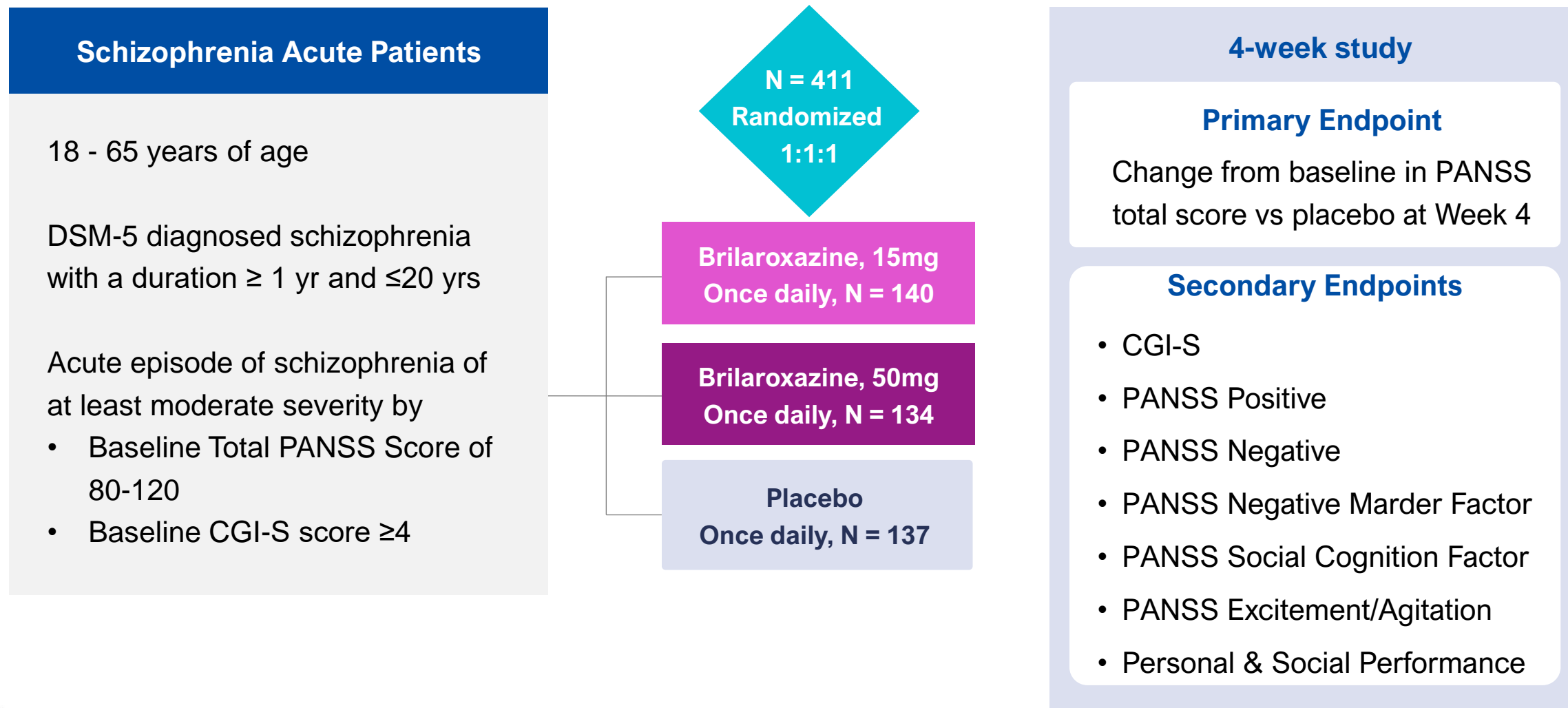
Brilaroxazine: Novel Serotonin Dopamine Signaling Modulator

Activities on critical pathways implicated in schizophrenia



Brilaroxazine Phase 3 RECOVER Trial For Schizophrenia

Randomized, 4-week, double-blind, placebo-controlled, multicenter trial in acute exacerbation of schizophrenia



RECOVER Trial Demographics And Baseline Characteristics

Balanced randomization with diverse representation of 411 patients; USA 60%, India 34%, Bulgaria 6%

	Brilaroxazine 15 mg (n = 140)	Brilaroxazine 50 mg (n = 134)	Placebo (n = 137)
Age (years) Mean (SD)	38.3 (10.88)	39.8 (10.85)	38.4 (10.71)
Male n (%)	96 (68.6)	96 (71.6)	103 (75.2)
Race, n (%)			
White	24 (17.1)	26 (19.4)	23 (16.8)
Black	64 (45.7)	59 (44.0)	66 (48.2)
Asian	49 (35.0)	46 (34.3)	44 (32.1)
Other	3 (2.1)	3 (2.2)	4 (2.9)
Baseline PANSS total score Mean (SD)	97.3 (10.15)	99.1 (9.56)	98.3 (9.48)
Baseline PANSS positive score Mean (SD)	26.20 (3.58)	26.47 (3.63)	26.53 (3.57)
Baseline PANSS negative score Mean (SD)	23.58 (4.60)	24.22 (4.60)	24.27 (4.23)
Baseline CGI score Mean (SD)	4.9 (0.62)	5.0 (0.53)	5.0 (0.56)

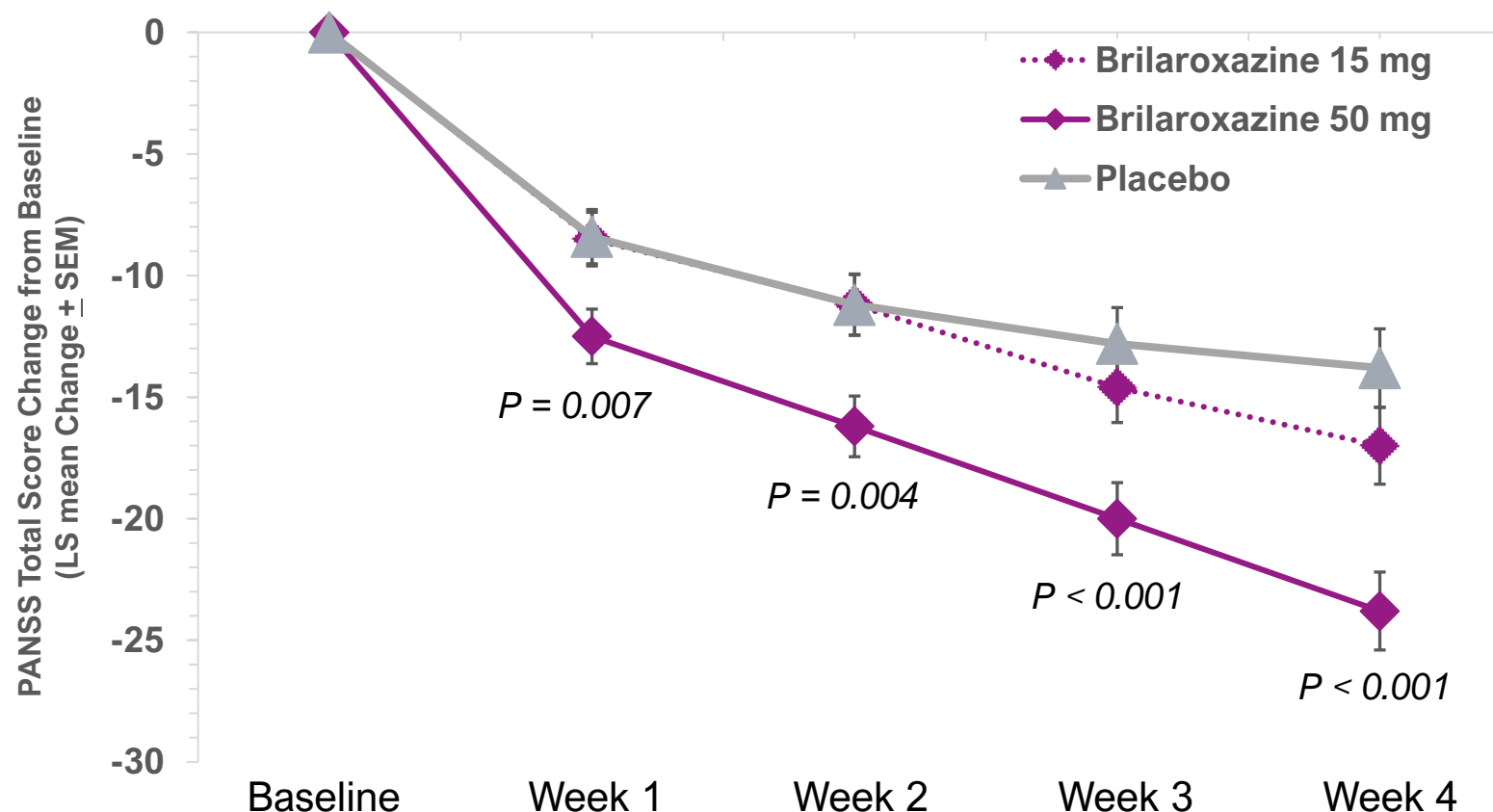
Primary Endpoint: PANSS Total Score At Week 4 For Brilaroxazine Vs. Placebo

10.1-point reduction in PANSS total score vs. placebo at week 4, $p < 0.001$ (-23.9 brilaroxazine 50 mg vs. -13.8 placebo)

Cohen's d effect size of 0.6

PANSS Total Score

- Successfully met PANSS Total Score primary endpoint for brilaroxazine 50 mg
- Statistically significant and clinically meaningful sustained decrease with brilaroxazine 50 mg
- Separation for brilaroxazine 50 mg from placebo within a week
- Brilaroxazine 15 mg numerically separated from placebo

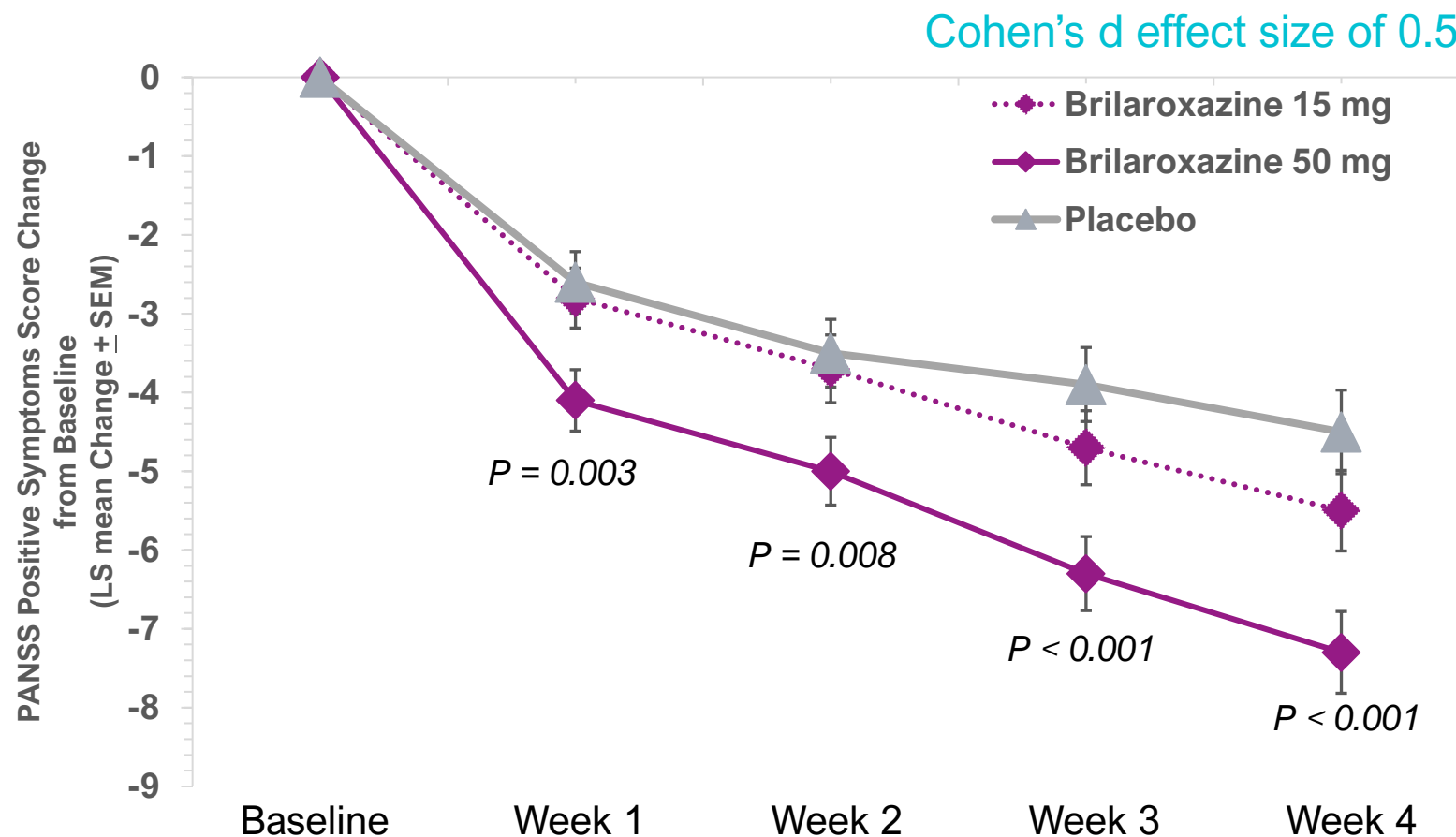


Secondary Endpoint: Positive Symptoms At Week 4 For Brilaroxazine Vs. Placebo

2.8-point reduction in positive symptoms vs. placebo at week 4, $p < 0.001$ (-7.3 brilaroxazine 50 mg vs. -4.5 placebo)

Positive Symptoms

- Successfully met the secondary endpoint positive symptoms
- Statistically significant and clinically meaningful sustained decrease with brilaroxazine 50 mg
- Separation for brilaroxazine 50 mg from placebo within a week
- Brilaroxazine 15 mg numerically separated from placebo

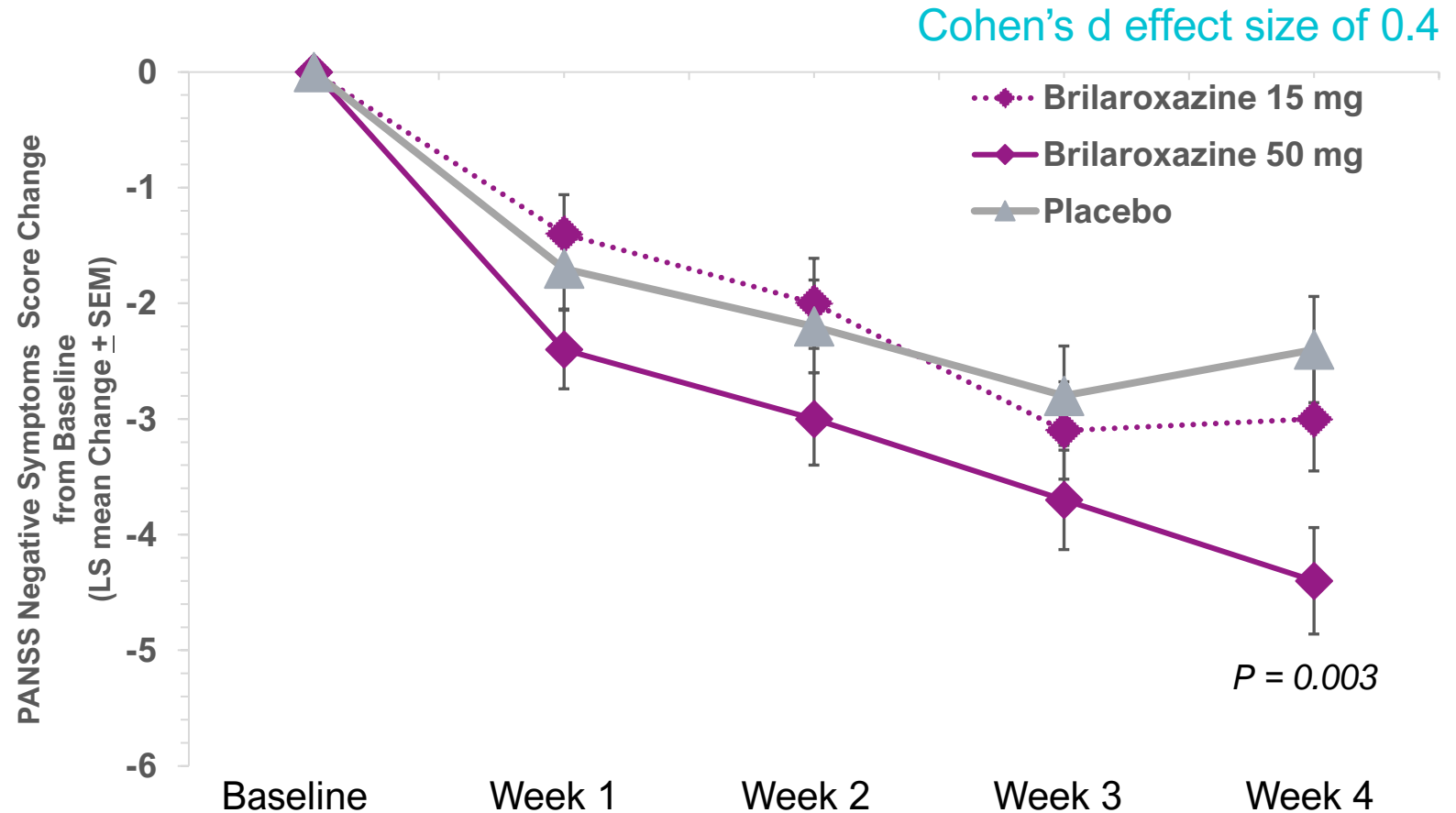


Secondary Endpoint: Negative Symptoms At Week 4 For Brilaroxazine Vs. Placebo

2-point reduction in negative symptoms vs. placebo at week 4, $p = 0.003$ (-4.4 brilaroxazine 50 mg vs. -2.4 placebo)

Negative Symptoms

- Successfully met the secondary endpoint negative symptoms
- Statistically significant and clinically meaningful decrease with brilaroxazine 50 mg
- Separation for brilaroxazine 50 mg from placebo within a week
- Brilaroxazine 15 mg numerically separated from placebo

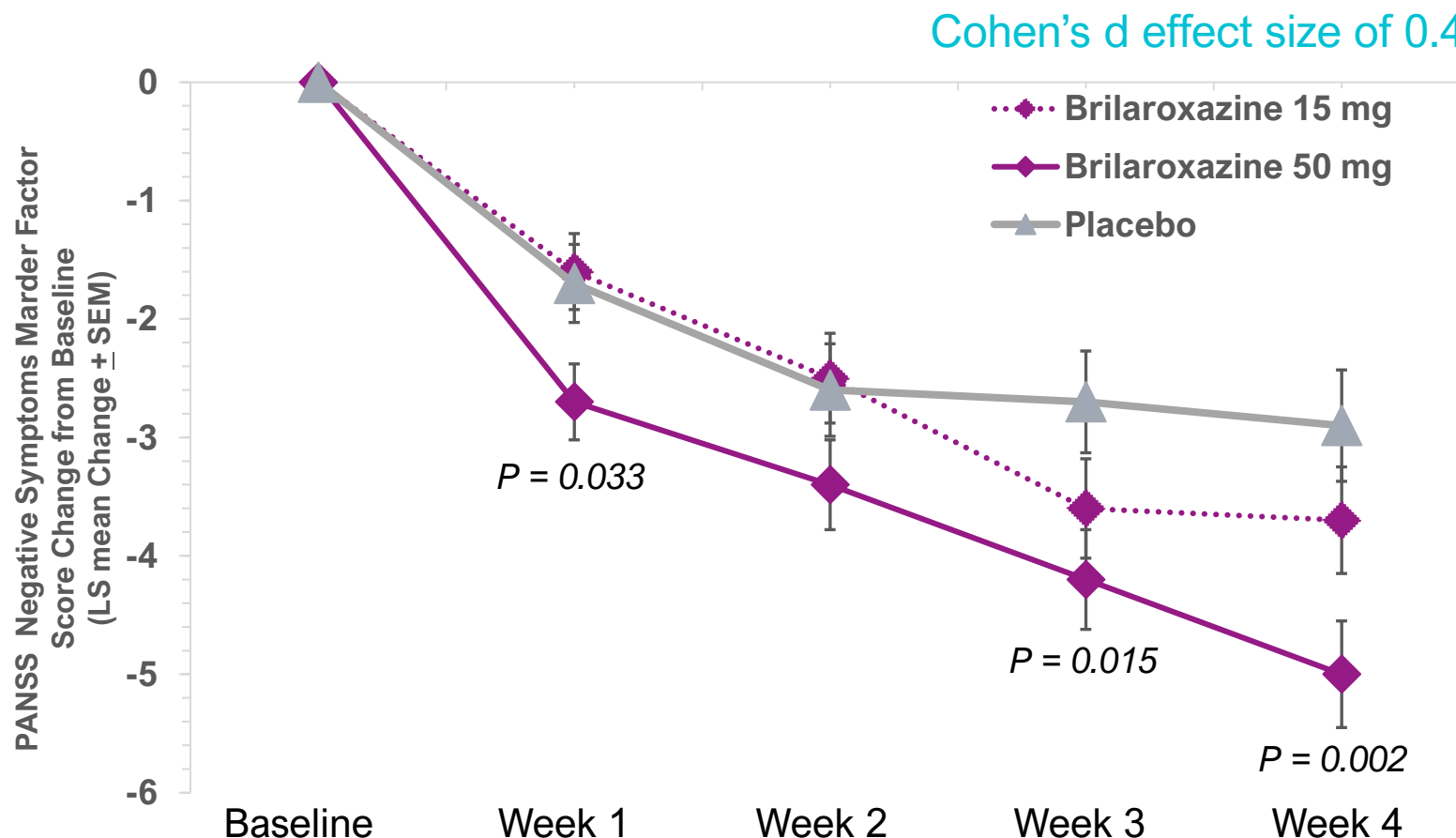


Secondary Endpoint: Negative Symptoms PANSS Marder Factor At Week 4

2.1-Point reduction in negative symptoms on Marder factor in brilaroxazine 50 mg vs. placebo at week 4, $p = 0.002$

Negative Symptoms Marder Factor

- Successfully met the secondary endpoint negative symptoms PANSS Marder factor
- Statistically significant and clinically meaningful decrease with brilaroxazine 50 mg
- Separation for brilaroxazine 50 mg from placebo within a week
- Brilaroxazine 15 mg numerically separated from placebo

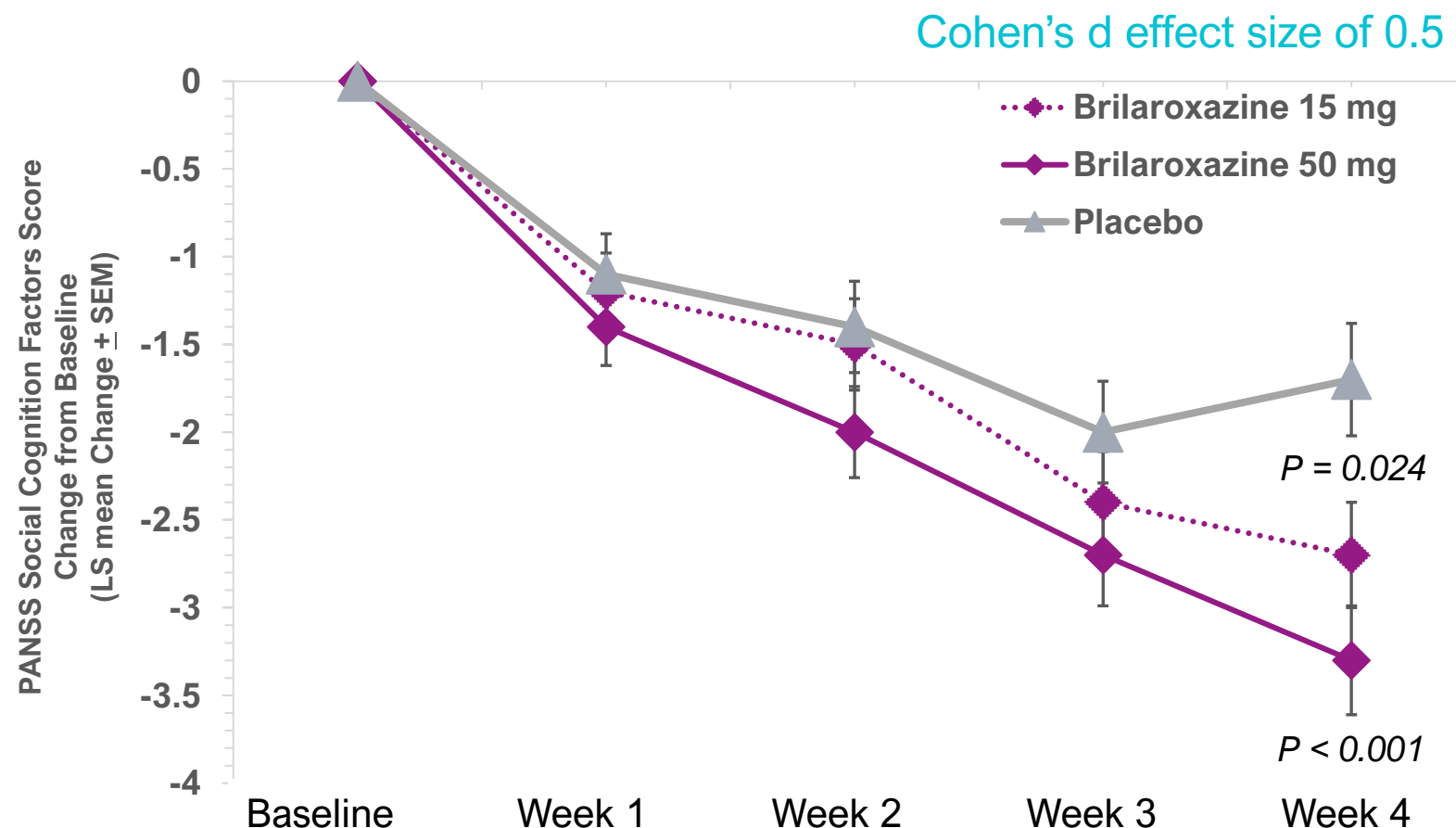


Secondary Endpoint: PANSS Social Cognition Factors At Week 4

1.6-point reduction in social cognition deficits in brilaroxazine 50 mg vs. placebo at week 4, $p < 0.001$

Social Cognition Deficits

- Successfully met the secondary endpoint social cognition symptoms
- Statistically significant and clinically meaningful decrease with both brilaroxazine 15 mg and 50 mg at week 4
- Separation for brilaroxazine 50 mg from placebo within a week



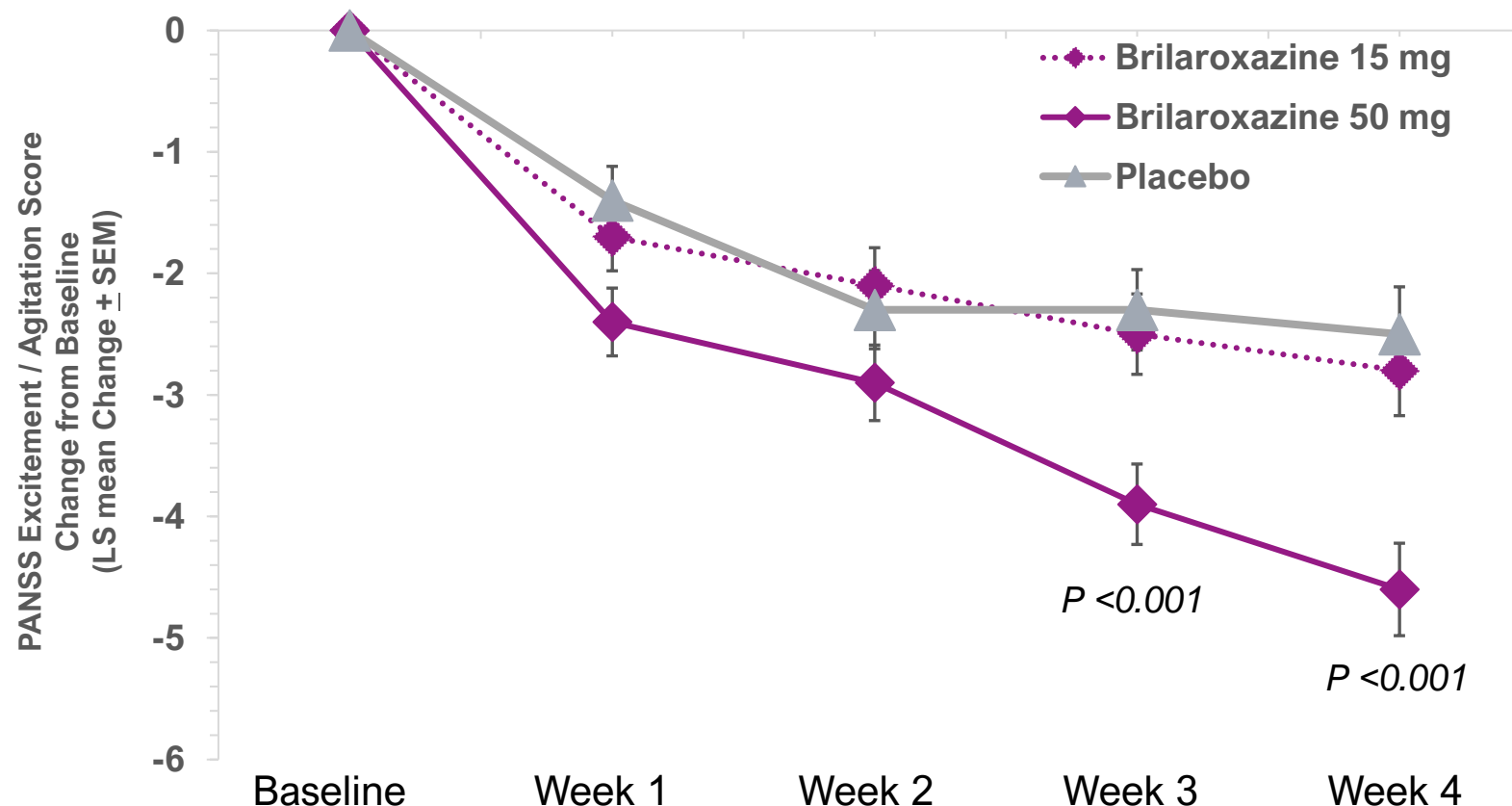
Secondary Endpoint: PANSS Excitement/Agitation At Week 4

2.1-point reduction in excitement/agitation symptoms in brilaroxazine 50 mg vs. placebo at week 4, $p < 0.001$

Cohen's d effect size of 0.5

Excitement / Agitation Symptoms

- Successfully met the secondary endpoint excitement/agitation symptom
- Statistically significant and clinically meaningful sustained decrease with brilaroxazine 50 mg

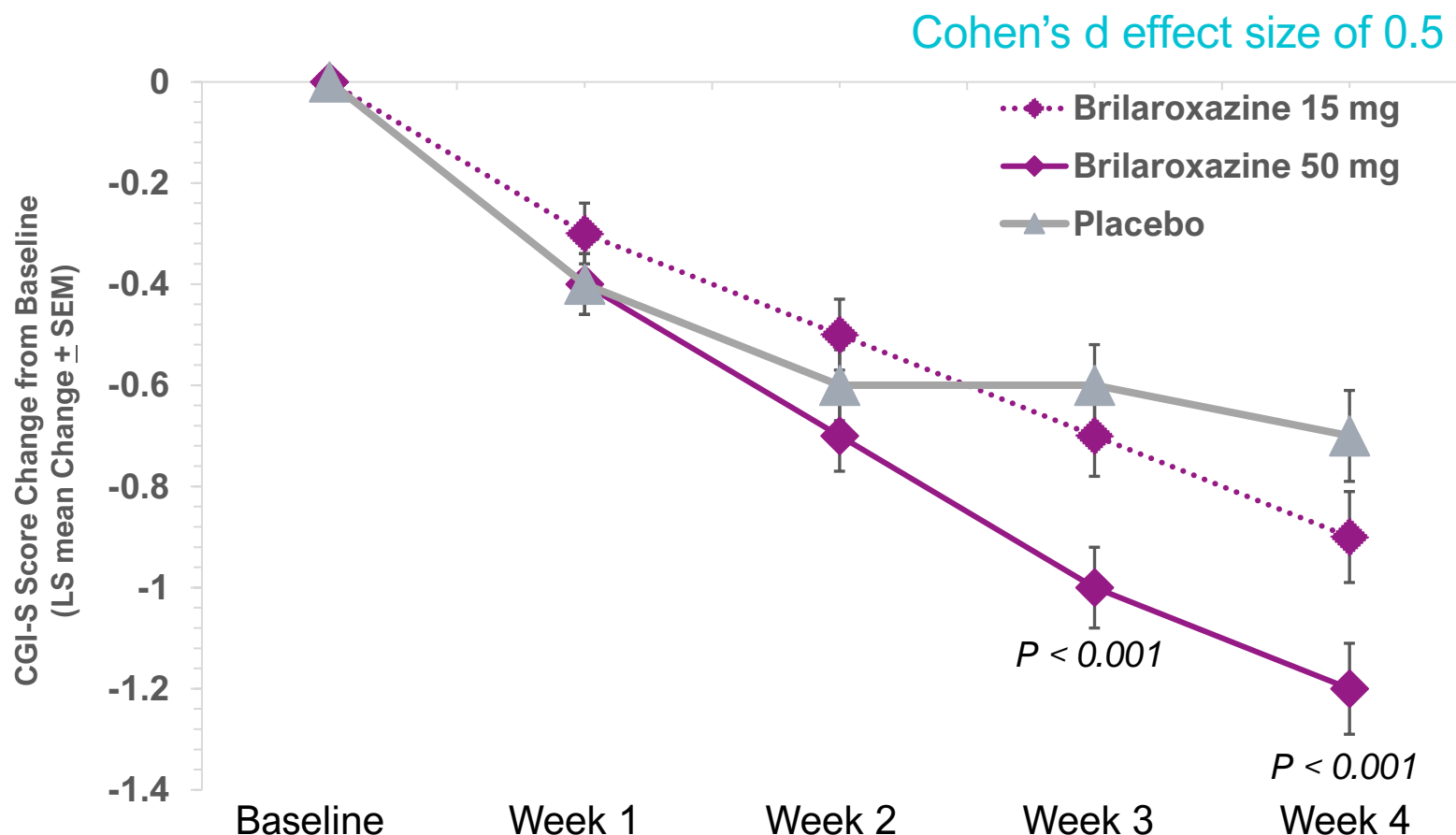


Secondary Endpoint: CGI-S At Week 4 For Brilaroxazine Vs. Placebo

≥1-point reduction in CGI-S score in brilaroxazine 50 mg vs. placebo at week 4, $p < 0.001$

CGI-S Score ≥ 1-Point Reduction

- Successfully met the secondary endpoint CGI-Severity score
- Statistically significant and clinically meaningful sustained decrease with brilaroxazine 50 mg
- Brilaroxazine 15 mg numerically separated from placebo at weeks 3 and 4

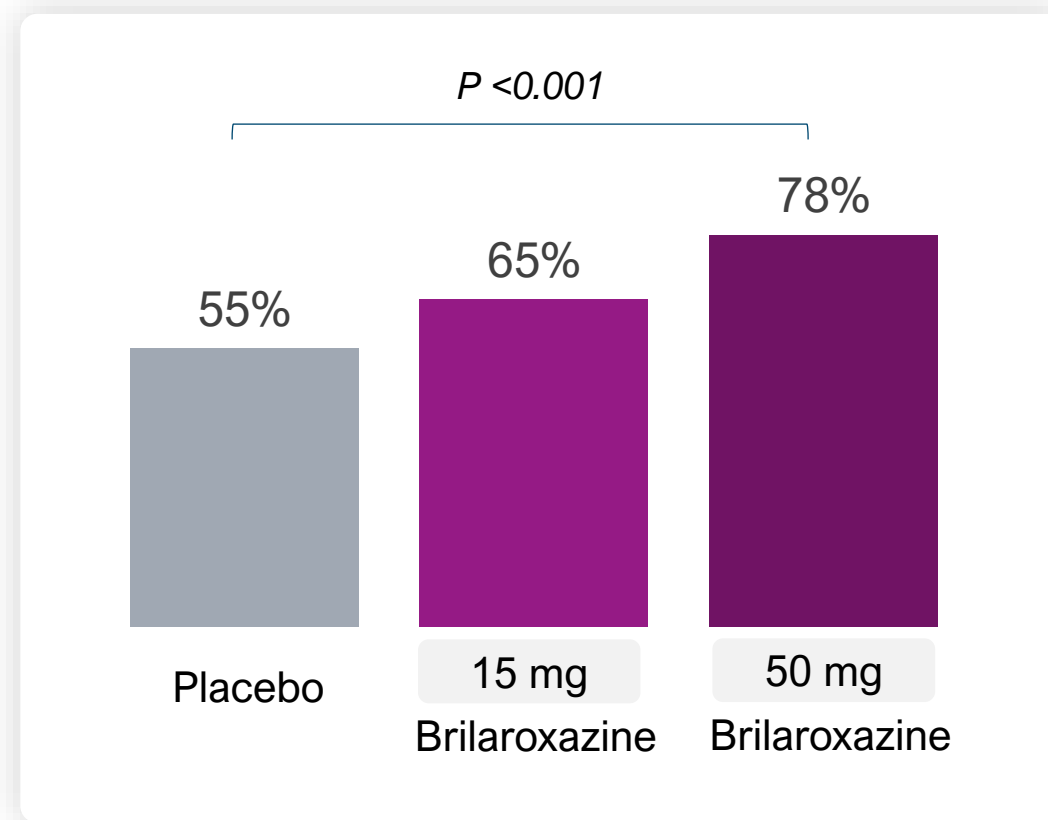


Secondary Endpoint: CGI-S At Week 4 For Brilaroxazine Vs. Placebo

Proportion of subjects with ≥ 1 point(s) improvement on the CGI-Severity scale from baseline

CGI-S score ≥ 1 -point improvement

- Study successfully met secondary endpoint CGI-Severity score
- 78% of subjects on brilaroxazine 50 mg achieved a statistically significant ≥ 1 -point improvement in CGI-Severity scale from baseline vs. placebo
- 65% of subjects on brilaroxazine 50 mg achieved ≥ 1 -point improvement in CGI-Severity scale from baseline vs. placebo



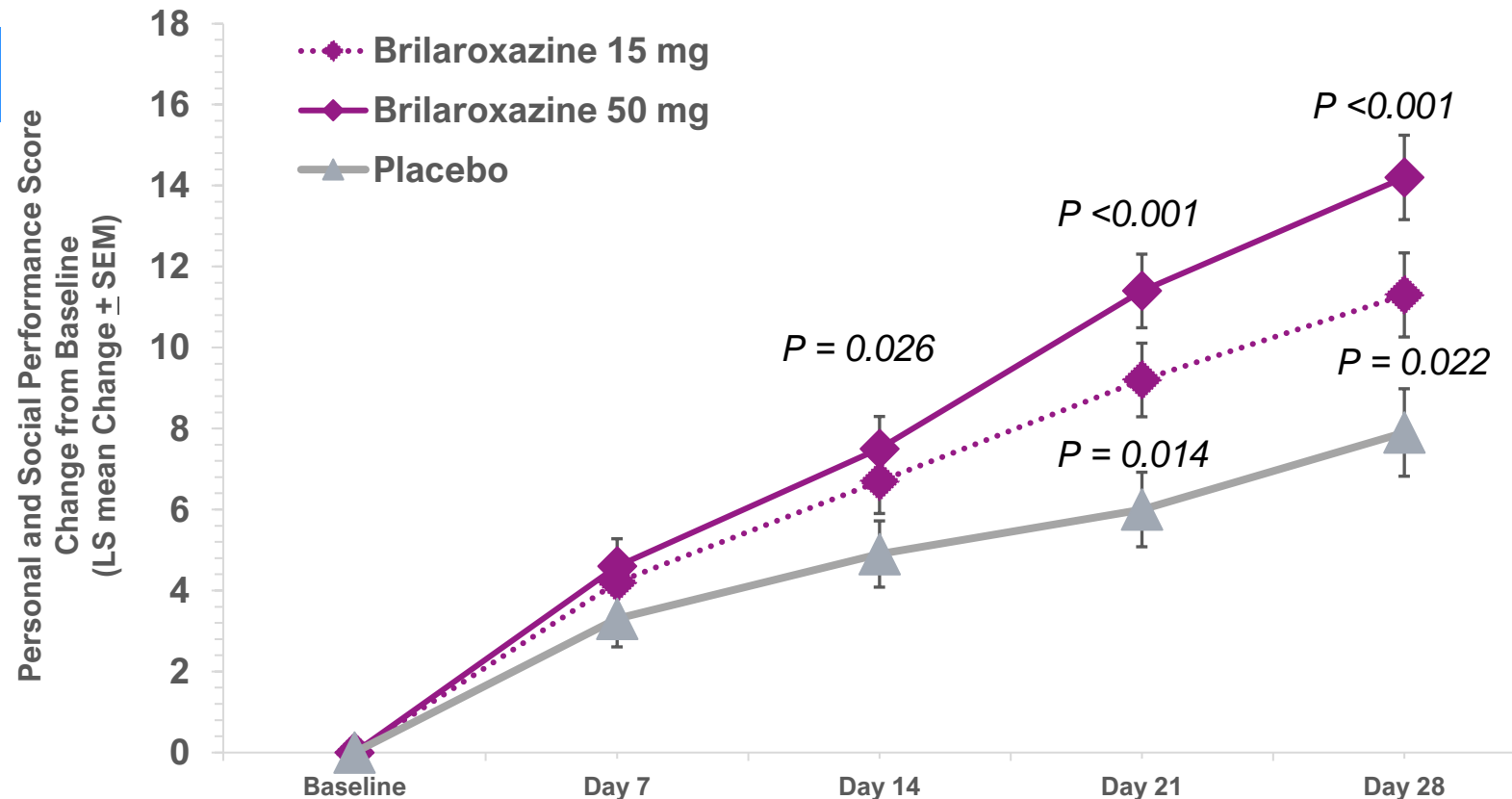
Secondary Endpoint: Personal And Social Performance (PSP) At Week 4

6.3-point improvement in PSP score in brilaroxazine 50 mg vs placebo at week 4, $p < 0.001$

Cohen's d effect size of 0.5

Personal and Social Performance

- Successfully met the secondary endpoint personal and social performance
- Statistically significant and clinically meaningful sustained improvement with both brilaroxazine 15 mg and 50 mg



Statistically Significant And Clinically Meaningful Improvements Across All Major Symptom Domains With Brilaroxazine 50 Mg Vs. Placebo At Week 4

	Brilaroxazine 50 mg vs. Placebo at week 4 Point Reduction / Improvement	Cohen's d Effect Size	P Value
PANSS Total Score	10.1	0.6	< 0.001 ✓
Positive Symptoms	2.8	0.5	< 0.001 ✓
Negative Symptoms	2.0	0.4	0.003 ✓
Negative Symptoms Marder Factor	2.1	0.4	0.002 ✓
PANSS Social Cognition	1.6	0.5	< 0.001 ✓
PANSS Excitement/Agitation	2.1	0.5	< 0.001 ✓
Personal and Social Performance	6.3	0.5	< 0.001 ✓
CGI-S score	≥1	0.5	< 0.001 ✓

RECOVER Trial Topline Tolerability Results: Brilaroxazine Vs Placebo

Well-tolerated safety profile

Brilaroxazine was generally well tolerated

- Overall TEAEs rates 34.5% in brilaroxazine 15 mg, 35.5% in 50 mg, and 30% in placebo
- One serious TEAE reported in brilaroxazine 50 mg was not related to the study drug
- Two serious TEAEs reported in the brilaroxazine 15 mg were deemed not to be related to the study drug
- No incidence of suicidal ideation
- No significant change in bodyweight, blood glucose levels, lipids levels, or endocrine hormones (prolactin, thyroid hormone) compared to placebo

The most common brilaroxazine TEAEs (>5%) were mild to moderate in severity

Common brilaroxazine TEAEs (>5%) were headache (<6%) and somnolence (≤7.5%) generally transient in nature

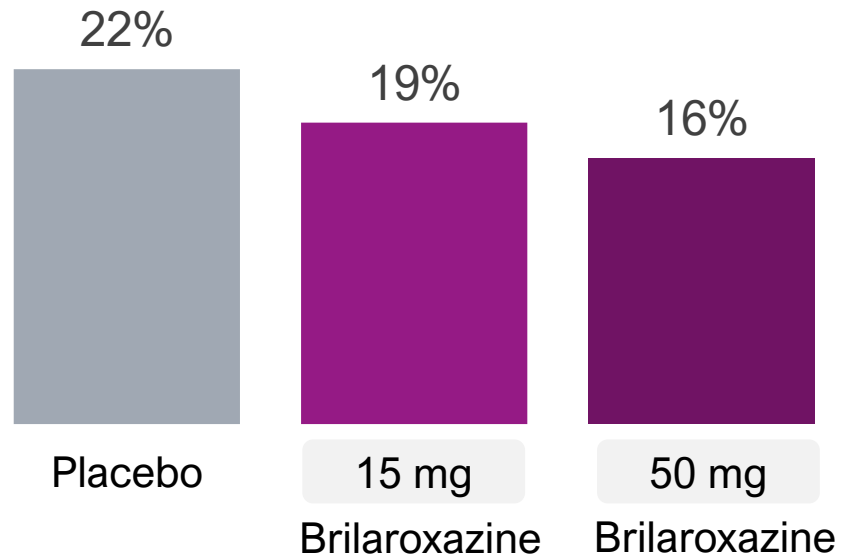
Brilaroxazine adverse events of special interest (AESI) were mild to moderate in severity

- Weight gain 2.1% in 15 mg and 5.9% in 50 mg brilaroxazine and 2.9% in placebo
- Akathisia 0.7% and EPS 0.7% in 50 mg brilaroxazine and none in 15 mg and placebo
- Elevated LDL level none in brilaroxazine and 2.9% in placebo
- Low HDL level 0.7% in 15 mg, 1.4% in 50 mg brilaroxazine and 1.4% in placebo

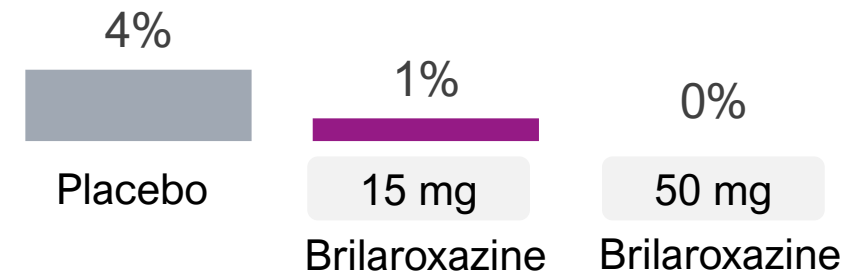
RECOVER Trial Discontinuation Rates: Brilaroxazine Vs. Placebo

19% (N=78) total discontinuation rate in the study

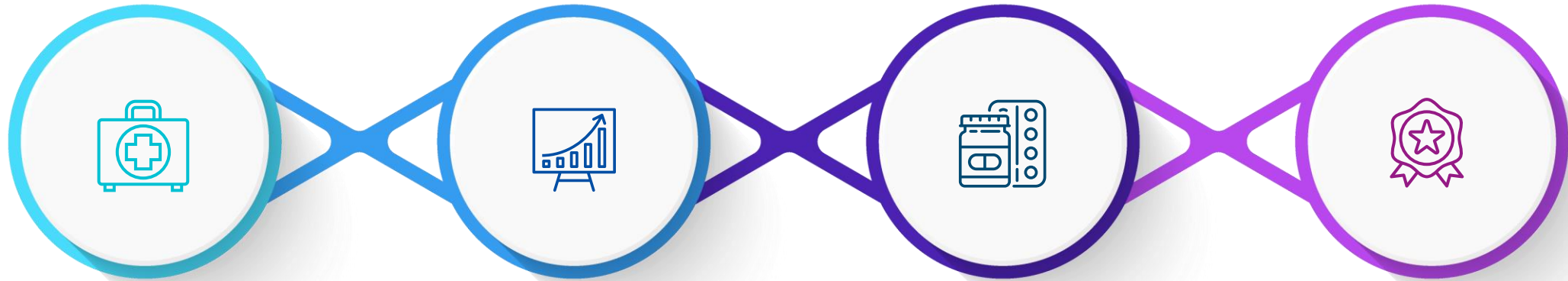
Discontinuation Rate



Discontinuation Due to Side Effects



Clinically Meaningful And Statistically Significant Improvements In Positive And Negative Symptoms Of Schizophrenia With Safety Profile Comparable To Placebo



Successfully met primary endpoint for brilaroxazine 50 mg with reduction in PANSS score

Improvement in all major symptom domains

Well-tolerated with side effects comparable to placebo

Low discontinuation rate comparable to placebo

Next Steps

Phase 3 RECOVER-2 trial expected to be initiated in Q1 2024 and completed in early 2025

Topline data from OLE trial expected in Q4 2024

Planned New Drug Application (NDA) submission to the FDA expected in 2025

Ongoing Clinical Program Sets The Stage Regulatory Path Forward

Regulatory discussions with FDA on planned New Drug Application (NDA) submission

PHASE 2 REFRESH NCT01490086	PHASE 3 RECOVER NCT05184335	PHASE 3 OLE NCT05184335	PHASE 3 RECOVER-2 TBD
<p>N = 234</p> <p>Acute schizophrenia or schizoaffective disorder</p> <p>Efficacy and safety of brilaroxazine vs placebo</p> <p>3:3:2 Randomized, 4-week, double-blind, placebo-controlled, multicenter</p> <p>Once daily brilaroxazine 15, 30, 50 mg</p> <p>FDA indicated potential for 'Superior Safety' label claim</p>	<p>N = 412</p> <p>Acute schizophrenia</p> <p>Efficacy and safety of brilaroxazine vs placebo</p> <p>1:1:1 Randomized, 4-week, double-blind, placebo-controlled, multicenter</p> <p>Once daily brilaroxazine 15, 50 mg</p> <p>Completed in Q3 2023</p>	<p>N = 100 completed</p> <p>Stable schizophrenia</p> <p>Long-term safety and tolerability of brilaroxazine</p> <p>Open label, one group. 1-year outpatient extension of RECOVER</p> <p>Once daily brilaroxazine 15, 30, 50 mg flexible dose</p> <p>Completion expected in Q4 2024</p>	<p>N = 450</p> <p>Acute schizophrenia</p> <p>Efficacy and safety of brilaroxazine vs placebo</p> <p>1:1:1 Randomized, 6-week, double-blind, placebo-controlled, multicenter</p> <p>Once daily brilaroxazine 30, 50 mg with primary & secondary endpoints same as RECOVER</p> <p>Completion expected in early 2025</p>

Brilaroxazine: Treating Complex Mental Illnesses And Schizophrenia

Multifaceted mechanism of action has direct and indirect impacts on multiple critical pathways implicated in disease

Differentiated Phase 3 Data

Statistically significant improvement across key symptom domains (PANSS total, positive, and negative score, social cognition, and CGI score)

Well-tolerated safety profile comparable to placebo

Novel Properties

Multifaceted activity
Serotonin-dopamine modulator

Pharmacological activity on pathways implicated in neuropsychiatric and inflammatory diseases

Broad Application

Approaching NDA submission in schizophrenia

Phase 2/3 expansion potential:

- Neuropsychiatric disorders (bipolar disorder, MDD, ADHD)
- Inflammatory diseases (PAH, IPF, psoriasis)

Upcoming Milestones

Initiation of RECOVER-2 Phase 3 trial expected in Q1 2024

Topline data from 1-year open-label extension (OLE) trial expected Q4 2024