Reviva Pharmaceuticals

KOL Webinar to Discuss Vocal Biomarker Results of brilaroxazine Phase 3 RECOVER Trial in Schizophrenia

September 4, 2024 at 11:00am PST

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 1-year Phase 3 open-label extension (OLE) trial evaluating the long-term safety and tolerability of brilaroxazine, the Company's registrational Phase 3 RECOVER-2 trial, 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, planned or intended additional trials and the timing thereof, planned or intended regulatory submissions and the timing thereof, trial results, market opportunity, ability to raise sufficient funding, competitive position, possible or assumed future results of operations, business strategies, potential growth, financing, partnership, expansion and other 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 COVID-19 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, 2023, and the Company's other filings from time to time with the Securities and Exchange Commission (the "SEC"). 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.

The Company's SEC filings are available on the SEC's website at www.sec.gov. Given these uncertainties, you should not place undue reliance on these forward-looking statements, which apply only as of the date of this presentation and should not be relied upon as representing the Company's views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-looking statements, other than as may be required by law. If the Company does update one or more forward-looking statements, no inference should be made that the Company will make additional updates with respect to those or other forward-looking statements.

This presentation also contains estimates and other statistical data made by independent parties and by the Company relating to market size and growth and other data about the Company's industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.

Agenda

Welcome and Introduction	Welcome and Introduction Laxminarayan Bhat, Founder, President and CEO, Reviva Pharmaceuticals
Review of Brilaroxazine Phase 3 RECOVER Trial Efficacy Results	Mark Opler, PhD, MPH Chief research Officer at WCG Inc and Executive Director at the PANSS Institute
Brilaroxazine Phase 3 RECOVER Trial Vocal Biomarker Results	Brian Kirkpatrick, MD, MSPH Professor, Psychiatric Research Institute, University of Arkansas for Medical Sciences, Arkansas
Q&A Session	Q&A Session

Reviva Clinical Development Pipeline

			Discovery	Preclinical	Phase I	Phase II	Phase III	Est. Market Opportunity ($B)
Brilaroxazine – Serotonin/ dopamine modulator (NCE)	Neuropsychiatric	Schizophrenia						$13.4 (1)
		Bipolar Disorder						$6.1 (2)
		Major Depressive Disorder						$14.9 (3)
		Attention Deficit Hyperactivity Disorder						$30.5 (4)
	Inflammatory	Pulmonary Arterial Hypertension						$12.1 (5)
		Idiopathic Pulmonary Fibrosis						$6.4 (6)
		Psoriasis (topical gel)						$57.7 (7)
RP1208 – Triple reuptake inhibitor (NCE)		Depression						$26.4 (8)
		Obesity						$77 (9)

(1) By 2032 per Schizophrenia Market by Market Research Future 2024. (2) By 2028 per Bipolar Disorder Market by Skyquest Report 2022. (3) By 2032 per Major Depressive Disorder Market by Future Market Insights 2022. (4) By 2032 per ADHD market by Polaris Market Research 2023. (5) By 2032 per Pulmonary Arterial Hypertension (PAH) by Precedence Research 2023. (6) By 2031 per Idiopathic Pulmonary Fibrosis (IPF) by SkyQuest 2024. (7) By 2032 per Psoriasis Market by Precedence Research 2023. (8) By 2028 per Anxiety and Depression market, Report Linker 2023. (9) By 2030 per Morgan Stanley Research 2023

Ongoing Clinical Program Sets the Stage for a Regulatory Path Forward

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

PHASE 2 REFRESH ✓ NCT01490086	**PHASE 3 RECOVER-1** ✓ NCT05184335	**PHASE 3 Long-term Safety** NCT05184335	**PHASE 3 RECOVER-2** **TBD**
N = 234 (4-week) **Acute schizophrenia or schizoaffective disorder**	**N = 411 (4-week)** **Acute schizophrenia**	**N = 100 completers (1-year)** **Stable schizophrenia**	**N = 450 (4-week)** **Acute schizophrenia**
Efficacy and safety	Efficacy and safety	Long-term safety and tolerability	Efficacy and safety *Primary and secondary endpoints consistent with RECOVER-1 trial*
15, 30, 50 mg	15, 50 mg	15, 30, 50 mg flexible dose	30, 50 mg
FDA indicated potential for 'Superior Safety' label claim in the End-of-Phase 2 (EOP2) meeting	Completed with topline results announced in October 2023	Topline data expected Q4 2024	Completion expected Q4 2025

Registrational Phase 3 RECOVER-2 trial will replicate the successful trial design of Phase 3 RECOVER-1 trial, replacing the low dose with 30 mg

Most non-clinical development is complete, and preparation is underway to file in Q1 2026

Reviva PHARMACEUTICALS

OLE: Open Label Extension

Results of brilaroxazine Phase 3 RECOVER-1 trial in schizophrenia

Overview of Today's KOL Webinar

- Review of brilaroxazine phase 3 RECOVER-1 trial efficacy results
- Presenting vocal biomarker results for schizophrenia and negative symptoms

Brilaroxazine phase 3 RECOVER-1 trial efficacy and safety results were presented in the KOL webinar on February 15, 2024.

Webinar recording: https://revivapharma.com/kol-event-021524/

Slide deck: https://revivapharma.com/wp-content/uploads/2024/02/Reviva-KOL-Webinar-021524.pdf

Reviva PHARMACEUTICALS

KOL Biography

Mark Opler, PhD, MPH

Chief Research Officer at WCG Inc and Executive Director of the PANSS Institute

Dr. Opler has served as a faculty member in the Departments of Psychiatry and Environmental Medicine at New York University School of Medicine and in the Department of Neuroscience at Columbia University, College of Physicians and Surgeons. His academic research focuses on the etiology, phenomenology, and treatment of serious and persistent mental disorders. He is a co-author and developer of several clinical assessment tools, including the SNAPSI, CGI-DS, and NY-AACENT. He is a contributor to the latest edition of the PANSS Manual©.

Dr. Opler has received research support from the US NIMH, the Brain & Behavior Foundation (formerly NARSAD), the Stanley Medical Research Institute, and the Qatar National Research Fund. He has co-authored more than 50 peer-reviewed publications and has contributed to multiple book chapters and review articles on clinical assessment, research methodology, and mental health.

He received his PhD and MPH from Columbia University and his BSc from SUNY at Stony Brook. He is a graduate of the Psychiatric Epidemiology Training Program at Columbia University and completed his postdoctoral fellowship at the New York State Psychiatric Institute.

KOL Biography

Brian Kirkpatrick, MD, MSPH

Professor, Psychiatric Research Institute, University of Arkansas for Medical Sciences, Arkansas

Brian Kirkpatrick, MD, MSPH, Professor in the University of Arkansas for Medical Sciences (UAMS) Department of Psychiatry, is a nationally and internationally renowned expert on schizophrenia and related disorders, whose pioneering research has advanced many life-changing treatments.

Dr. Kirkpatrick graduated from the University of Texas Medical School at Houston and completed his residency in psychiatry at the University of North Carolina at Chapel Hill (UNC). After residency, he participated in the UNC Robert Wood Johnson Clinical Scholars Program, receiving a Master of Science in Public Health with a concentration in epidemiology. He also completed a fellowship in neuropharmacology at UNC.

Dr. Kirkpatrick joined the Maryland Psychiatric Research Center at the University of Maryland School of Medicine in Catonsville and later served as vice chair of psychiatry at the Medical College of Georgia. He subsequently served as chair of the Department of Psychiatry at Scott & White Hospital and the Texas A&M School of Medicine, and the Department of Psychiatry and Behavioral Sciences at the University of Nevada, Reno School of Medicine. He joined the UAMS Department of Psychiatry in 2022.

Throughout his career, Dr. Kirkpatrick has focused on schizophrenia and related disorders. He co-chaired the Consensus Development Conference on Negative Symptoms sponsored by the National Institute of Mental Health (NIMH). He has received competitive funding from NIMH, the National Institute of Diabetes and Digestive and Kidney Diseases, the Brain and Behavior Research Foundation, and the Scottish Rite Foundation. He served as an associate editor of Clinical Schizophrenia and Related Psychoses and is on the editorial board of Schizophrenia Bulletin.

Brilaroxazine Phase 3 Study (RECOVER)
Review of Efficacy Results

Dr. Mark Opler, PhD, MPH

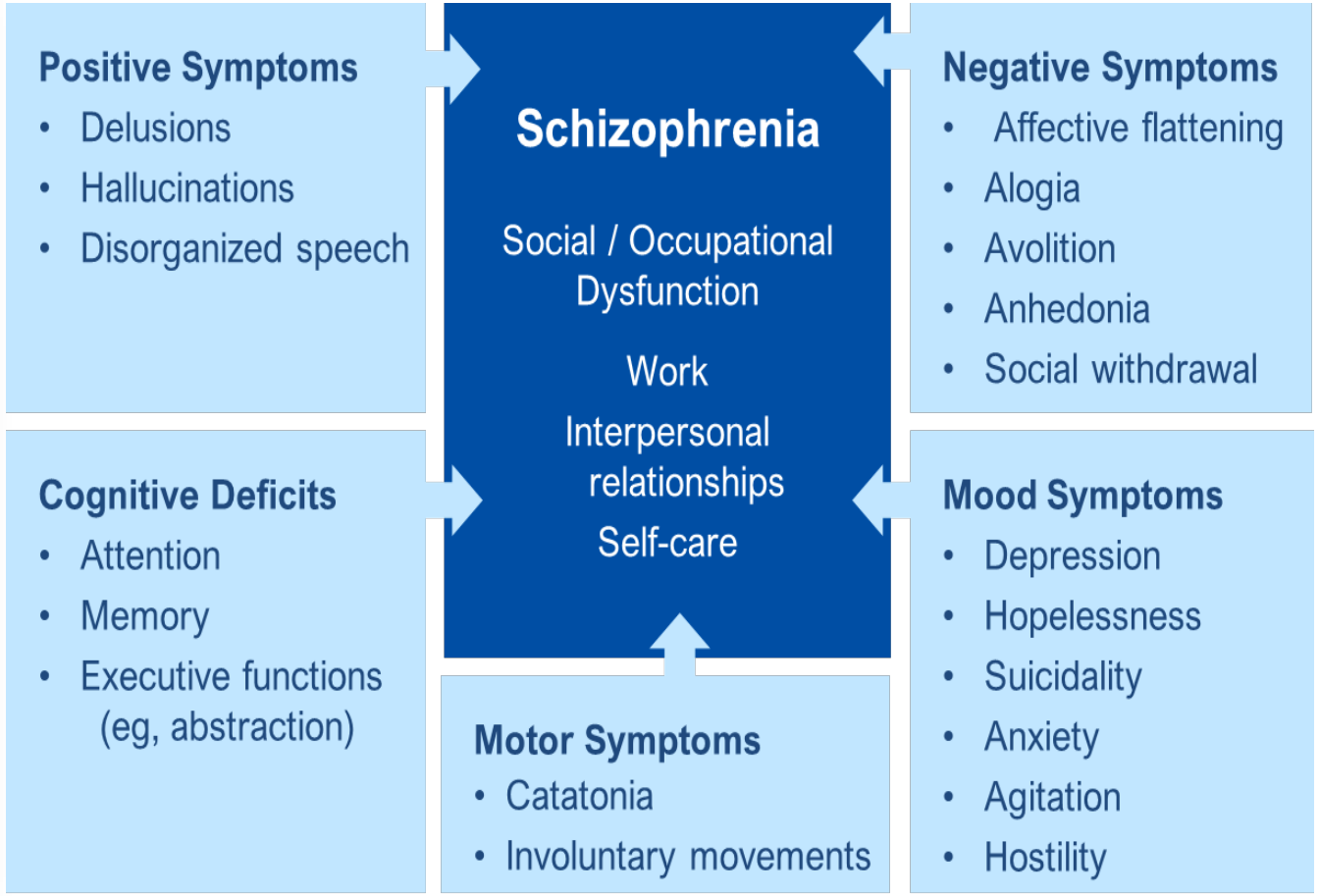
Chief research Officer at WCG Inc and Executive Director at the PANSS Institute

Dr. Opler has served as a faculty member in the Departments of Psychiatry and Environmental Medicine at New York University School of Medicine and in the Department of Neuroscience at Columbia University, College of Physicians and Surgeons.

Schizophrenia: Common Psychiatric Condition With Multiple Symptom Domains

Most patients need lifelong treatment

- 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

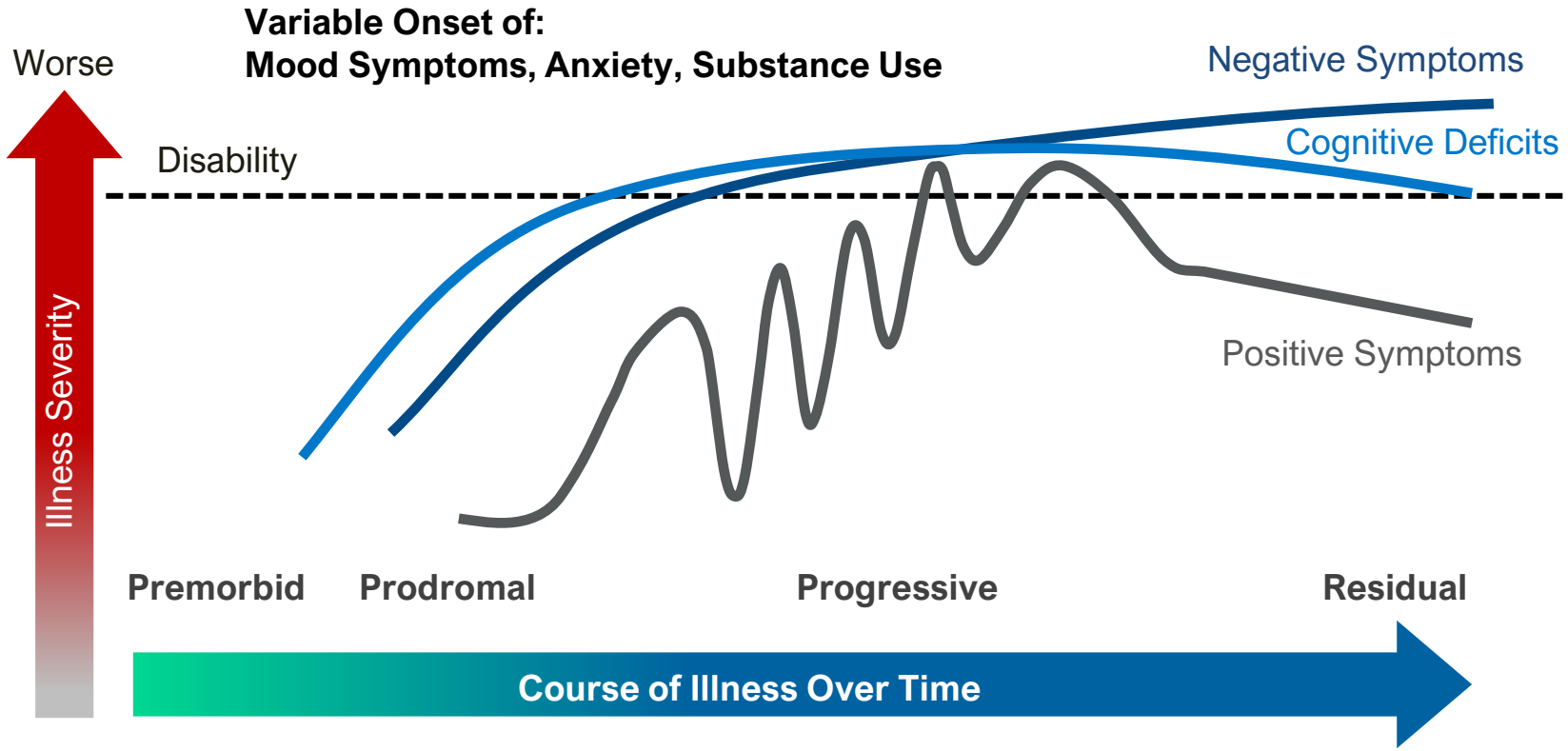


Source: https://www.mentalhelp.net/schizophrenia/statistics/; https://www.who.int/news-room/fact-sheets/detail/mental-disorders; https://fherehab.com/schizophrenia/statistics; https://www.nimh.nih.gov/health/statistics/schizophrenia; Kane JM et al. J Clin Psychology 2019, 80(2):18com12123..

Clinical Features Of Schizophrenia Demonstrate Illness Complexity and Multiple Symptom Domains

Cognitive deficits and “lack of insight” are common, and the person is unaware or in denial that he has the illness, which can make treatment and adherence to health care much more challenging!

- Varying symptoms among patients longitudinally:
- Chronicity and time course
- Multiple neural circuits, receptors/transmitters implicated
- Recent focus on immune and inflammatory processes across psychiatric and neurologic disorders

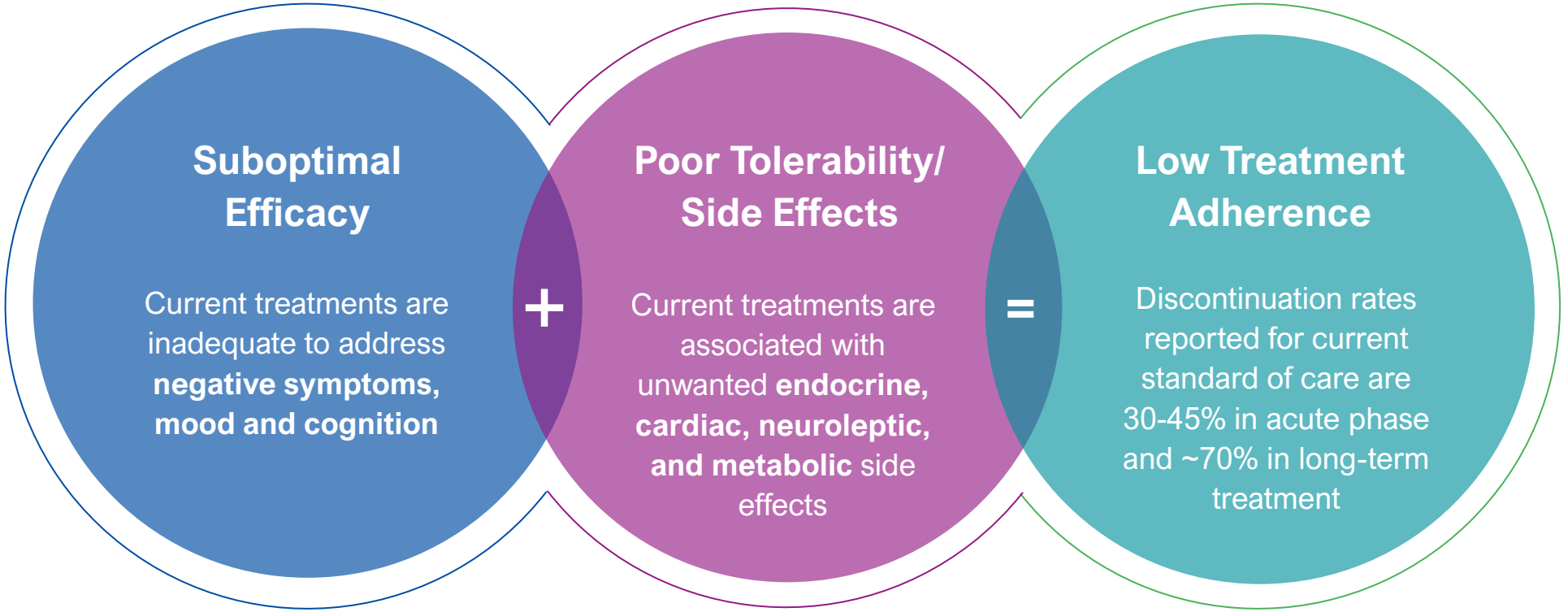


Adapted from: Correll CU. J Clin Psychiatry. 2013;74(2):e04; link

Correll CU. J Clin Psychiatry. 2013;74(2):e04; Maguire GA. Am J Health Syst Pharm. 2002;59(17 Suppl 5):S4-S11; Lasminarayan Bhat et. al. Medical Research Archives. 2023 (accepted and in press);

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



Critical unmet needs in the treatment of schizophrenia are negative symptoms and non-adherence to treatment

Source: Bhat L, et al. Medical Research Archives 2023, 11(4):3834. Guo J et al. Schizophrenia 2023, 9:31. Stroup T S and Gray N, World Psychiatry 2018, 17:341-356; Kikkert MJ et al. prim Care Companion CNS Disord 2017, 19(6):17n02182. Levin, S.Z. et al., Schizophrenia Research 2015, 164:122-126; Acosta FJ et al. World Journal of Psychiatry 2012, 2(5):74

Schizophrenia: Clinical Evaluation

Scales and tools for evaluating brilaroxazine treatment effects in RECOVER-1 trial for schizophrenia

- **PANSS:** Positive and Negative Syndrome Scale (Kay, Opler, et al.), gold-standard outcome for antipsychotic efficacy, used in multinational clinical trials for >30 years.
  - *PANSS Total score:* Accepted primary endpoint by regulatory agencies with demonstrated reliability and validity across languages and cultural contexts as overall measure of disease severity.
  - *PANSS Positive Factor:* Hallucinations, delusions, and related features of psychosis.
  - *PANSS Negative & Social Cognition Factors:* Measures of social & emotional functioning.
  - *PANSS Positive & Agitation Factor:* Acute symptoms of excitement and hostility
- **PSP:** Personal and Social Performance Scale (PSP) evaluates interpersonal, daily functioning, and quality of life, critical domains for patients with schizophrenia working towards recovery.
- **CGI:** Clinical Global Impressions Scale is a standardized tool to summarize global patient status.

Maintaining Data Quality. RECOVER used state-of-the-art methods developed by WCG Inc., similar to those used in other clinical development programs which have led to regulatory approval to help ensure accuracy & data quality:

- Clinical rater training and calibration was conducted for all outcome measures.
- Independent review of video-recorded assessments was used to verify PANSS scores and standardize ratings.
- Blinded data analytics were conducted to monitor and reduce potential sources of noise and random error.

Brilaroxazine Phase 3 RECOVER-1 Trial For Schizophrenia

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

Schizophrenia Acute Patients

18 - 65 years of age

DSM-5 diagnosed schizophrenia with a duration ≥ 1 yr and ≤20 yrs

Acute episode of schizophrenia of at least moderate severity by

- Baseline Total PANSS Score of 80-120
- Baseline CGI-S score ≥4

N = 411
Randomized
1:1:1

- **Brilaroxazine, 15mg Once daily, N = 140**
- **Brilaroxazine, 50mg Once daily, N = 134**
- **Placebo Once daily, N = 137**

4-week study

Primary Endpoint

Change from baseline in PANSS total score vs placebo at Week 4

Secondary Endpoints

- CGI-S
- PANSS Positive
- PANSS Negative
- PANSS Negative Marder Factor
- PANSS Social Cognition Factor
- PANSS Excitement/Agitation
- Personal & Social Performance

For details see: www.clinicaltrials.gov (search key word, RP5063); PANSS: Positive and Negative Syndrome Scale; CGI-S: Clinical global impression – severity scale

RECOVER-1 Trial Demographics And Baseline Characteristics

Balanced randomization with diverse representation of 411 patients; USA 245 (60%), India 140 (34%), Bulgaria 26 (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)

PANSS: Positive and Negative Syndrome Scale

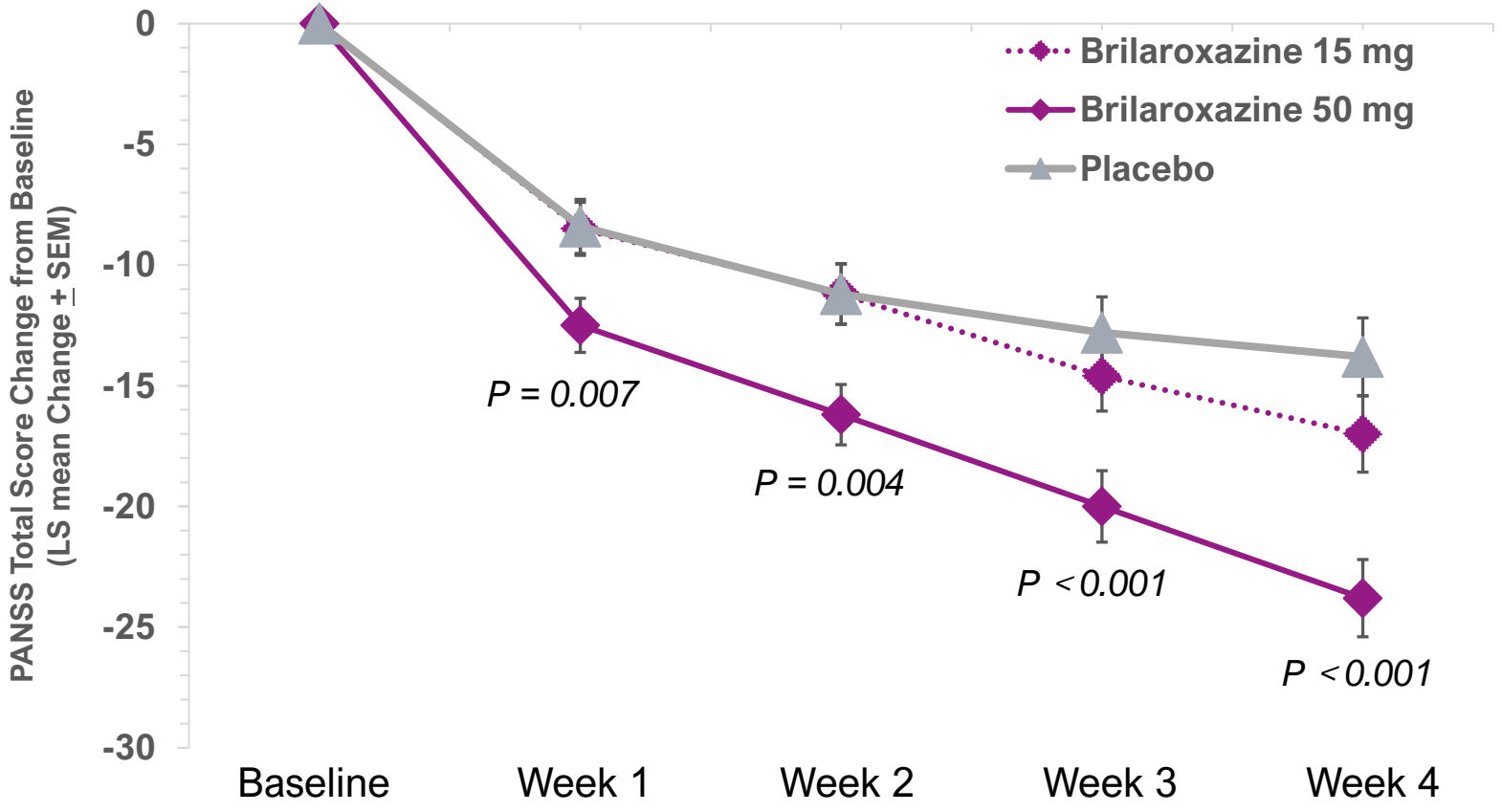
RECOVER-1 Trial Primary Endpoint: PANSS Total Score

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)

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
- No significant difference in treatment effect between the US and ex-US patients

Cohen's d effect size of 0.6



PANSS: Positive and Negative Syndrome Scale

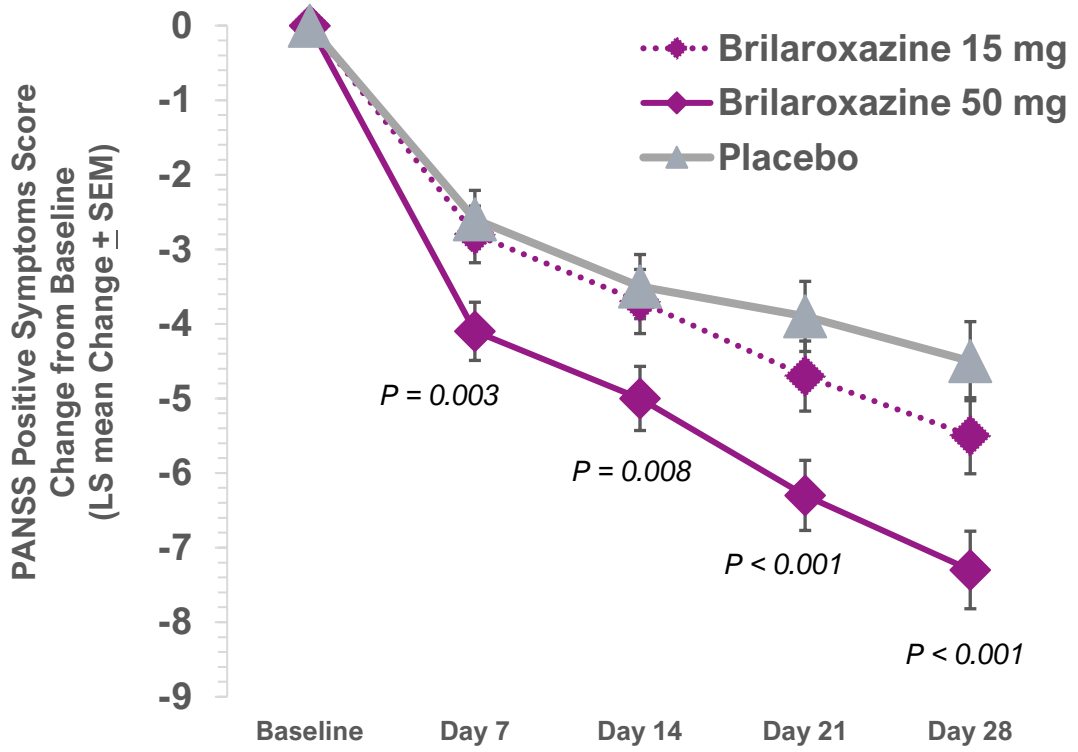
Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

Efficacy Secondary Endpoints: Positive Symptoms and Agitation/Excitement

RECOVER-1: Significant decrease in positive symptoms & agitation/excitement in brilaroxazine 50 mg vs. placebo at week 4

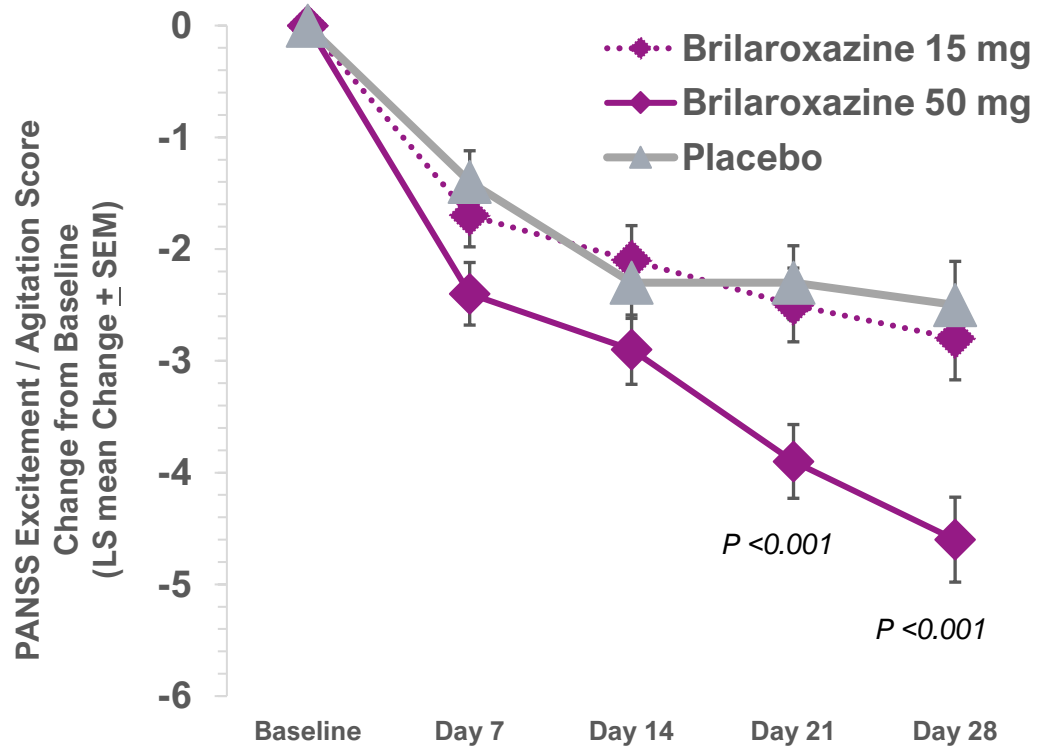
Decrease in Positive Symptoms

Cohen's d effect size of 0.5



Decrease in Agitation/Excitement Symptoms

Cohen's d effect size of 0.5



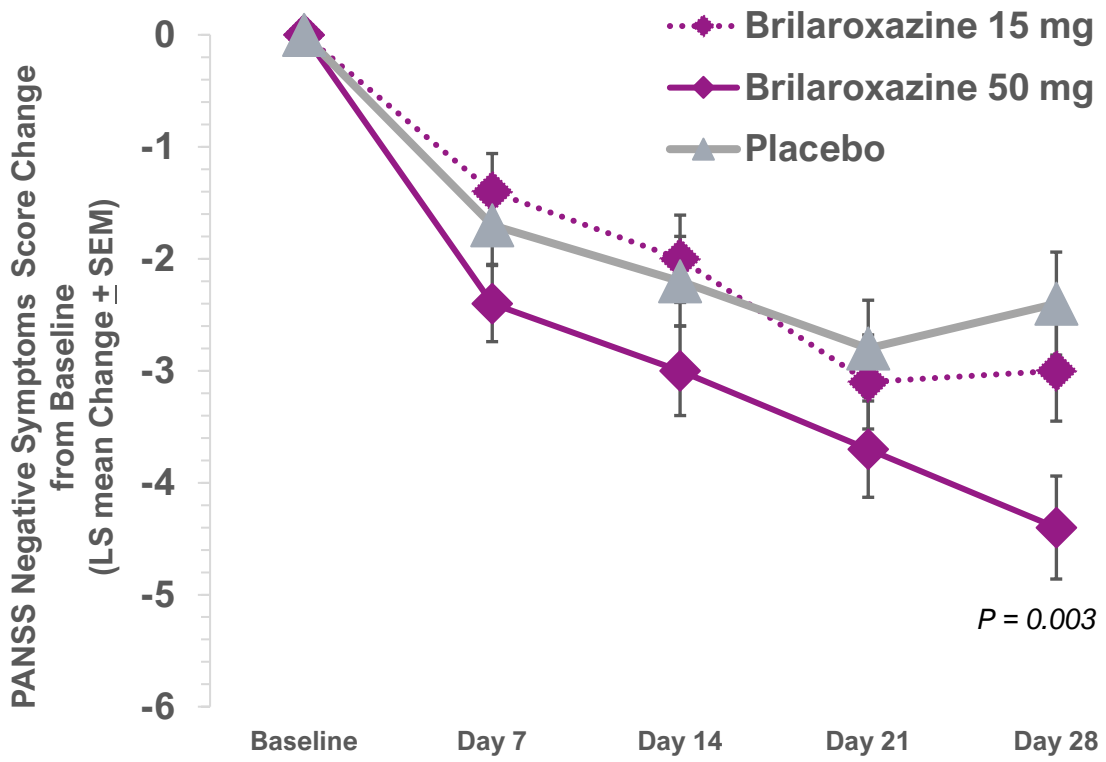
Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

Efficacy Secondary Endpoint: Negative Symptoms

RECOVER-1: Significant decrease in negative symptoms in brilaroxazine 50 mg vs. placebo at week 4

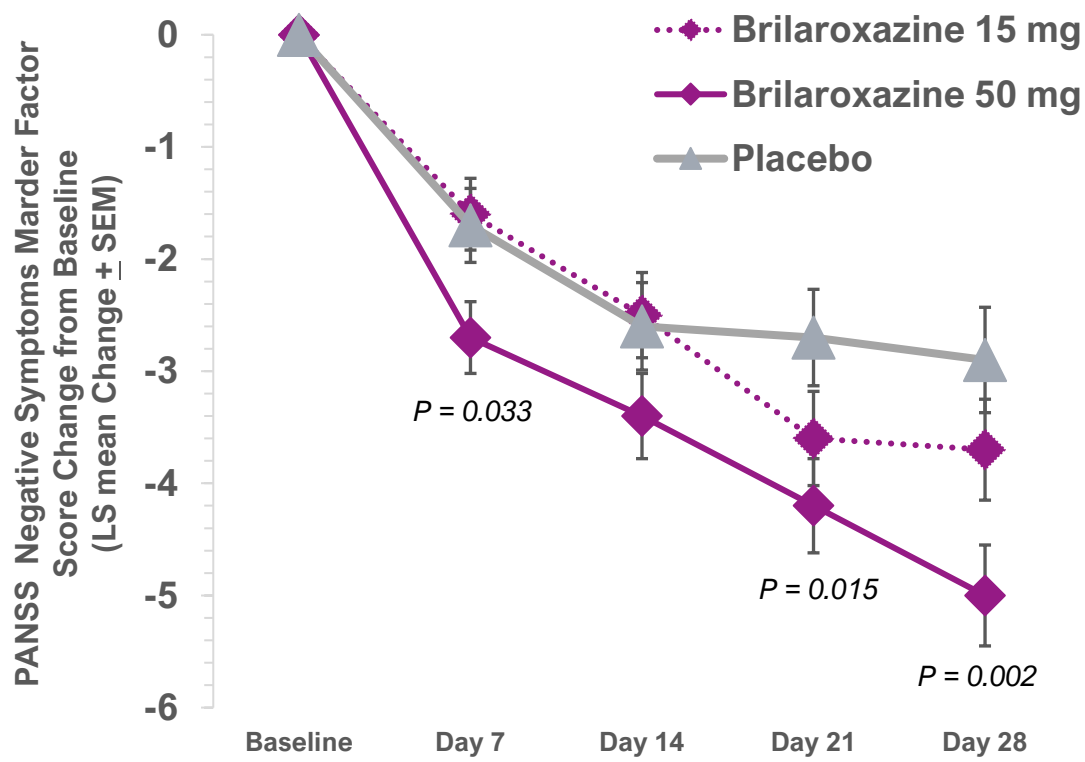
Decrease in Negative Symptoms

Cohen's d effect size of 0.4



Decrease in Negative Symptoms (Marder Factor)

Cohen's d effect size of 0.4



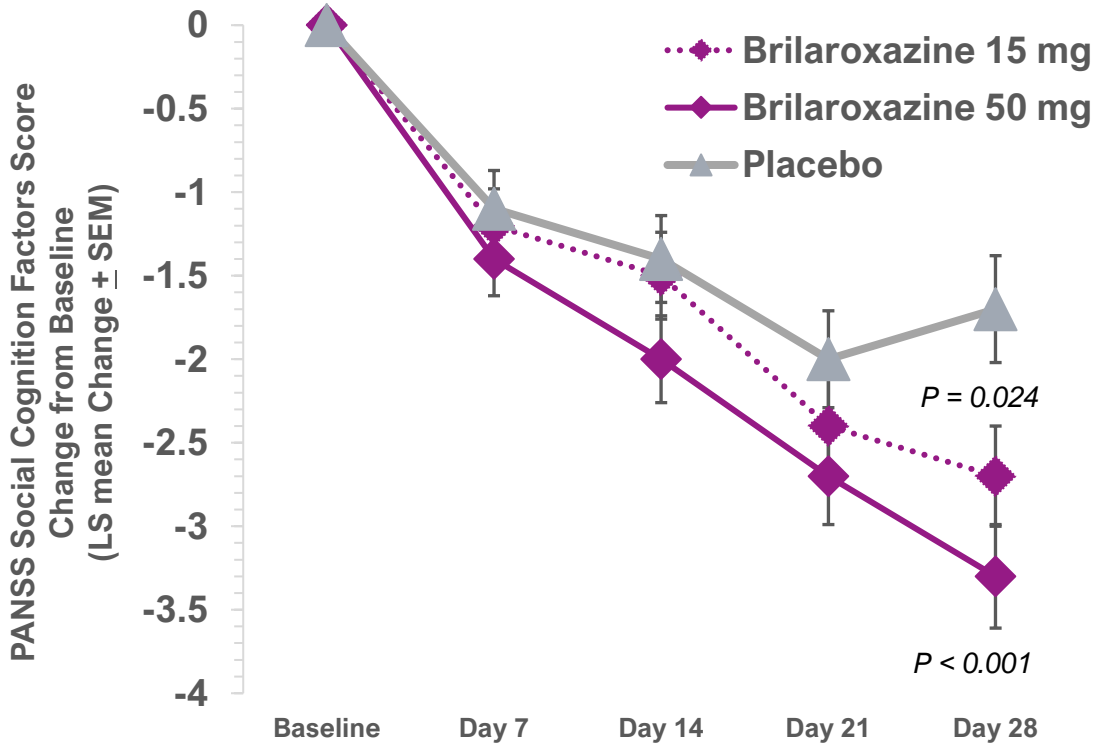
Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

Efficacy Secondary Endpoints: Social Cognition and Social Functioning

RECOVER-1; Significant decrease in social cognition deficits and improvement in personal & social performance

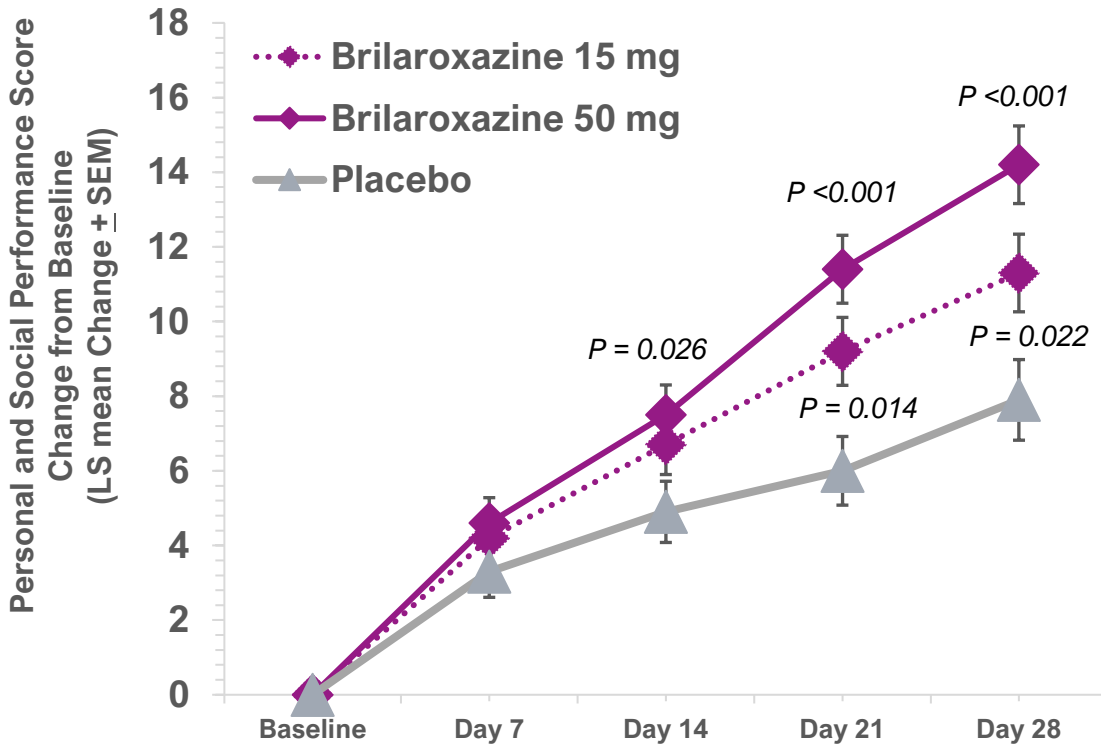
Decrease in Social Cognition Deficits

Cohen's d effect size of 0.5



Improvement in Personal & Social Performance

Cohen's d effect size of 0.5



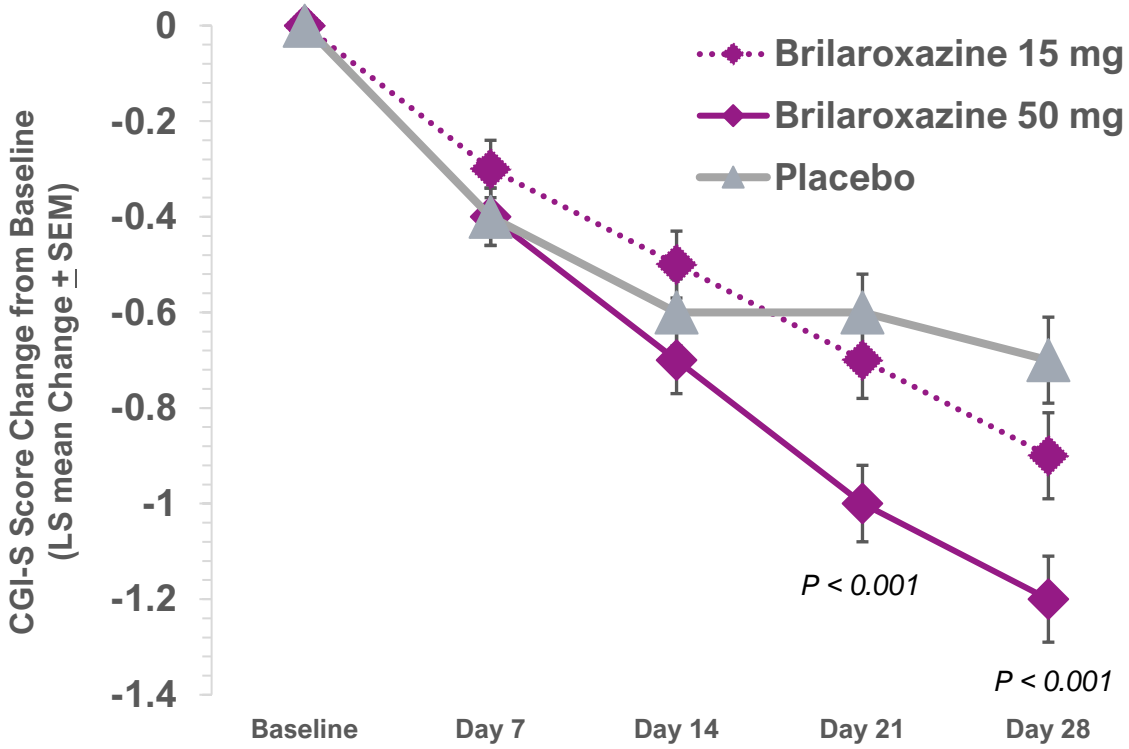
Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

Efficacy Secondary Endpoint: CGI-S Scores

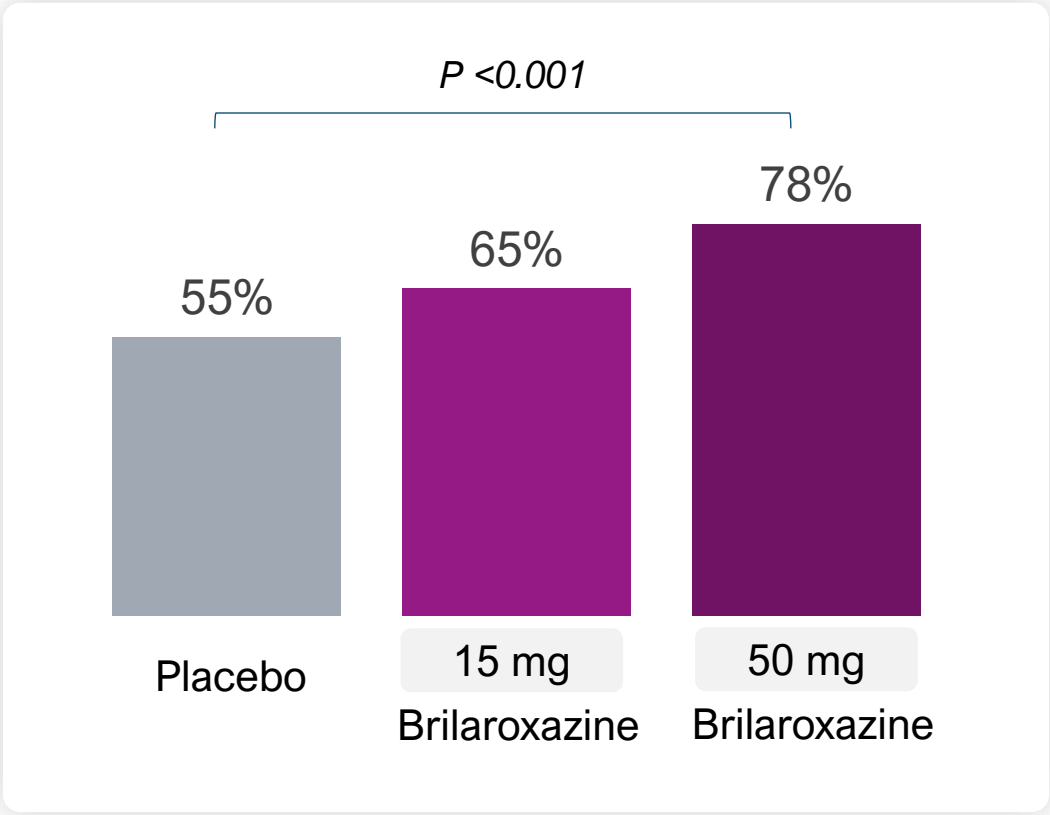
RECOVER-1: ≥1-Point reduction in CGI-S score in brilaroxazine 50 mg vs. placebo at week 4, p < 0.001

CGI-S Score ≥ 1-Point Reduction

Cohen's d effect size of 0.5



Proportion of Subjects with ≥ 1-Point Reduction



CGI-S: Clinical global impression – severity scale

Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

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	6.1	*0.5*	*< 0.001* ✓
CGI-S score	≥1	*0.5*	*< 0.001* ✓

PANSS: Positive and Negative Syndrome Scale; CGI-S: Clinical global impression – severity scale

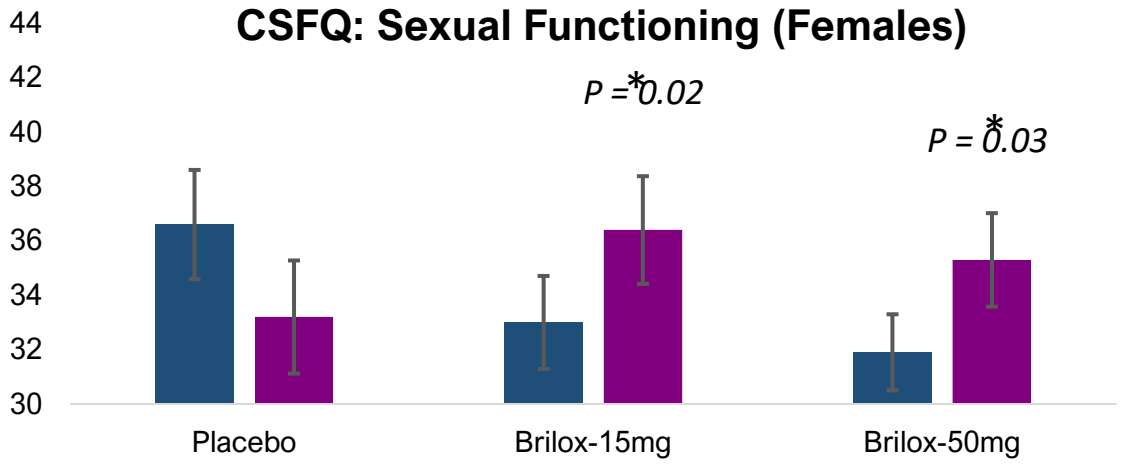
Surrogate Outcome Efficacy & Safety: CSFQ Score Changes for Sexual Functioning

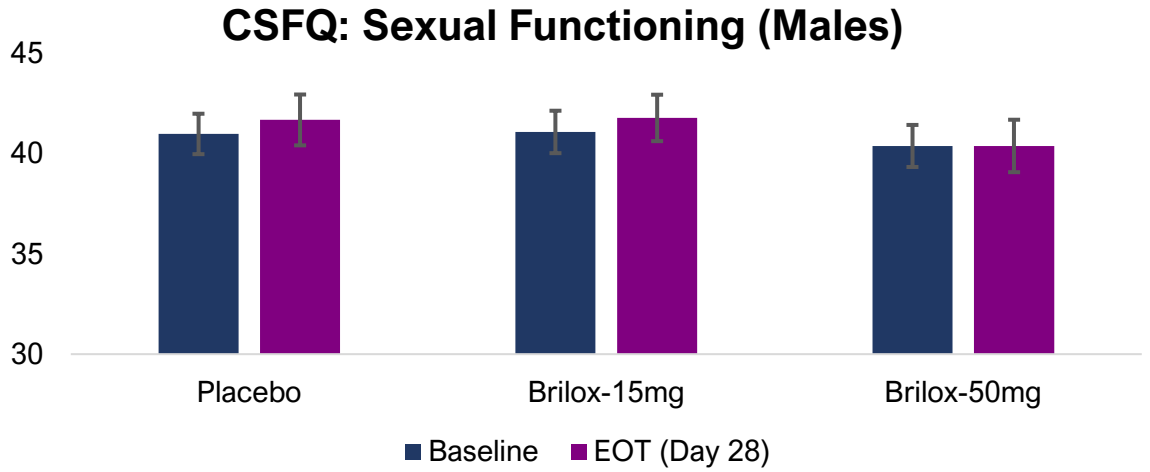
RECOVER-1: Significant Improvement in sexual functioning with Brilaroxazine vs Placebo (Females)

Sexual Functioning

- Brilaroxazine (15 and 50 mg) significantly improved sexual functioning in females and comparable to placebo.

- CSFQ scores ≤41 for females and ≤47 for males indicate sexual dysfunction
- Prevalence of sexual dysfunction in women 60% and men 55% men with schizophrenia
- Sexual dysfunction linked to negative symptoms, social cognition and social functioning
- Sexual dysfunction impacts quality of life, treatment adherence, and may develop depression and suicidality
- Hyperprolactinemia and hypothyroidism in schizophrenia linked sexual dysfunction





CSFQ: Change in Sexual Functioning Questionnaire; Anita H et al. Handbook of sexualy-related measures, 2010, page 290; Edinoff AN et al. Psychiatry Intnl 2022, 3:29-42; Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

Efficacy & Safety Biomarker: Change in Prolactin Hormone

RECOVER-1: Clinically significant decrease in prolactin hormone levels in brilaroxazine (15 and 50mg) vs placebo

Decrease in Prolactin

- Clinically significant decrease in prolactin levels on Day 14 and Day 28 in brilaroxazine (15 and 50 mg) vs placebo

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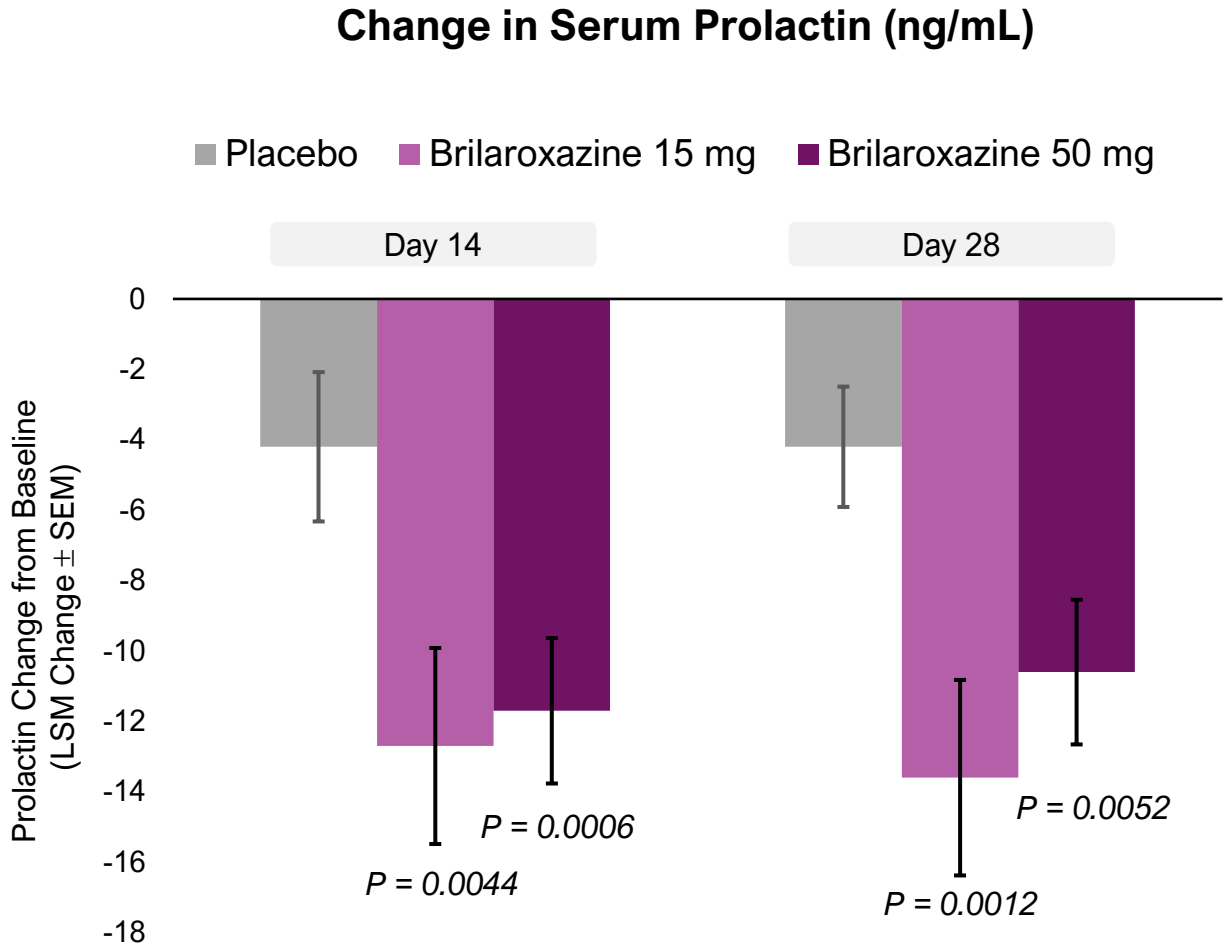
- Hyperprolactinemia is common condition in patients with schizophrenia / psychiatric disorders
- Hyperprolactinemia is associated with immune disorders / diseases and believed to play crucial role in their pathogenesis
- Hyperprolactinemia is associated with variety of adverse effects: weight gain, breast tenderness and enlargement, sexual dysfunction (lack of libido), and erectile dysfunction in men.



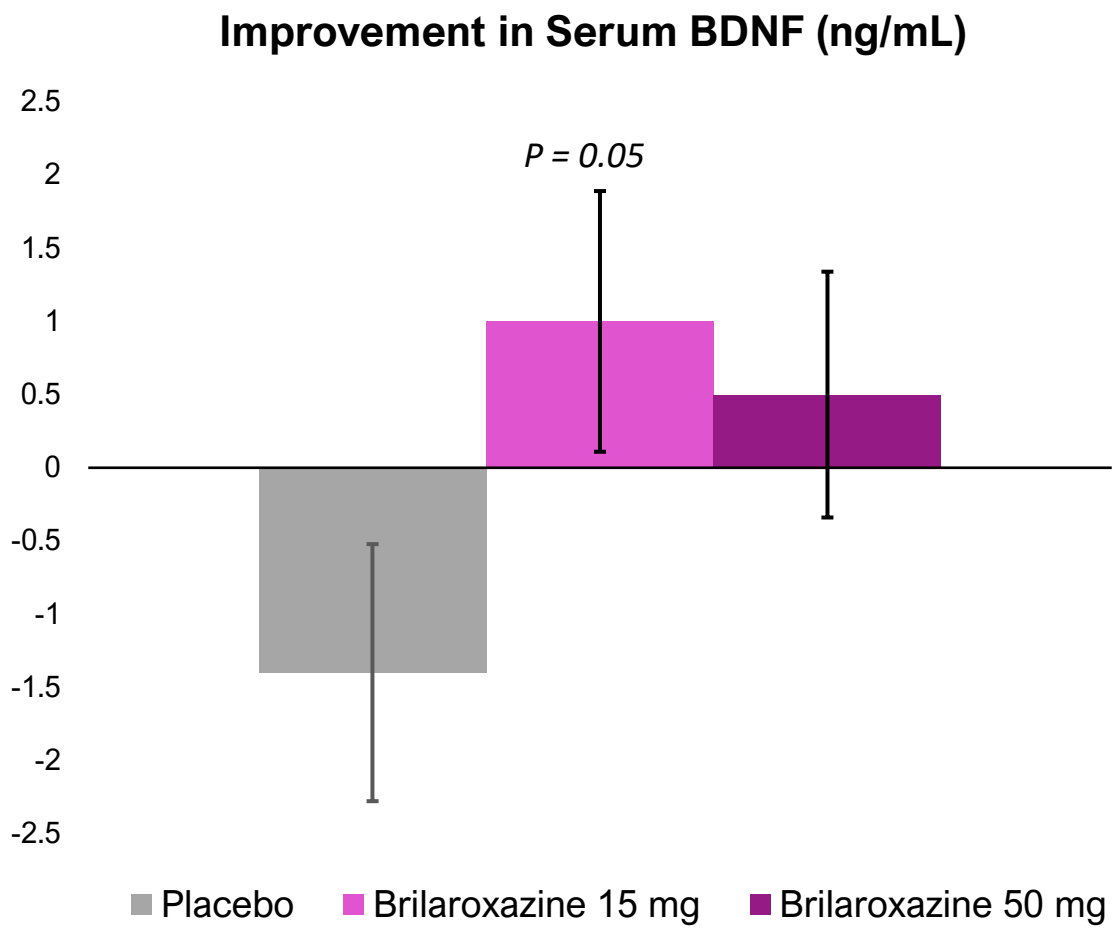
Efficacy Biomarker: Change in Brain-Derived Neurotropic Factor (BDNF)

RECOVER-1: Clinically significant improvement in BDNF levels with Brilaroxazine 15 mg vs Placebo

BDNF Improvement

- Brilaroxazine improved BDNF compared to placebo, 15mg dose showed significant improvement.

- Reduced levels of BDNF reported in schizophrenia and depression patients
- BDNF is linked to negative symptoms and cognitive / memory impairments in schizophrenia
- BDNF is linked with neuroinflammation
- Improvement in BDNF levels reported to decrease proinflammatory cytokine levels (e.g. IL-6, IL-8 etc) in schizophrenia and depression patients

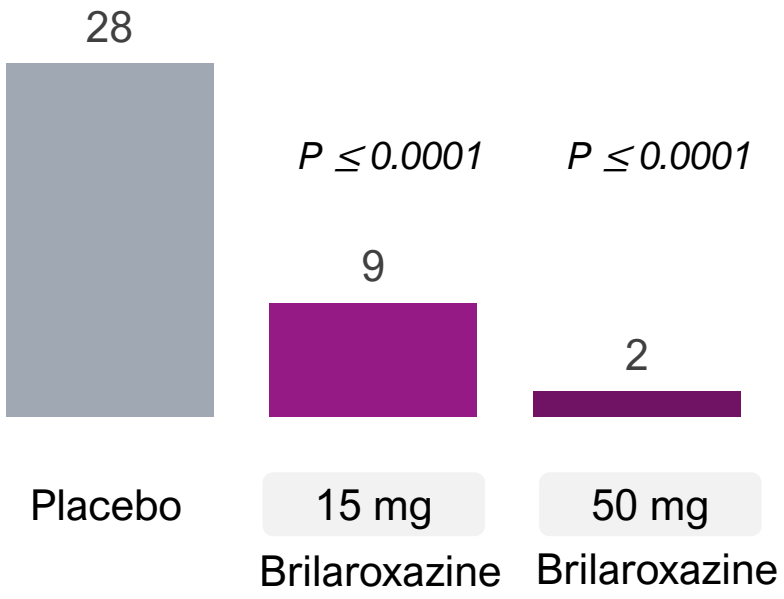


BDNF: Brain Derived Neurotrophic Factor. Nieto RR et al. Front Psychiatry 2021, 12: 662407; Xu H et al. Psychoneuroendocrinology 2019, 125:105121. Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

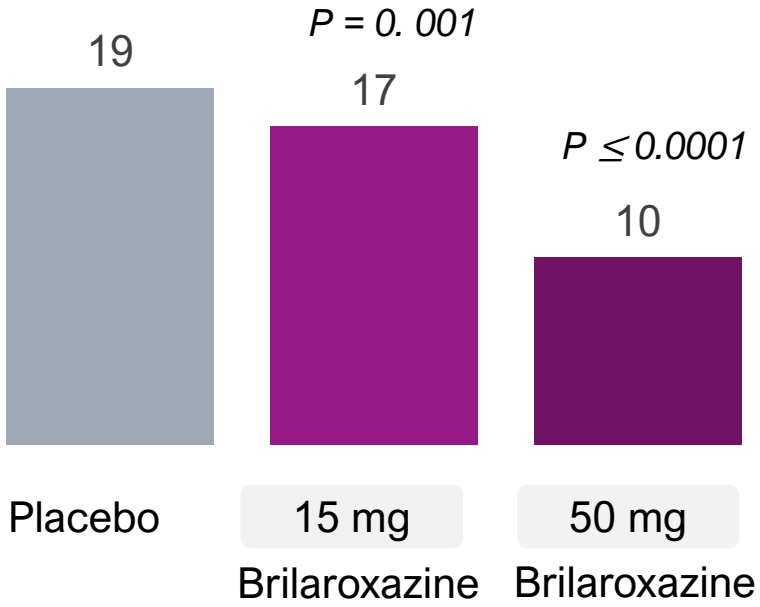
Efficacy & Safety Biomarkers: Change in Serum Cytokines & Chemokines

RECOVER-1: Clinically significant decrease in cytokine IL-8 and chemokine MIP-1 in Brilaroxazine vs Placebo

Decrease in Proinflammatory Cytokine IL-8 (ng/mL)



Change in Proinflammatory Chemokine MIP-1 (ng/mL)



Elevated IL-8 levels have been reported in psychiatric diseases, particularly in schizophrenia, bipolar disorder, obstructive sleep apnea and autism spectrum disorder
(Tasi S-J. Prog Neuropsychopharmacol Biol Psychiatry 2021)

Elevated level of MIP-1 found in schizophrenia, depression and Alzheimer's patients

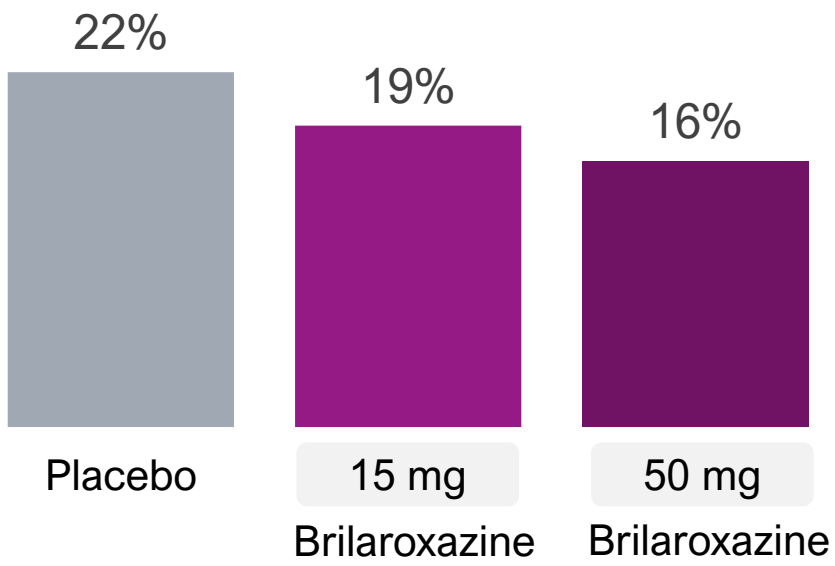
(Frydecka D et al. Brain Behavior and immunity 2018,; Hong S et al Schizophrenia Res 2016)

Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

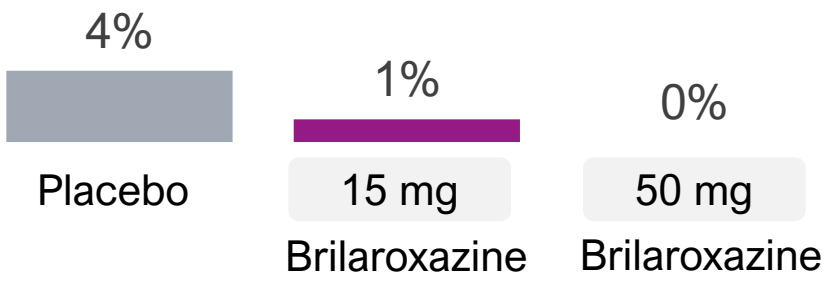
Surrogate Efficacy & Safety Outcome: Treatment Adherence

RECOVER-1: Discontinuation rates in brilaroxazine treatment groups lower than placebo

Discontinuation Rate



Discontinuation Due to Side Effects



Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

Brilaroxazine: Consistent Findings in 50 mg Dose in Phase 2 & Phase 3 Studies

Robust efficacy on primary endpoint and key secondary endpoints and low discontinuation rate, lower than placebo

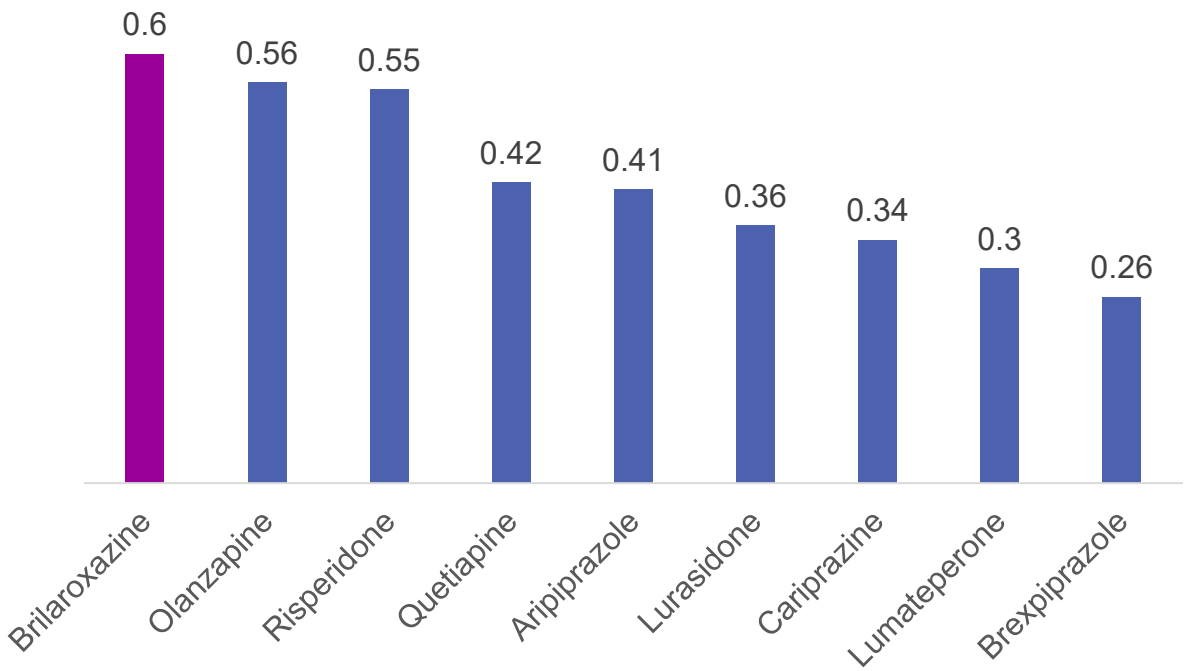
Key Metrics	PHASE 3 RECOVER (N=411 | 4-wk) NCT05184335	PHASE 2 REFRESH (N=234 | 4-wk) NCT01490086
Primary Endpoint (Brilaroxazine 50 mg vs Placebo)		
PANSS Total Score	-10.1 P<0.001 (Effect Size, 0.6)	-10.7 P<0.01
Secondary Endpoint (Brilaroxazine 50 mg vs Placebo)		
PANSS Positive Score	-2.8 P<0.001 (Effect Size, 0.5)	-3.04 P=0.03
PANSS Negative Score	-2.1 P<0.003 (Effect Size, 0.4)	-2.04 P=0.04
CGI-S Score	Improvement ≥ 1, 78% P<0.001 (Effect Size, 0.5)	Improvement ≥ 1, 72% P=0.02
Discontinuation Rate (Brilaroxazine 50 mg vs Placebo)		
Related to any reasons	16% (50mg) vs 22% (placebo)	12% (50mg) vs 28% (placebo)
Related to TEAEs in 50mg	0	1.7% (1-subject)

Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291); Bhat, et al. J Neurol Neuromed 2018, 3(5): 39-50. (3) Cantillon, M. et al. Schizophrenia Research 2017, 189: 126-133

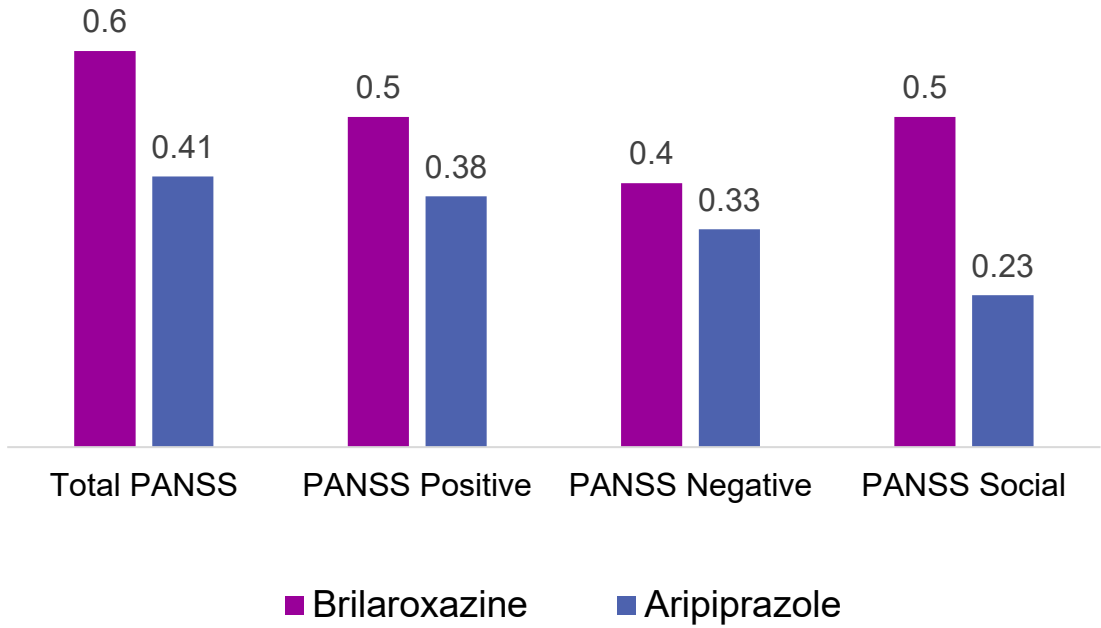
Comparison of Treatment Effect Size from Phase 3 Studies

Primary endpoints and major secondary efficacy endpoints

Brilaroxazine[1] vs Marketed Antipsychotics[2,3]



Brilaroxazine[1] vs Aripiprazole[2]



Source: (1) Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291); (2) Huhn M et al. Lancet 2019, 394:939-951; (3) Correll CU et al. JAMA Psychiatry 2020, 77(4):349-358

RECOVER Trial Conclusions: Treatment Effect for Schizophrenia

Brilaroxazine demonstrates high efficacy across multiple symptom domains with strong treatment adherence

Consistent, Wide-Spectrum Efficacy	Well-Conducted Trial, High-Quality Data	Strong Efficacy/ Side-Effect Ratio	Potential to Significantly Impact Unmet Needs
Brilaroxazine was consistent across multiple domains associated with schizophrenia, from positive and negative symptoms to social functioning and quality of life	Data quality was continuously monitored by WCG Inc., utilizing validated methods to reduce error and placebo response via standardized training & calibration of the PANSS and blinded monitoring of clinician and site performance	Compared to existing marketed drugs, brilaroxazine shows significant wide-spectrum efficacy across primary and secondary endpoints with high levels of treatment adherence	Brilaroxazine may address many unmet needs in both acute and chronic phases of schizophrenia which are critical to functional recovery across the lifespan

Objective Vocal Biomarker Analysis Confirms Significant Impact of Brilaroxazine on Vulnerable Subgroup of Patients with Schizophrenia

Brilaroxazine Phase 3 Study (RECOVER-1)
Vocal Biomarker Results

Brian Kirkpatrick, MD, MSPH
Professor, Psychiatric Research Institute
University of Arkansas for Medical Sciences, Arkansas

What are Negative Symptoms?

A decrease or absence of a normal psychological function, especially those commonly found in schizophrenia

Expressivity

- **Blunted affect**: a decrease in the nonverbal aspects of communication that are used to emphasize or clarify what is being said.
  - Facial expression
  - Vocal expression
  - Body language/expressive gestures
- **Alogia** (poverty of speech): few words spoken little information conveyed

Motivation and Pleasure

- **Avolition**: reduced initiation and persistence in activities, and a reduction in the desire to do so
- **Anhedonia**: a decrease in the frequency and intensity of pleasure, and the expected or anticipated intensity of pleasure from future activities
- **Asociality**: reduced social activity and decreased interest in having close relationships with others

Vocal Biomarkers for Schizophrenia & Negative Symptoms

- Vocal characteristics in persons with schizophrenia have been well documented, studied for decades
- Evaluated using objective, automated methods such as natural language processing (NLP) & acoustic processing, producing highly reliable, objective data

Speech Production: The most potent speech biomarker of negative symptoms (from 2 meta-analyses; Cohen et al., 2014; Parola et al., 2020).

Speech Latency (Turns): Response times to produce speech in response to interview questions

Interviewer: How are you doing today?

Patient: OK, I guess not much going on

An *a priori* hypothesis, based on an extensive literature, that turn latency would be an objective measure of negative symptoms

Larsen et al. 2024, 15:1342835; Parola et al. Schizophrenia Bulletin 2023, 49(2): S125-141; Abbas et al. JMIR Formative Research 2022, 6(1):e26276).

Vocal Biomarker Analysis Methodology for RECOVER-1 Trial Data

Turn latencies tap core schizophrenia pathology

Turn latencies reflect integration of

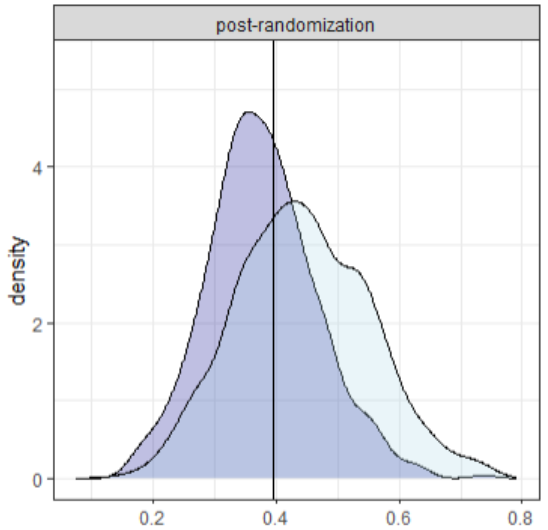
- Cognitive
- Social
- Motivational systems

Turn latencies are scientifically reliable and useful.

- Highly reliable (100+ turn in a session)
- Interpretable (in milliseconds)
- Easy to measure without added testing burden.
- Easy and fast to compute
- Easy to norm for international trials
- Sensitive to change, high temporal resolution as a “state” measure.

Vocal Biomarker Speech Latency Heterogeneity in RECOVER-1 Trial

Speech Latency is highly heterogeneous across patients

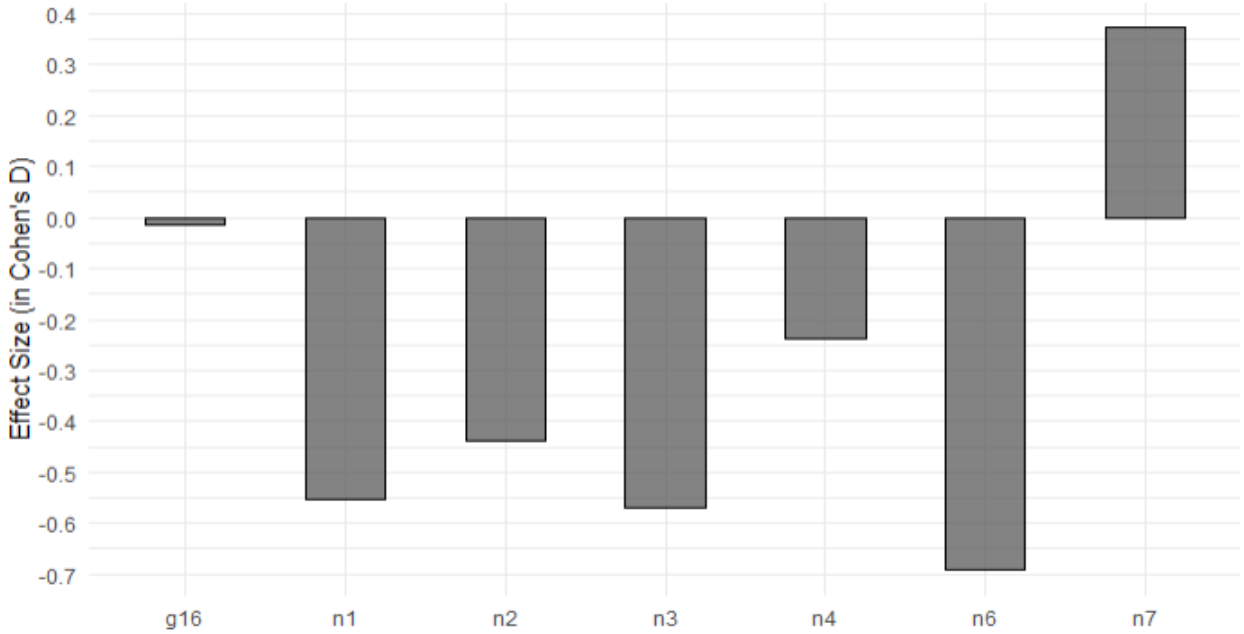


Machine Learning [of post-randomization data] identifies:

- **Vocal Biomarker Positive** (@ baseline, N = 220)
  - Slow responses: 550ms longer [nearly 2 seconds on average]
  - **More severe negative symptoms (d = 0.95)**
  - Slightly Younger (d = 0.57), but similar in sex.
- **Vocal Biomarker Negative** (@ baseline, N = 187)
  - Fast responses [1.4 seconds on average]
  - **More severe positive symptoms (d = 0.31)**

Profile of Vocal Biomarker (VBM) Positive Patients in RECOVER-1 Trial

VBM Positive patients showed a distinct signature in *rater's scores* of negative symptoms at baseline, characterized by more severe blunted affect (N1), emotional withdrawal (N2), poor rapport (N3), social withdrawal (N4), impaired communication (N6) and alogia (N7)



During their screening interviews, VBM-pos patients talked much less & at a slower pace, had shorter interviews with fewer turns, and raters gave them higher negative symptom scores.

Did their treatment responses differ?

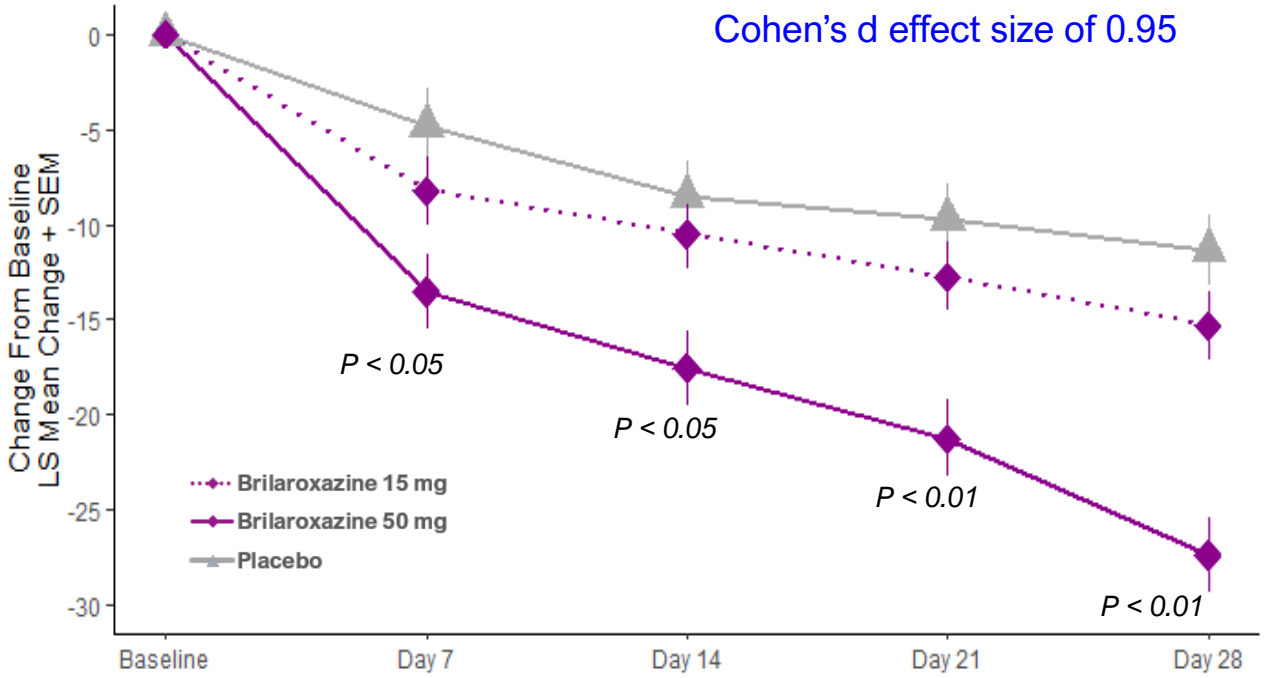
RECOVER-1 Trial Primary Endpoint & Speech Latency Relationship

PANSS Total Score/Speech Latency in Brilaroxazine vs Placebo

VBM/PD = Vocal Biomarker Speech Latency and pharmacodynamic or treatment effect relationship

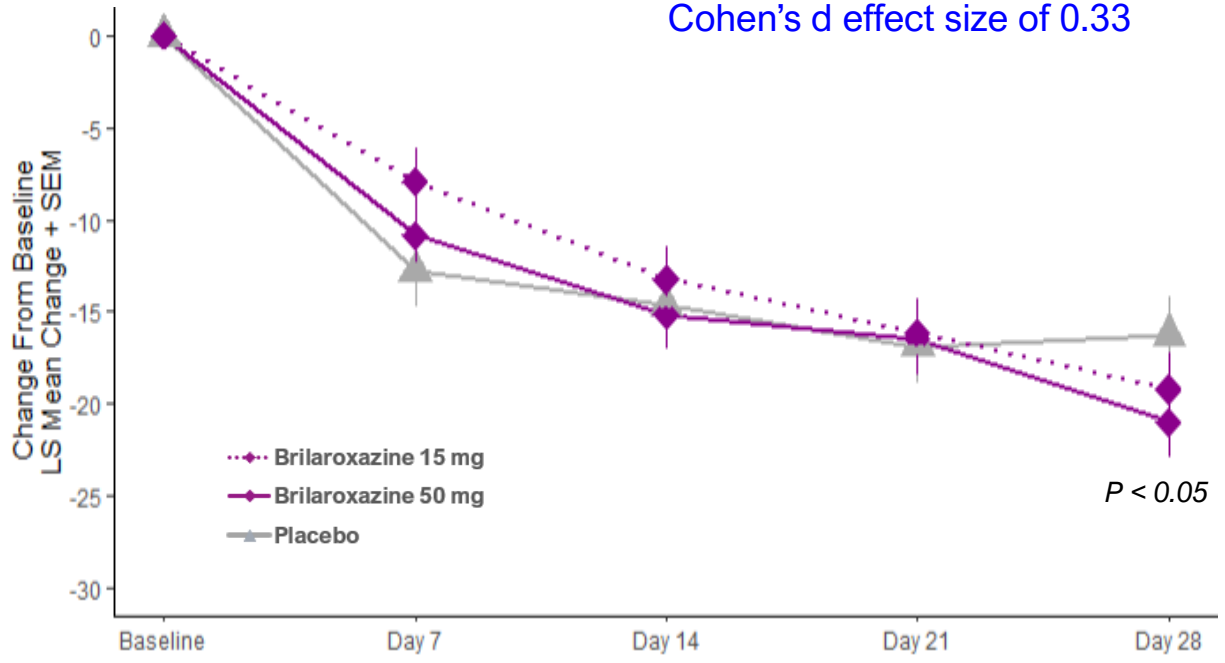
VBM/PANSS Total in VBM Positive Patients

Cohen's d effect size of 0.95



VBM/PANSS Total in VBM Negative Patients

Cohen's d effect size of 0.33



VBM positive patients show significantly greater reduction in PANSS total scores, but both groups had a significant improvement

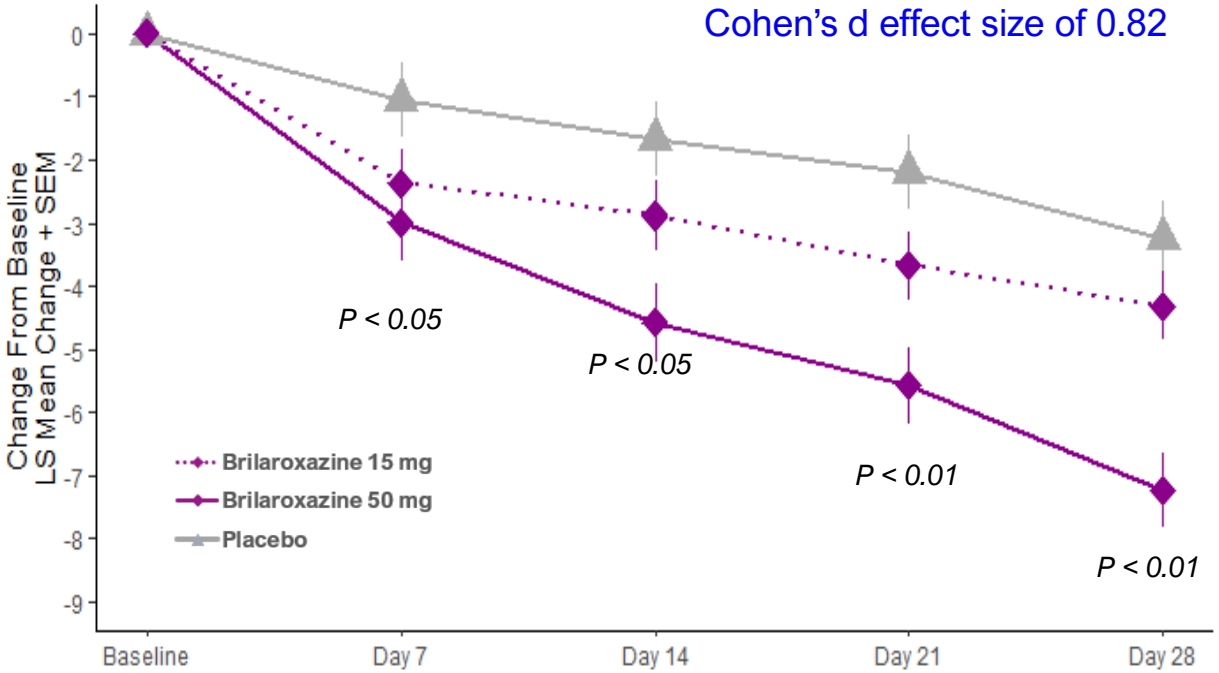
RECOVER-1 Trial Secondary Endpoint & Speech Latency Relationship

PANSS Positive Symptoms /Speech Latency in Brilaroxazine vs Placebo

VBM/PD = Vocal Biomarker Speech Latency and pharmacodynamic or treatment effect relationship

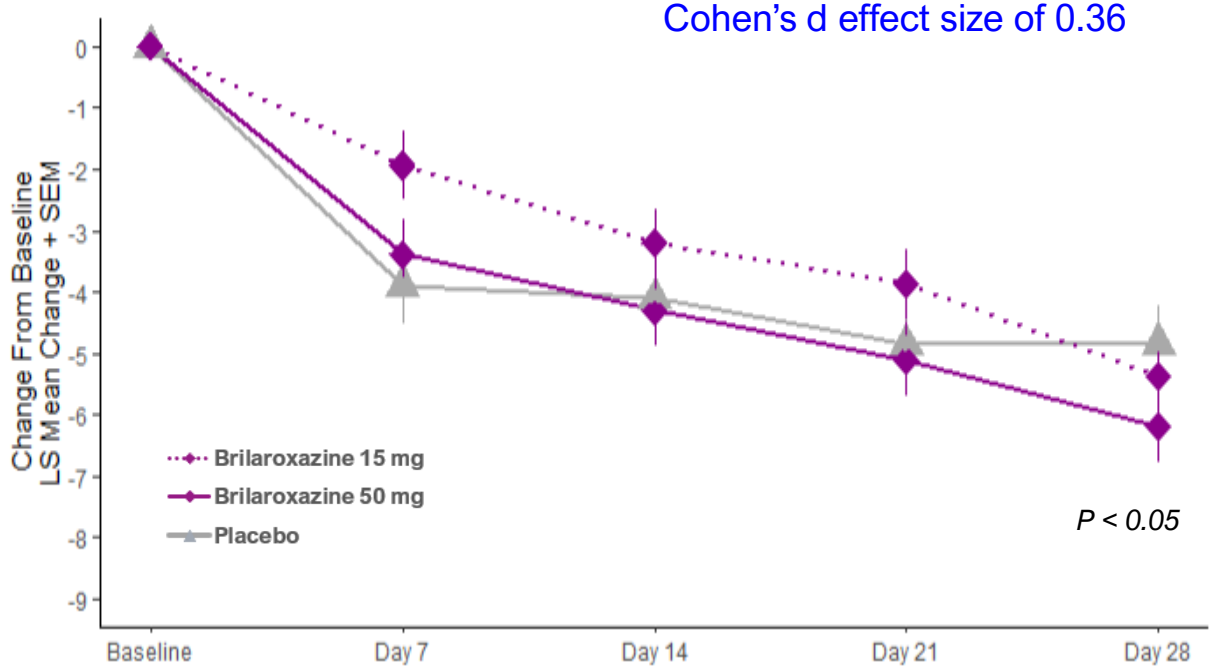
VBM/PANSS Positive in VBM Positive Patients

Cohen's d effect size of 0.82



VBM/PANSS Positive in VBM Negative Patients

Cohen's d effect size of 0.36



VBM positive patients show significantly greater reduction in positive symptoms, but both groups had a significant improvement

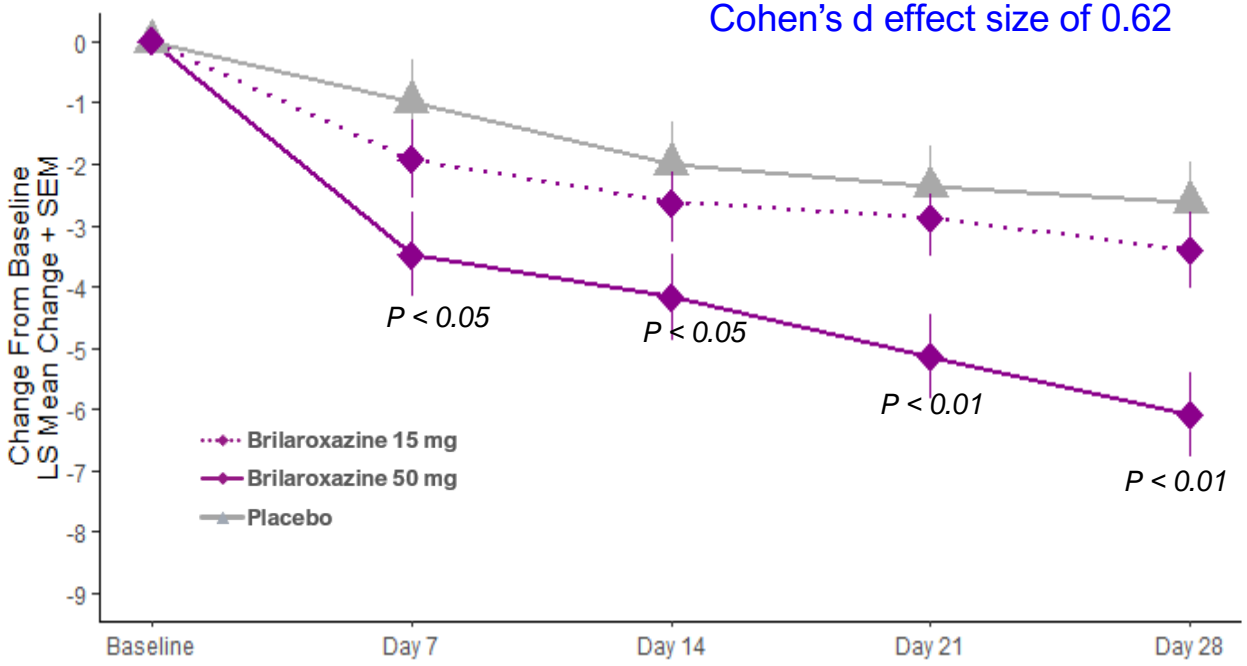
RECOVER-1 Trial Secondary Endpoint & Speech Latency Relationship

PANSS Negative Symptoms (Marder Factor) / Speech Latency in Brilaroxazine vs Placebo

VBM/PD = Vocal Biomarker Speech Latency and pharmacodynamic or treatment effect relationship

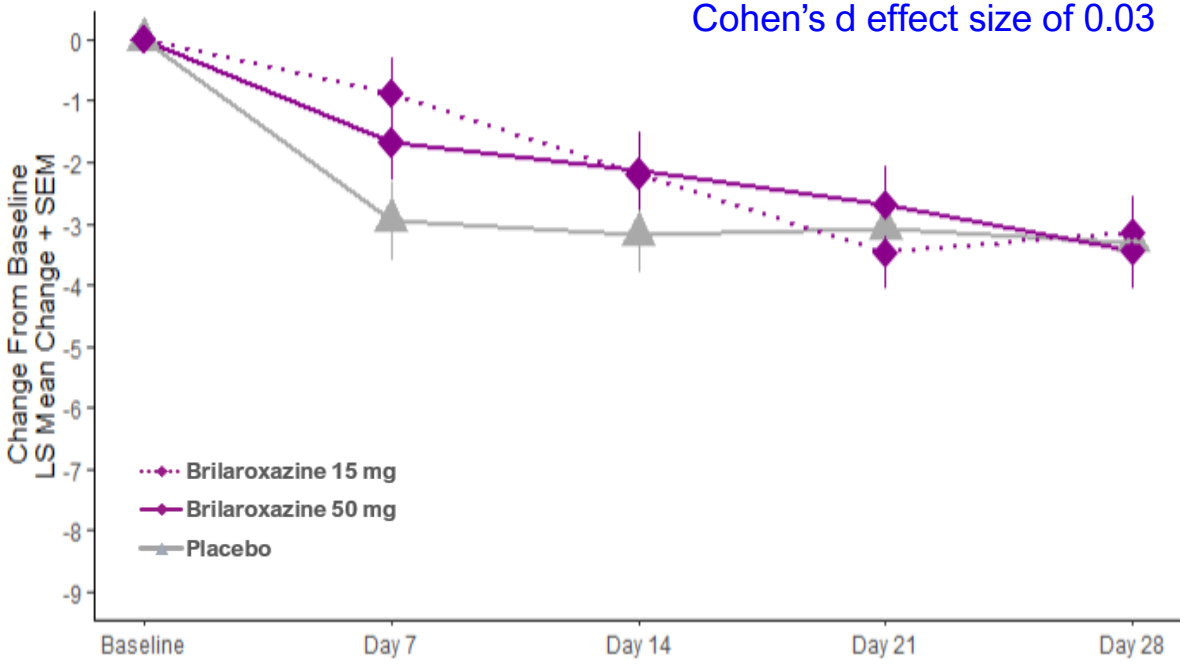
VBM/PANSS Negative in VBM Positive Patients

Cohen's d effect size of 0.62



VBM/PANSS Negative in VBM Negative Patients

Cohen's d effect size of 0.03



VBM positive patients show significantly greater reduction in PANSS negative symptoms

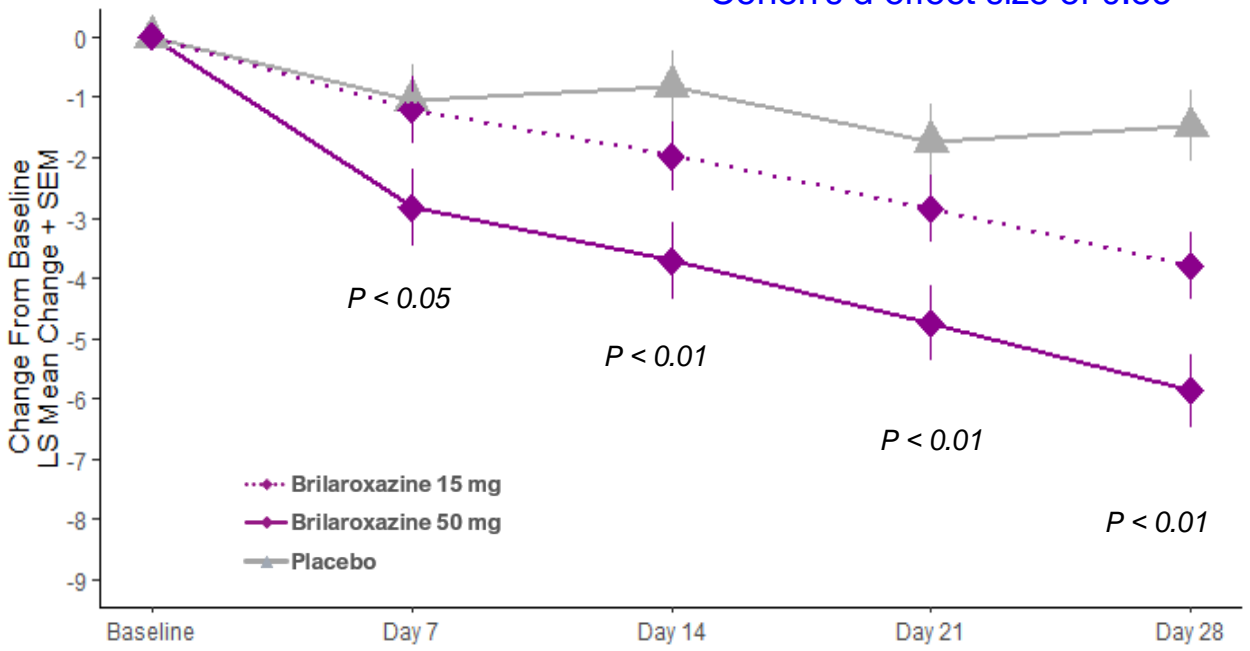
RECOVER-1 Trial Secondary Endpoint & Speech Latency Relationship

PANSS Cognitive (Disorganization) Factor/Speech Latency in Brilaroxazine vs Placebo

VBM/PD = Vocal Biomarker Speech Latency and pharmacodynamic or treatment effect relationship

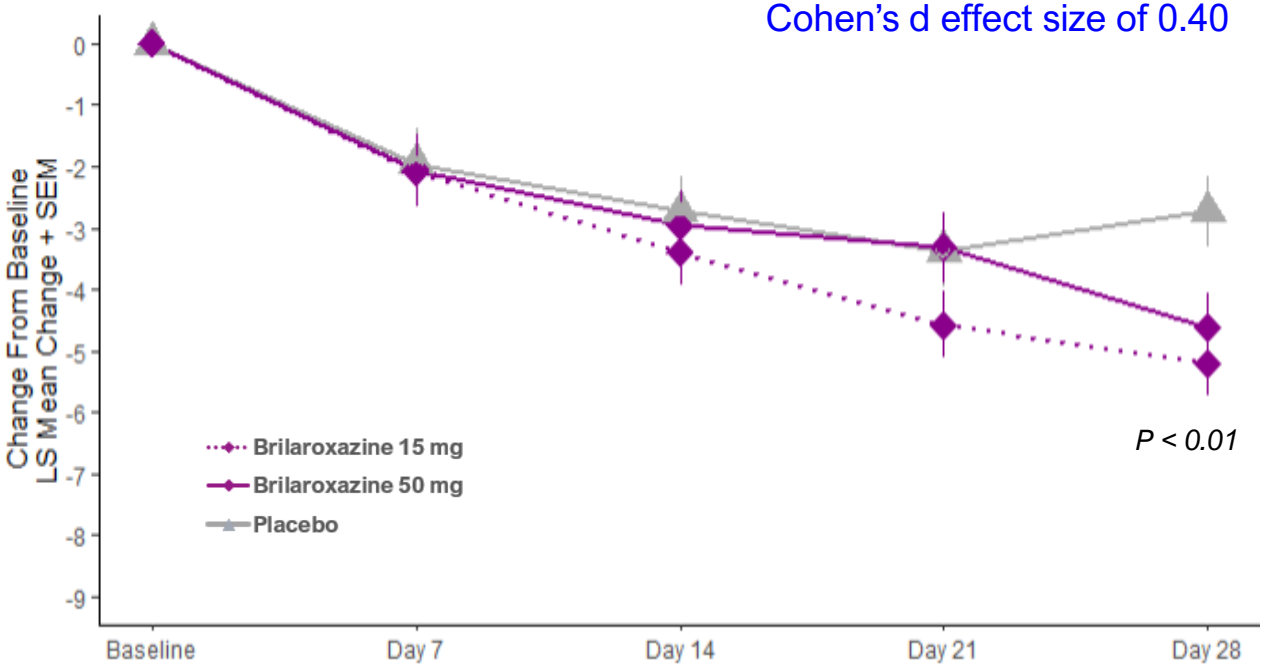
VBM/PANSS Cognition in VBM Positive Patients

Cohen's d effect size of 0.85



VBM/PANSS Cognition in VBM Negative Patients

Cohen's d effect size of 0.40



VBM positive patients show a greater reduction in cognitive/disorganization scores, but both groups had a significant improvement

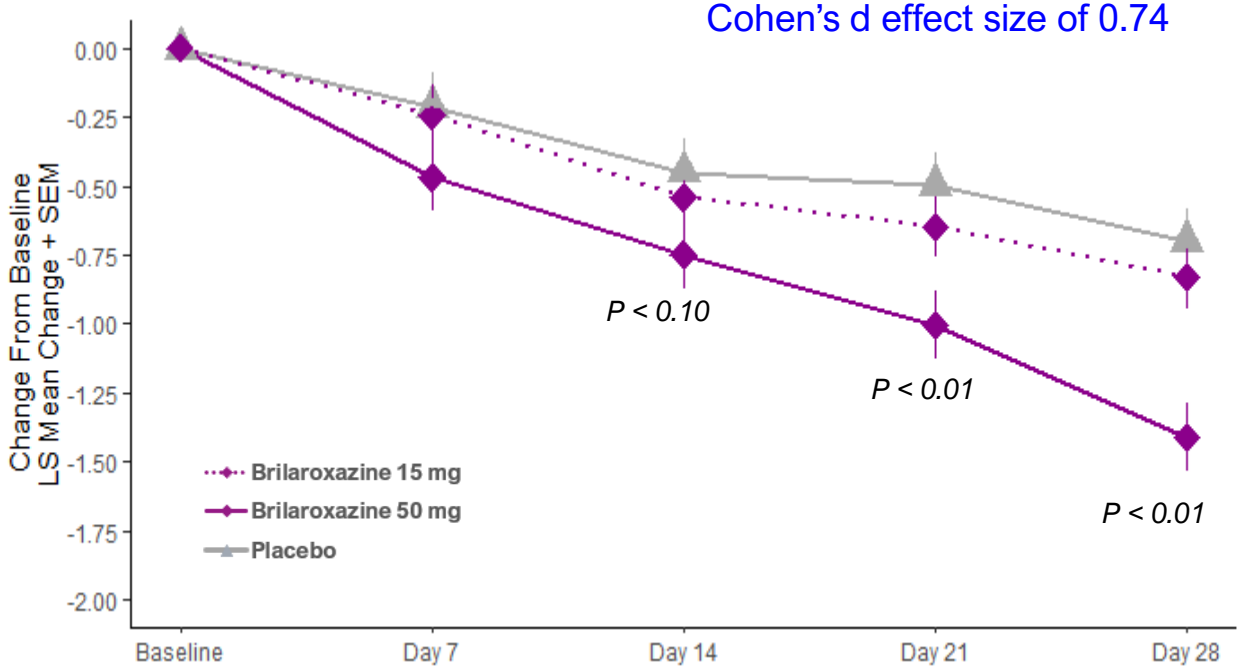
RECOVER-1 Trial Secondary Endpoint & Speech Latency Relationship

CGI-S/ Speech Latency in Brilaroxazine vs Placebo

VBM/PD = Vocal Biomarker Speech Latency and pharmacodynamic or treatment effect relationship

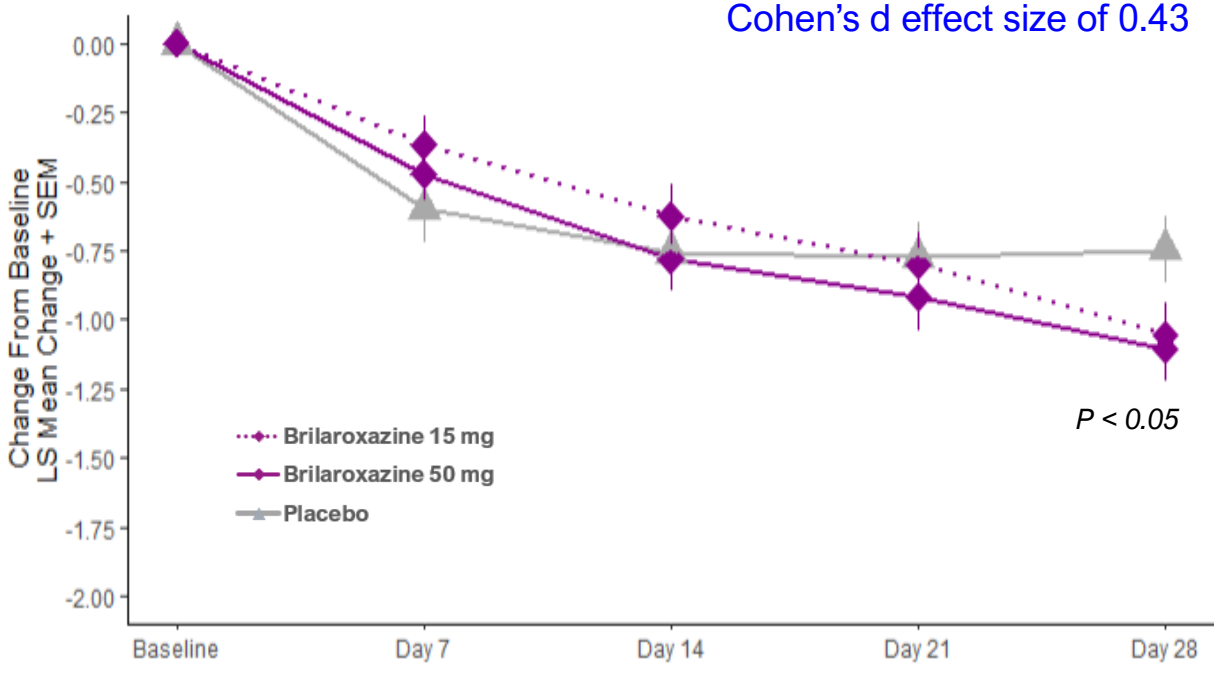
VBM/CGI-S in VBM Positive Patients

Cohen's d effect size of 0.74



VBM/CGI-S in VBM Negative Patients

Cohen's d effect size of 0.43



VBM positive patients show significantly greater reduction in CGI scores, but both groups had a significant improvement

RECOVER-1 Trial Secondary Endpoint & Speech Latency Relationship

Personal and Social Performance (PSP) Subscales / Speech Latency in Brilaroxazine vs Placebo

	Full sample		VBM-pos		VBM-neg	
Outcome measure	**Cohen's D**	**p value <**	**Cohen's D**	**p value <**	**Cohen's D**	**p value <**
PSP Total	0.48	0.05	0.34	NS	***0.62***	***0.05***
Socially useful activities	0.51	0.01	0.30	NS	***0.72***	***0.01***
Personal and social relationships	0.37	0.05	***0.62***	***0.05***	0.18	ns
Self-care	0.54	0.01	***0.77***	***0.01***	0.35	ns
Disturbing & aggressive behavior	0.42	0.05	0.27	ns	***0.57***	***0.05***

Brilaroxazine causes robust improvement in this measure of function in both groups, but in different areas—as these two groups have different symptom profiles

Reviva PHARMACEUTICALS

Speech Latency, a Vocal Biomarker for Schizophrenia/Negative Symptoms

Summary

- Speech turn latency is an *automated*, *objective* measure with an extensive literature in schizophrenia that has
  - a clear, real-world interpretation
  - face validity as a measure of negative symptoms
- In the RECOVER 1 trial, turn latency delineated two groups that differed on the severity of negative and positive symptoms
- In *both vocal biomarker groups*, brilaroxazine had robust efficacy for total PANSS score, positive symptoms, and two measures of function (CGI-S, PSP)
- In the vocal biomarker positive group, which had moderate to severe negative symptoms, brilaroxazine had robust efficacy for negative symptoms
- Turn latency measures and human raters' scale scores cross-validate each other
- Turn latency provides further support for the efficacy of brilaroxazine for both symptoms and function

Brilaroxazine Key Points of Clinical Differentiation

Favorable efficacy, safety and treatment adherence profile in brilaroxazine 50mg vs placebo

Blood Biomarkers

Prolactin hormone

Thyroid T3 hormone

BDNF

Cytokines

IL-8

IL-6

MIP-1

Significant treatment effects on major symptom domains & unmet needs

10.1-point reduction in PANSS total score

78% patients, ≥1-point decrease in CGI score

2.8-point reduction in positive symptoms

2.1-point reduction in agitation/excitement

2-point reduction in negative symptoms

1.6-point improvement in social cognition

6.1-point improvement in functional outcome

Improvement in sexual functioning (females)

Improvement in treatment adherence

Digital Biomarkers

Vocal biomarker based on speech latency:

Negative Symptoms

function

Cognition

Efficacy overall

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Q&A