Reviva Pharmaceuticals

KOL Webinar on Phase 3 RECOVER Trial of Brilaroxazine in Schizophrenia

February 15, 2024 at 9:00am 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, 2022, 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.

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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
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 Safety, Tolerability and Compliance Results	Larry Ereshefsky PharmD, BCPP, FCCP, Retired professor of Psychiatry, Pharmacology and Psychiatry, The University of Texas; Chief Scientific Officer, Owner, Follow the Molecule LLC
Q&A Session	Q&A Session

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

Larry Ereshefsky, PharmD, BCPP, FCCP

Retired professor of Psychiatry, Pharmacology and Psychiatry the University of Texas

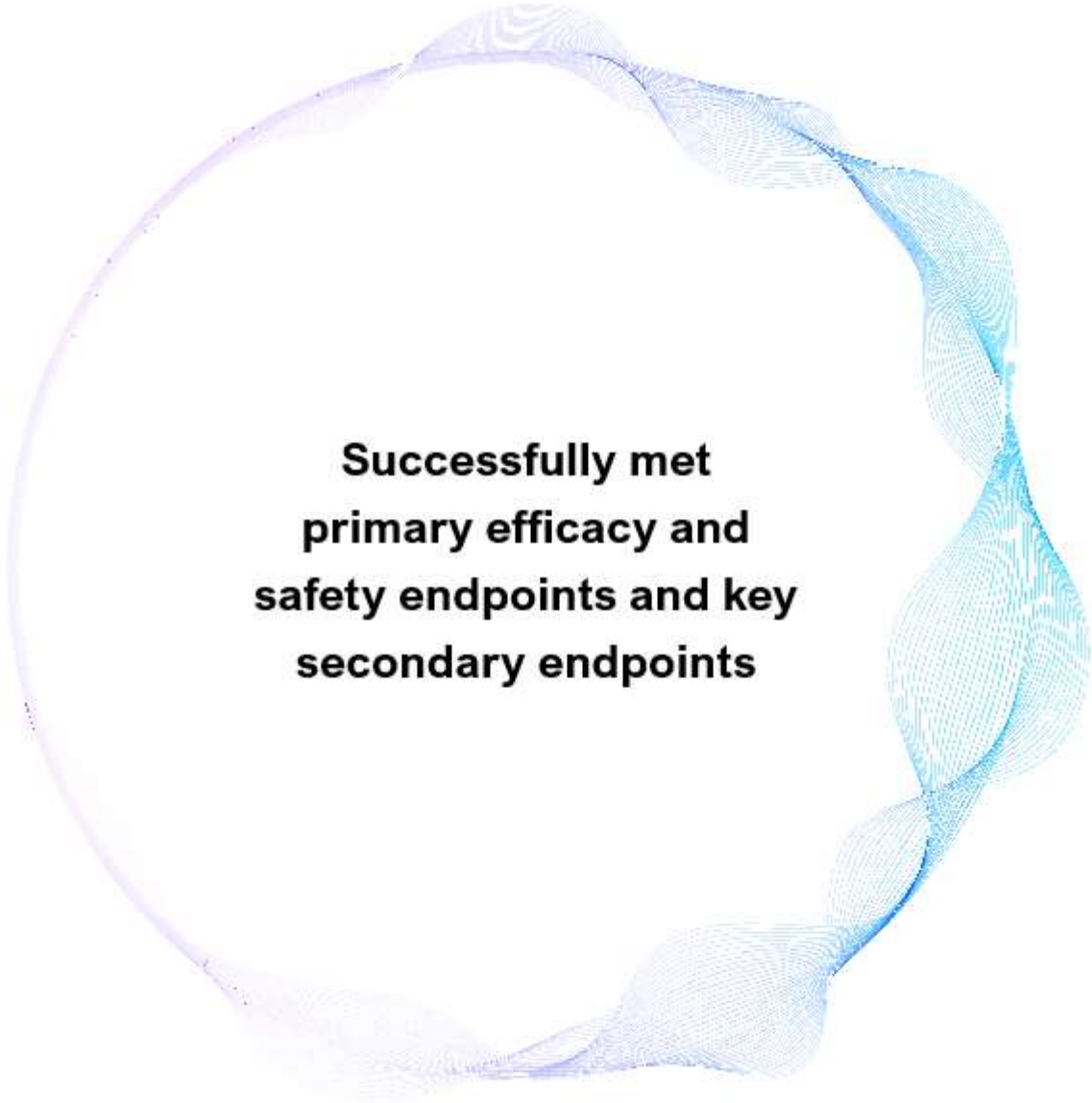
Chief Scientific Officer, Owner of Follow the Molecule LLC

Larry Ereshefsky over his 45 years' career applies his experience as a clinician, scientist and investigator, to develop treatments and innovate clinical methodologies to make a difference in the lives of patients with Neurodegenerative and Psychiatric Disorders. He has contributed significantly to several drug approvals spanning neurology and psychiatry. He has designed, implemented, supervised, and/or conducted >125 CNS and clinical pharmacology clinical trials ranging from first into patient through to proof of concept, implements Asian Bridging strategies, and has overseen large global Phase III registration trials. He is a leader in the use of signal detection and subject strategies to minimize placebo. Dr. Ereshefsky's contributions, from the unique perspective of a clinical scientist (clinical psychiatric pharmacist and psychopharmacologist) has supported clinical development planning, PK/PD evaluations, translational strategies, and methodological innovation for Schizophrenia, Depression, Bipolar Disorder, Parkinson's (PD), Alzheimer's Diseases (AD), and pain indications. He currently focuses on strategies to de-risk early development through proof of concept.

Currently he is the Chief Science Officer (CSO) and owner of Follow the Molecule LLC, providing consulting services to pharma, CROs, and technology vendors. He is also CSO for Clinical Sciences by CenExel Research.

He is a retired Regents Professor of Pharmacy, Psychiatry, and Pharmacology from The University of Texas. Previously, he was the CSO and EVP for California Clinical Trials, acquired by PAREXEL International where his role was VP, Principal Pharmacologist and Therapeutic Area Leader for CNS Early Phase with Global responsibilities. He previously served as CSO for APEX Innovative Sciences (minority owner) including their 2 x 80 bed early phase research units (CNS Network, CA and Hassman Research Institute, NJ). His leadership in developing/applying a translational 'tool-kit' for drug development includes neurocircuitry/biomarker based (RDoC) strategies, i.e., continuous CSF sampling, QEEG, ERP, PSG, sMRI, fMRI, MRS, PET, QST pain models, and cognitive and behavioral paradigms. As co-head of The Advanced Pharmacology and Evaluation Lab at UT, his team made pioneering contributions to understand the relationship of CYP pharmacogenetics, drug interactions, and the environment upon the PK/PD of drugs. He served twice on the FDA Psychopharmacological Drugs Advisory Committee. His PharmD and Residency in Psychopharmacology and Clinical Pharmacy were at the University of Southern California and LA County Medical Center and is Board Certified in Clinical Psychopharmacy.

Results of brilaroxazine Phase 3 RECOVER trial in schizophrenia



Reviva PHARMACEUTICALS

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

OLE: Open Label Extension

Brilaroxazine Phase 3 Study (RECOVER) Efficacy Results

Dr. Mark Opler, PhD, MPH

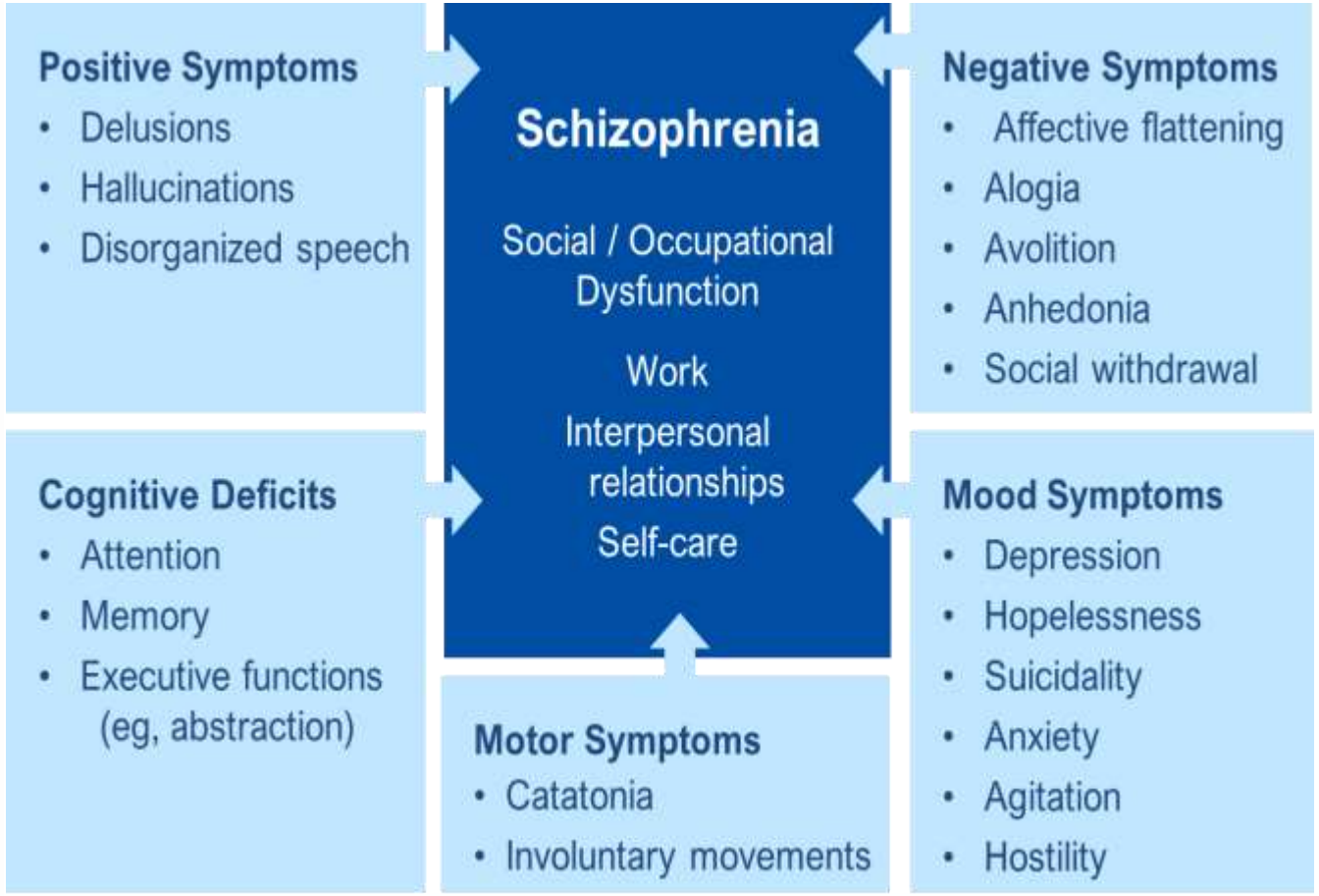
Chief research Officer at WCG Inc and Executive Director at the PANSS Institute

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

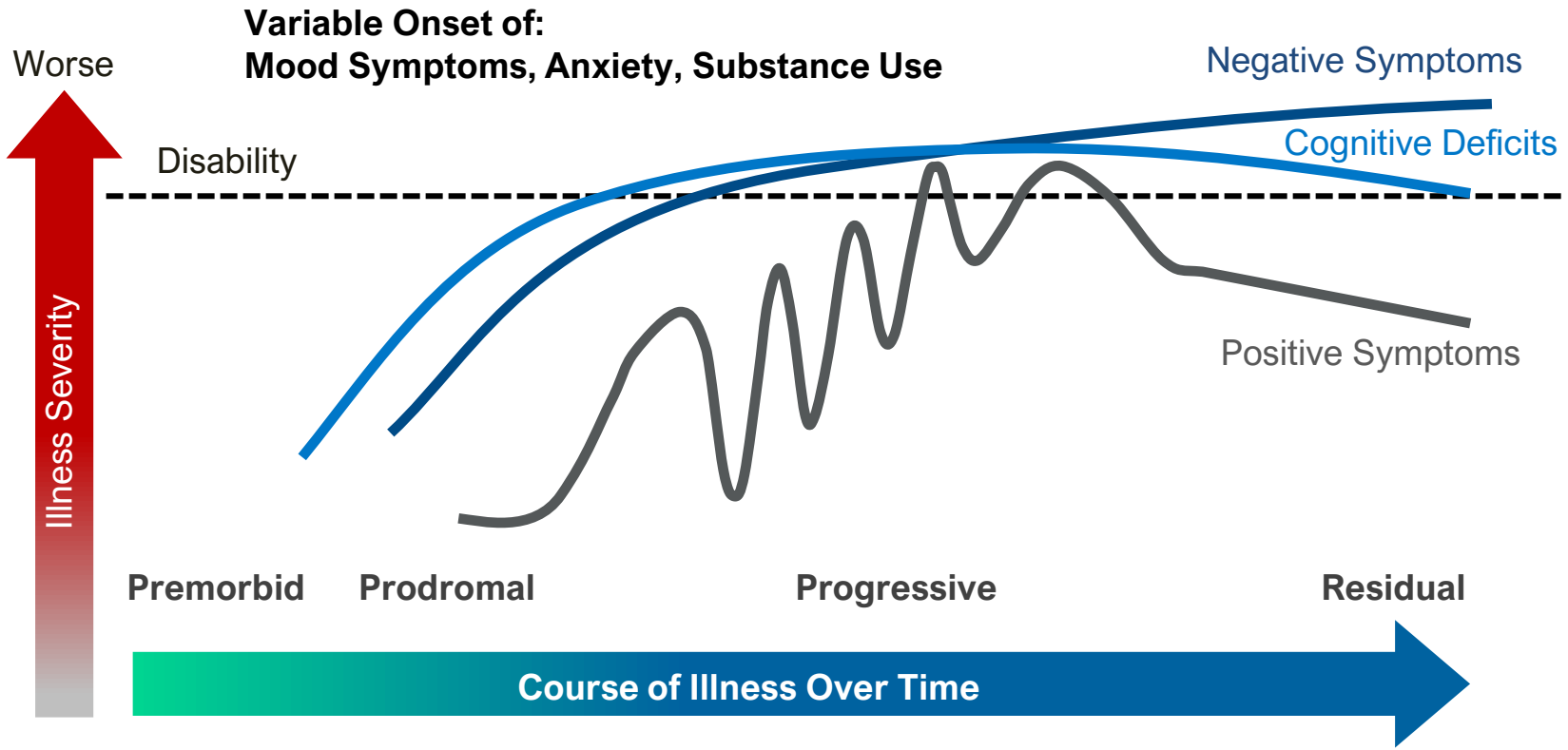


Source: https://www.mentalhelp.net/schizophrenia/statistics/; https://www.who.int/news-room/fact-sheets/detail/mental-disorders; https://fherehab.com/schizophrenia/statistics; https://www.nimh.nih.gov/health/statistics/schizophrenia; Kane JM et al. J Clin Psychology 2019, 80(2):18com12123..

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



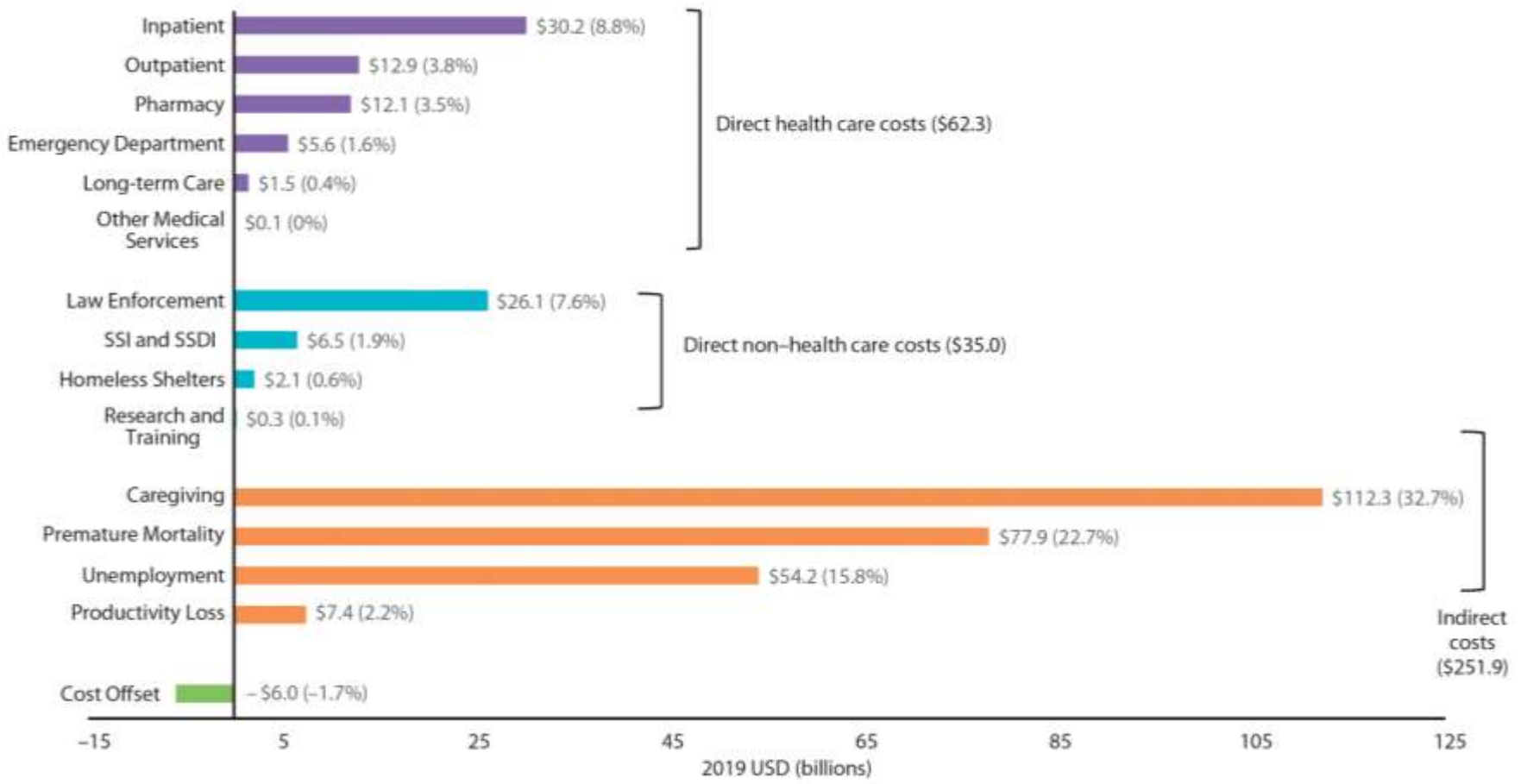
Adapted from: Correll CU. J Clin Psychiatry. 2013;74(2):e04; link

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);

Impact of Schizophrenia Beyond the Patient and Direct Healthcare Costs

Schizophrenia affects the physical, psychological, emotional, social, and financial life of caregivers

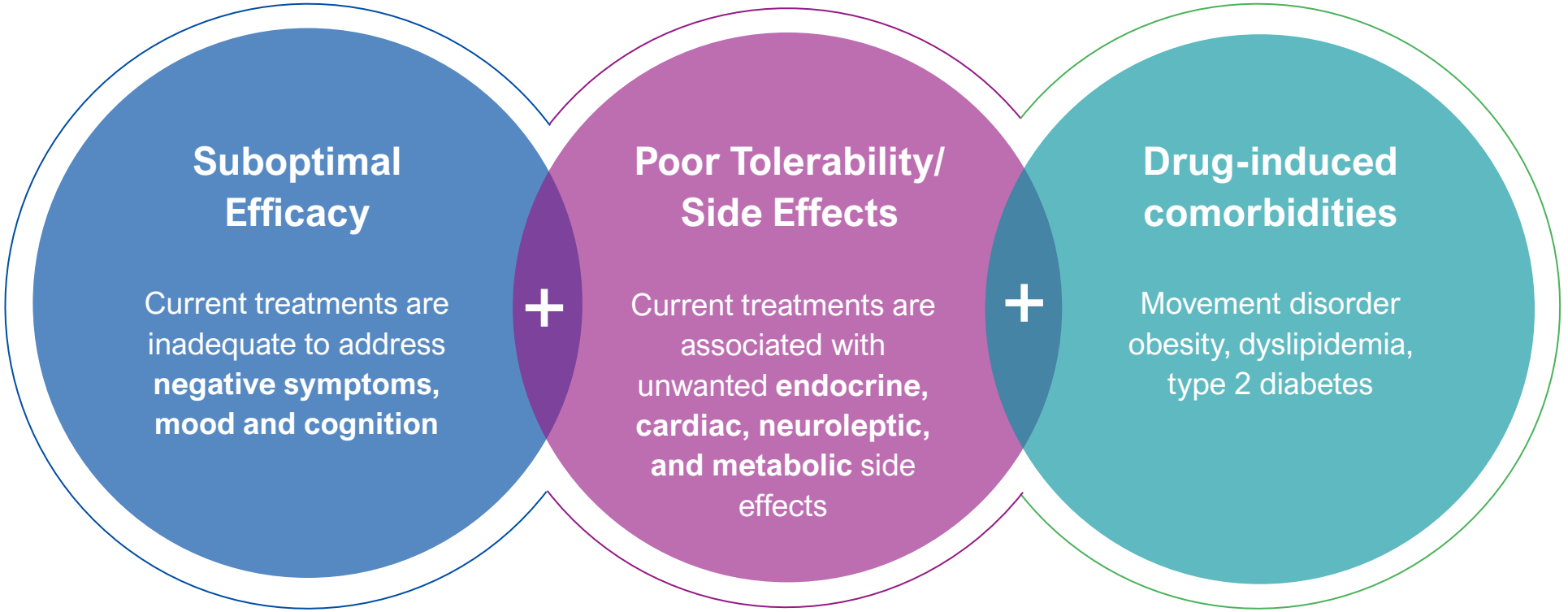
- Estimated societal burden of schizophrenia in the US in 2019 was $343.2 billion
- Indirect costs contributed the most, driven largely by costs associated with caregiving ($112.3 billion)
- 60% of patients with schizophrenia live with a caregiver
- In many States ‘Board and Care facilities’ take up the burden



Kadakia A, et. Al. J Clin Psychiatry. 2022;83:e1-e9; Millier A, et al. J Psychiatr Res. 2014;54:85-93; Wu EQ, et al. J Clin Psychiatry. 2005;66:1122-1129.

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

Source: Torres-Gonzalez F et al, Neuropsychiatric Disease and Treatment 2014, 10:97-110; Stroup T S and Gray N, World Psychiatry 2018, 17:341-356; Levin, S.Z. et al., Schizophrenia Research 2015, 164:122-126; Ermakov EA. et al., Frontiers in neuroscience 2022, 13:880568; Reale M et al. Frontiers in Psychiatry 2021, 12:536257; Monji A et al. Japanese Society of Psychiatry and Neurology 2009, 63:257-265; Bhat L, et al. Medical Research Archives 2023, 11(4):3834

Schizophrenia: Clinical Evaluation

Scales and tools for evaluating brilaroxazine treatment effects in RECOVER 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 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 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 Black Asian Other	24 (17.1) 64 (45.7) 49 (35.0) 3 (2.1)	26 (19.4) 59 (44.0) 46 (34.3) 3 (2.2)	23 (16.8) 66 (48.2) 44 (32.1) 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

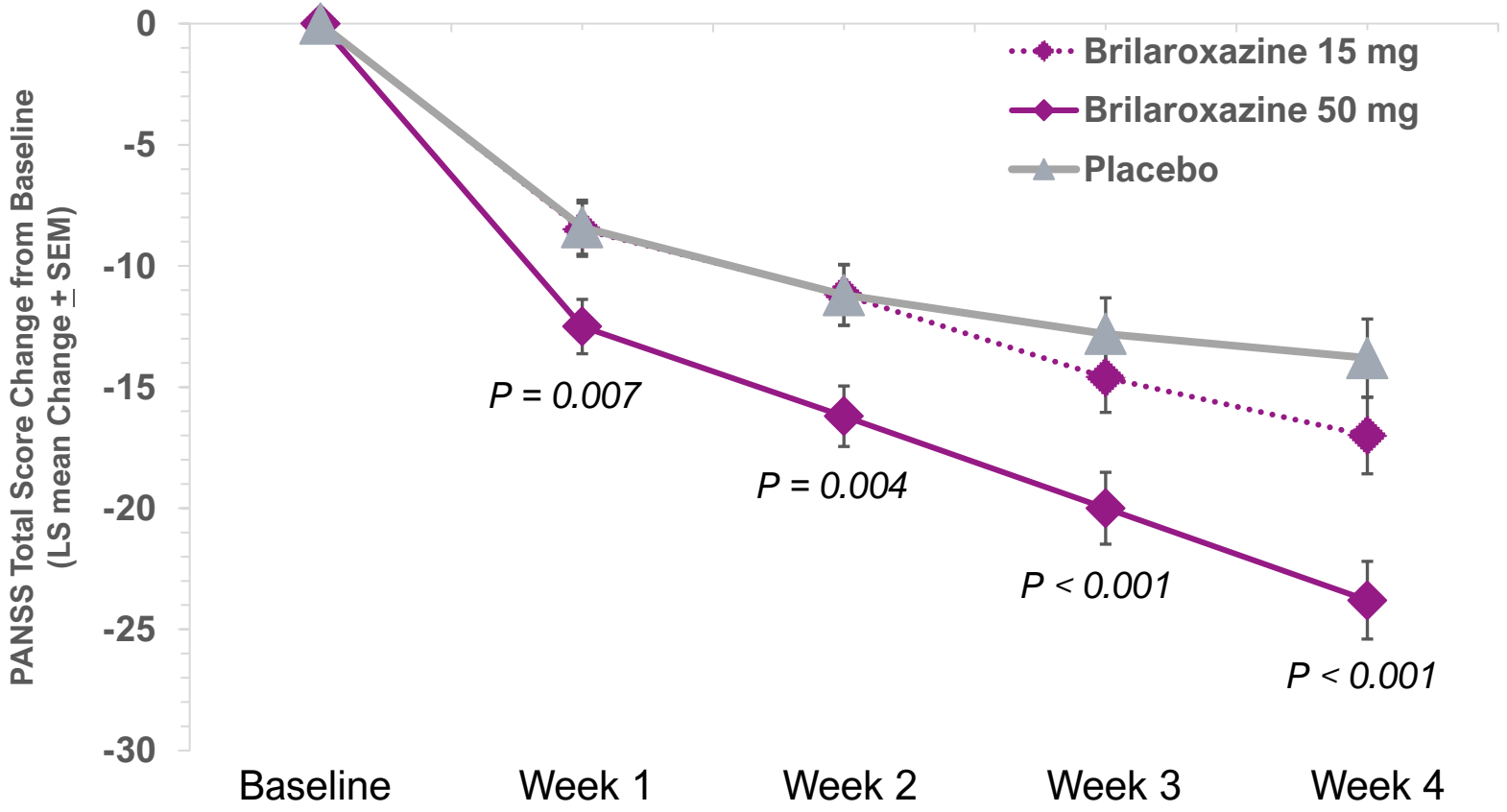
Primary Endpoint: PANSS Total Score at Week 4 for Brilaroxazine Vs. Placebo

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



PANSS: Positive and Negative Syndrome Scale

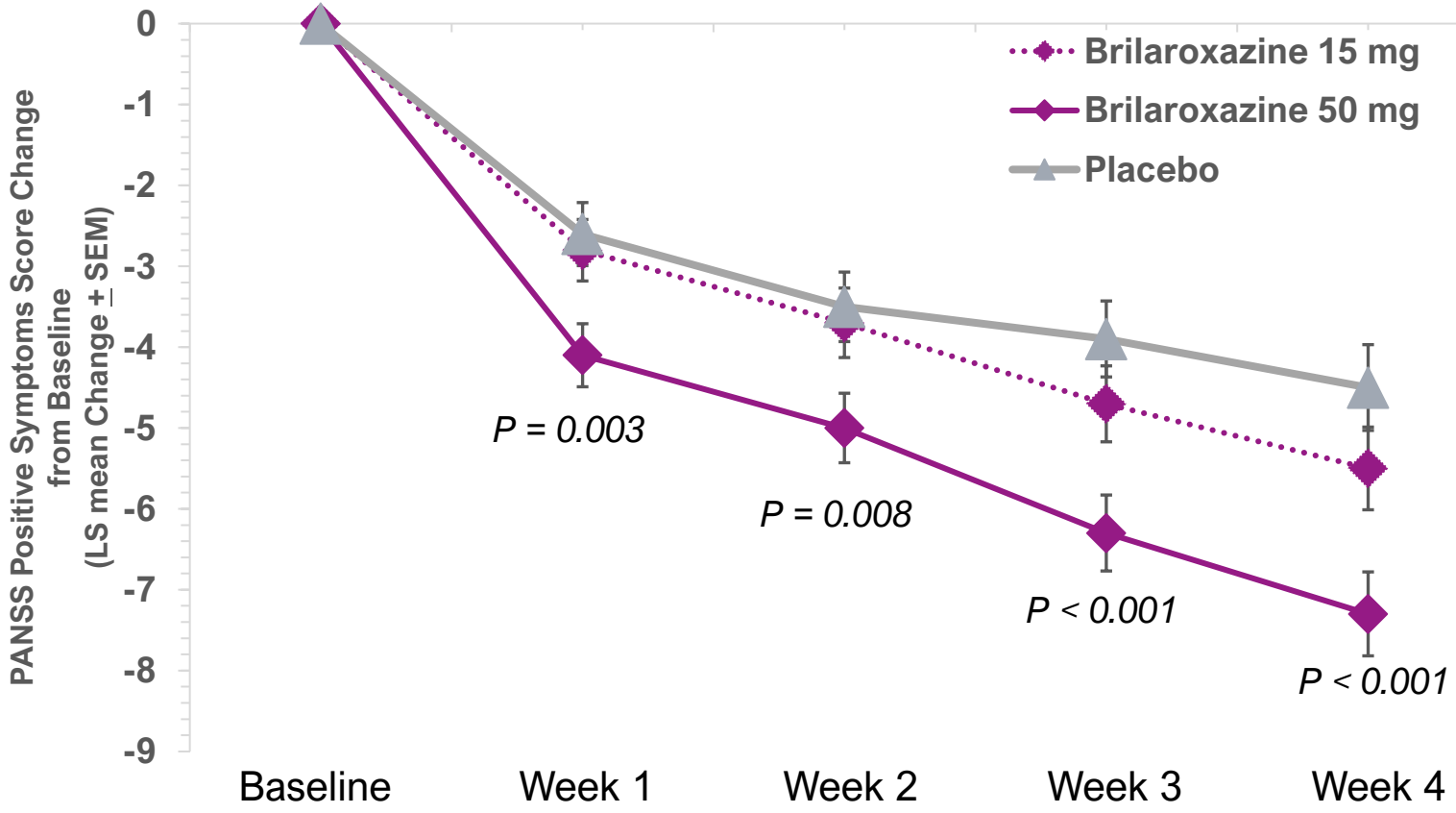
Secondary Endpoint: Positive Symptoms at Week 4 for Brilaroxazine Vs. Placebo

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

Cohen's d effect size of 0.5



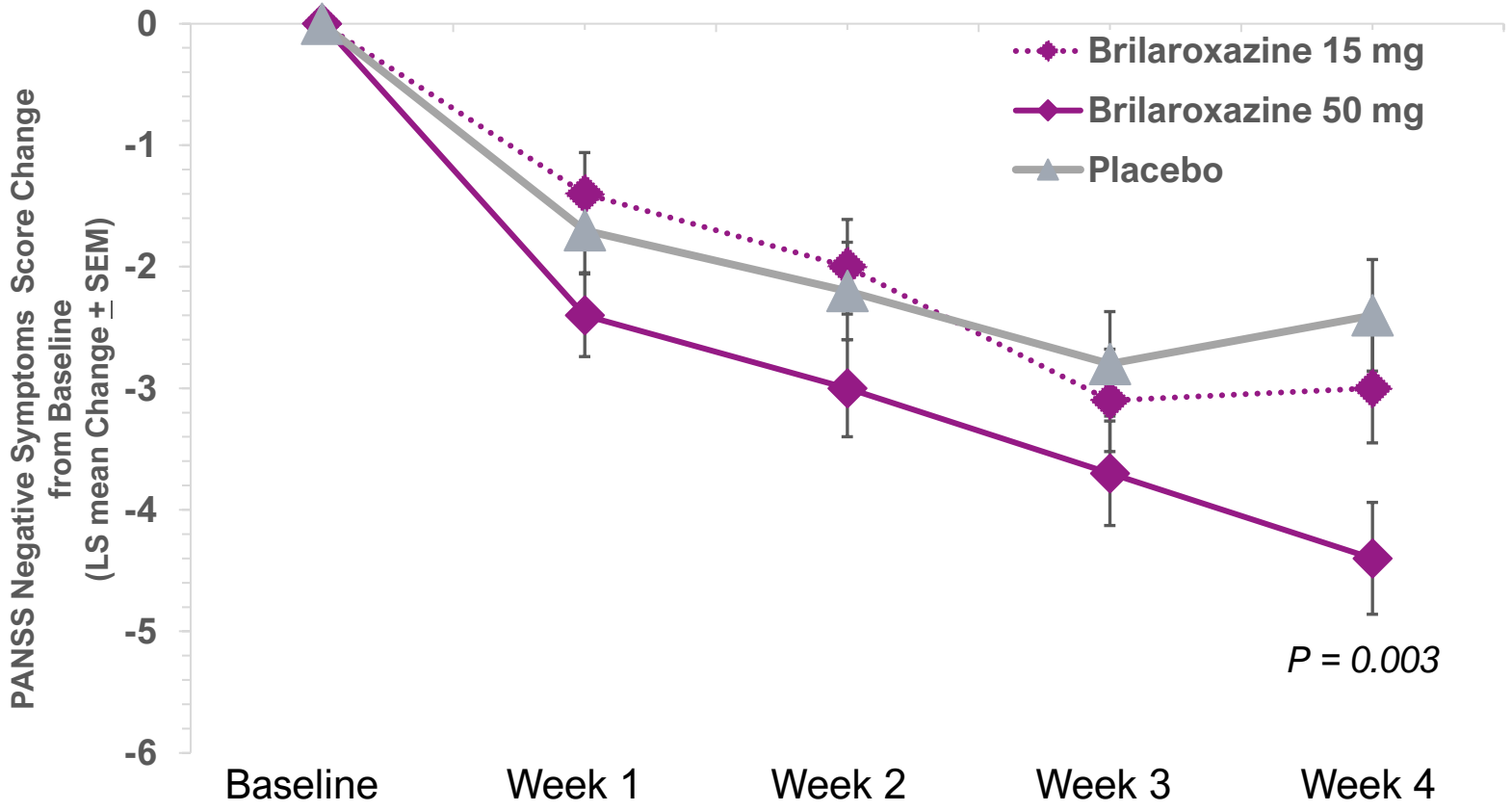
Secondary Endpoint: Negative Symptoms at Week 4 for Brilaroxazine Vs. Placebo

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

Cohen's d effect size of 0.4

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



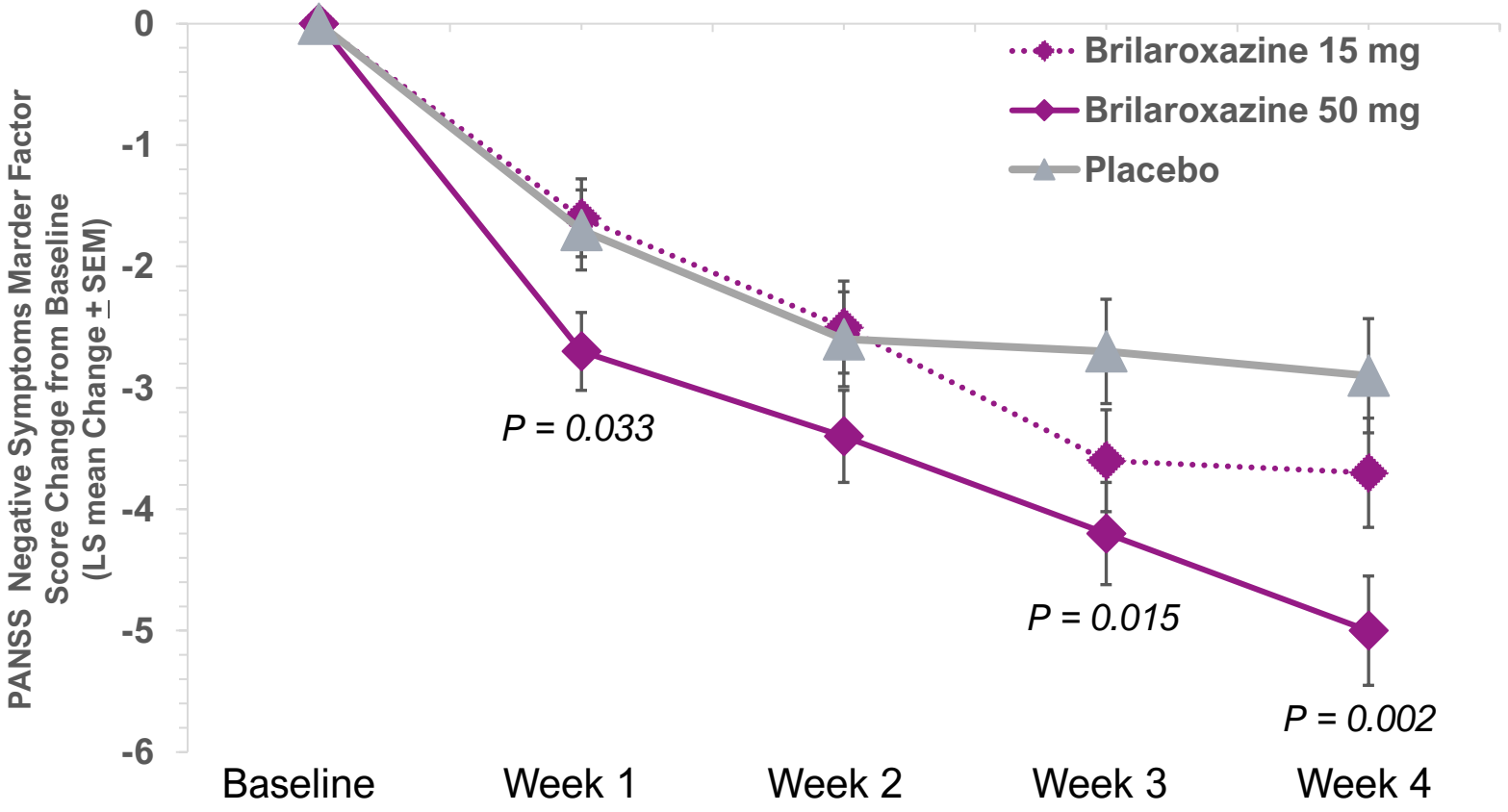
Secondary Endpoint: Negative Symptoms PANSS Marder Factor at Week 4

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

Cohen's d effect size of 0.4

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



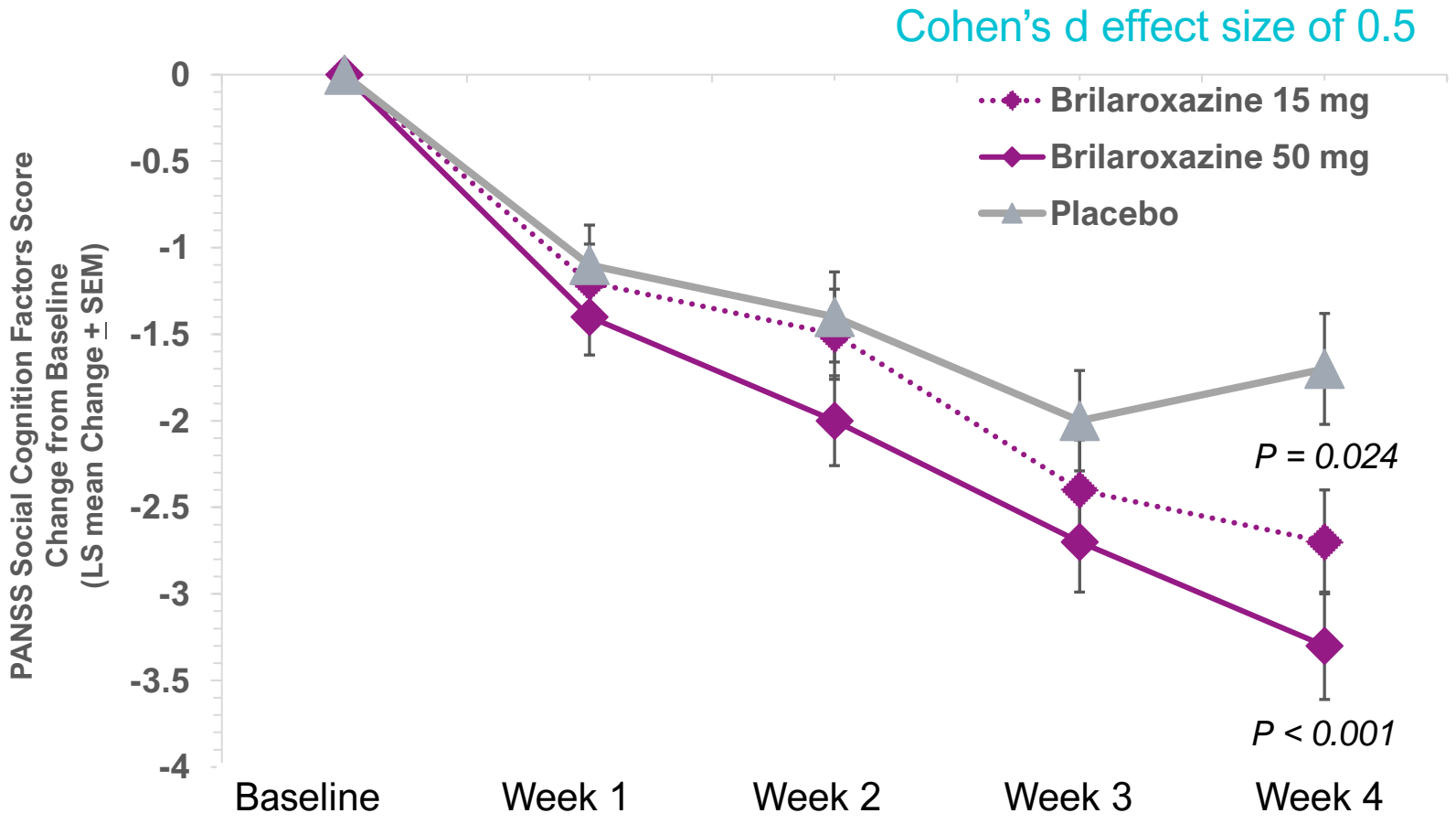
PANSS: Positive and Negative Syndrome Scale

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



PANSS: Positive and Negative Syndrome Scale

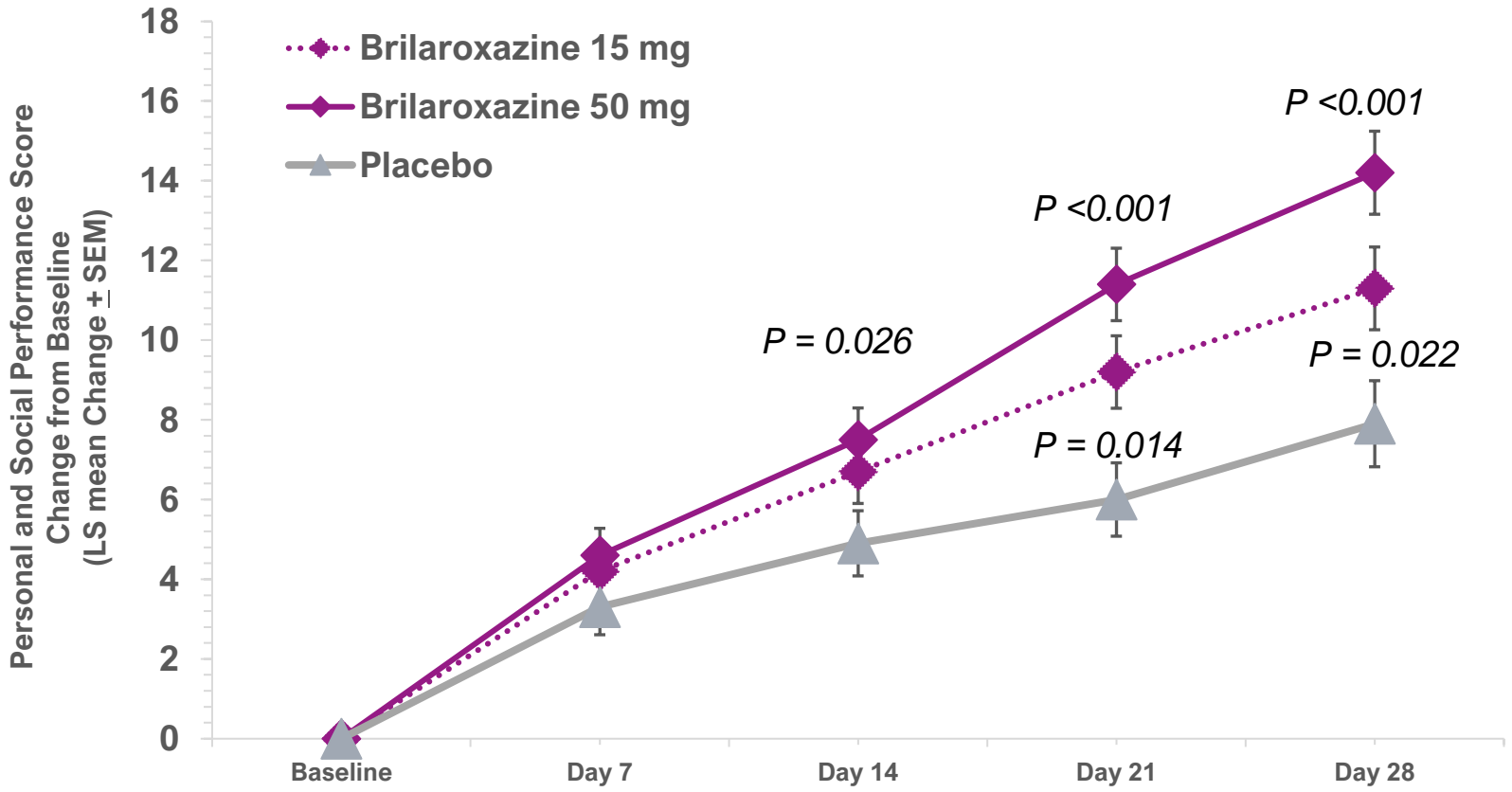
Secondary Endpoint: Personal and Social Performance (PSP) at Week 4

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



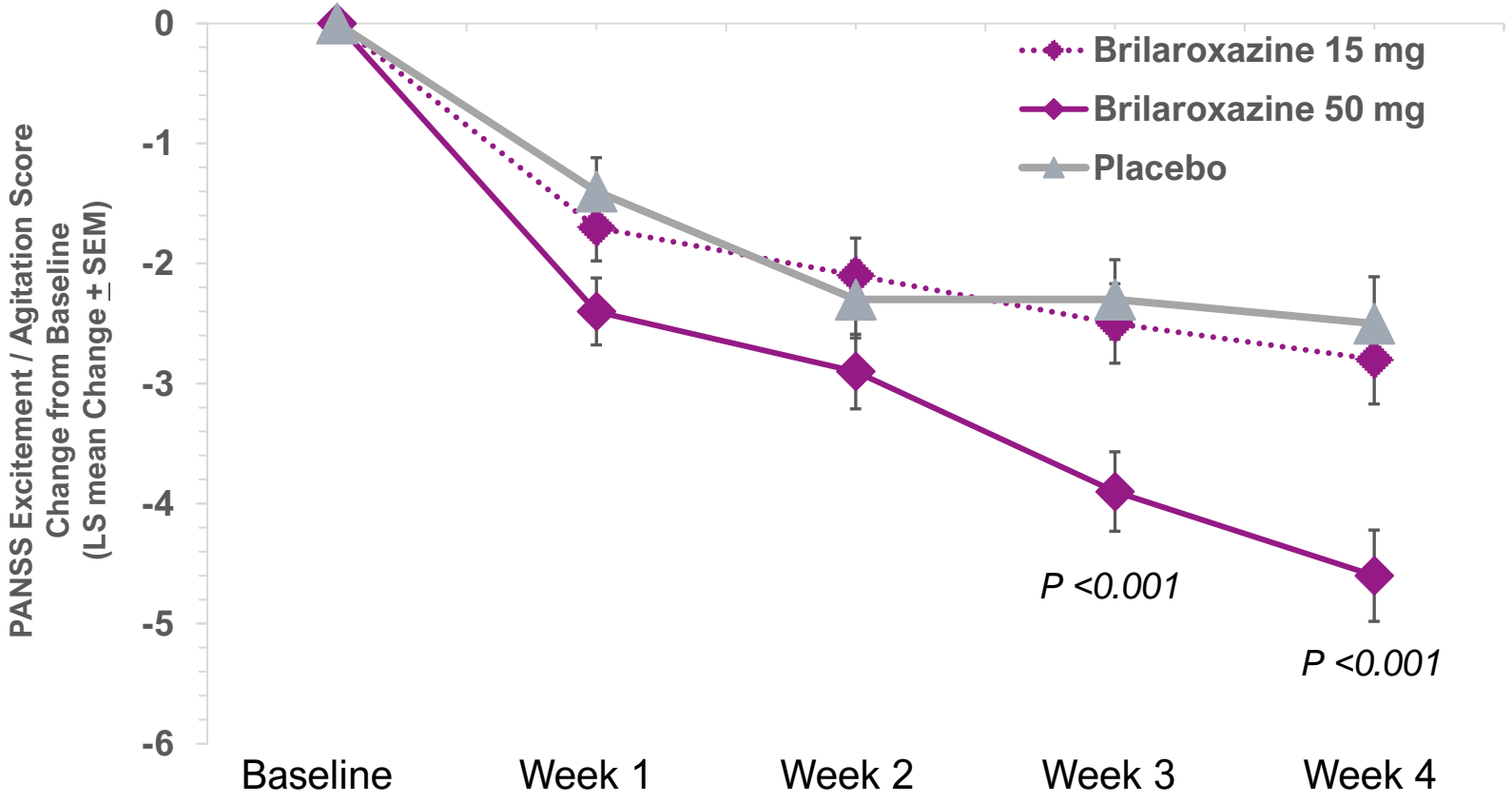
Secondary Endpoint: PANSS Excitement / Agitation at Week 4

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



PANSS: Positive and Negative Syndrome Scale

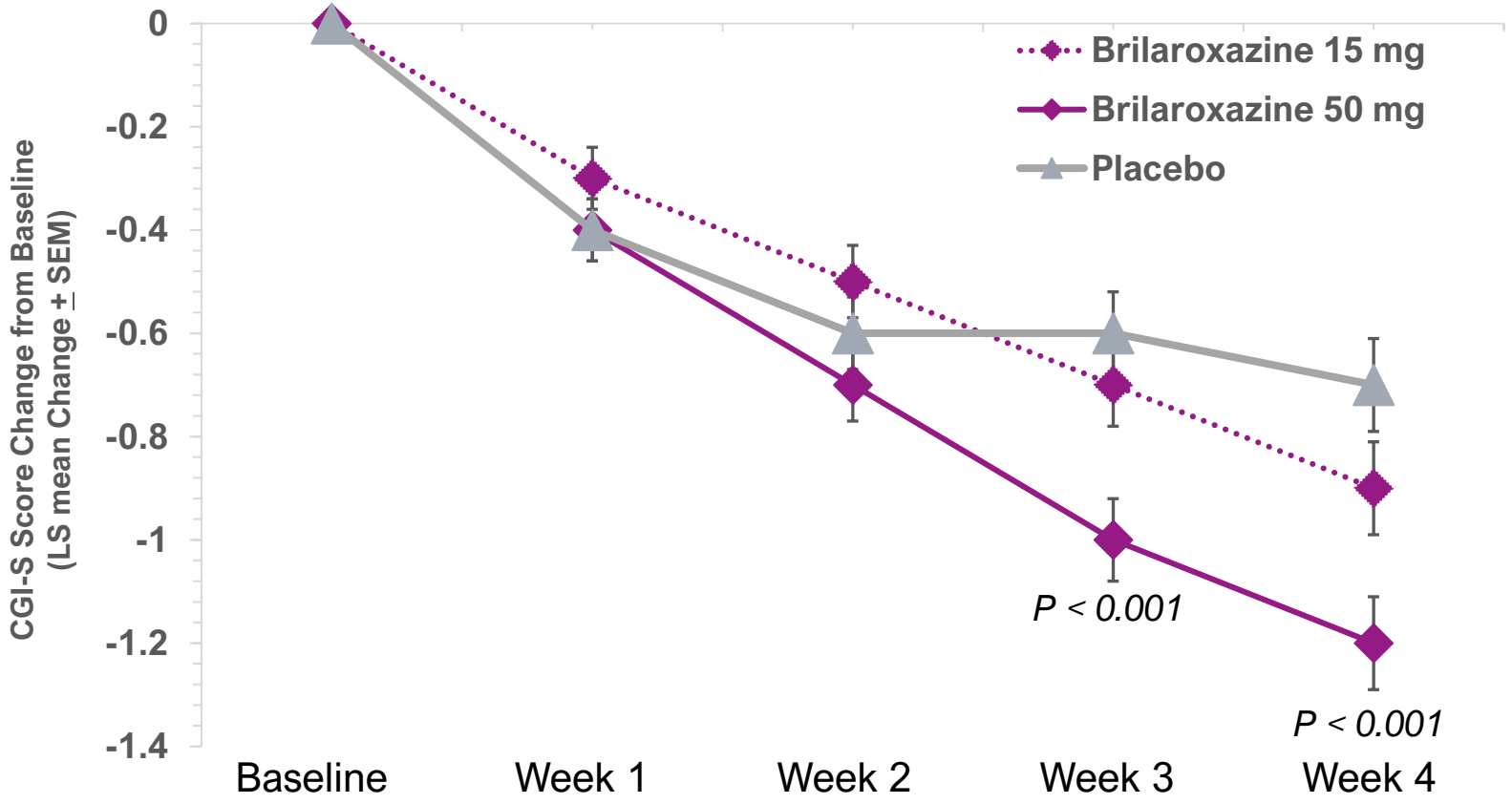
Secondary Endpoint: CGI-S At Week 4 for Brilaroxazine Vs. Placebo

≥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

Cohen's d effect size of 0.5



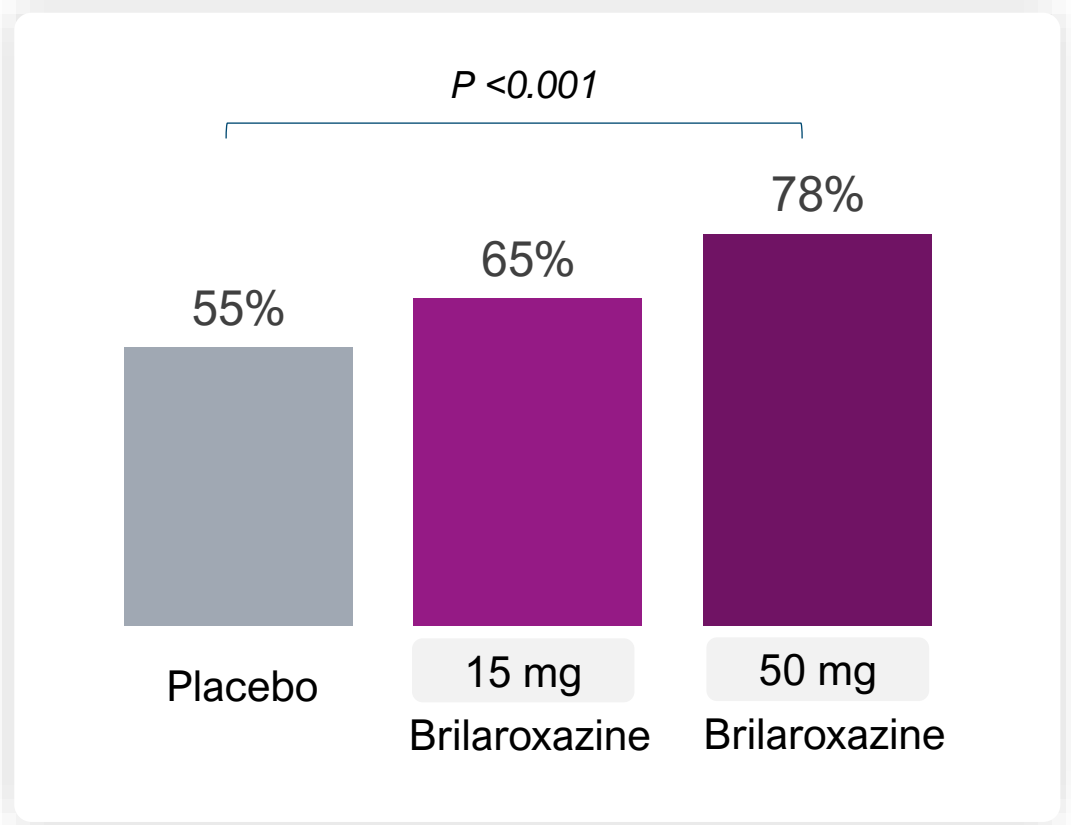
CGI-S: Clinical global impression – severity score

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 15 mg achieved ≥ 1-point improvement in CGI-Severity scale from baseline vs. placebo



CGI-S: Clinical global impression – severity scale

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* ✓

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

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

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

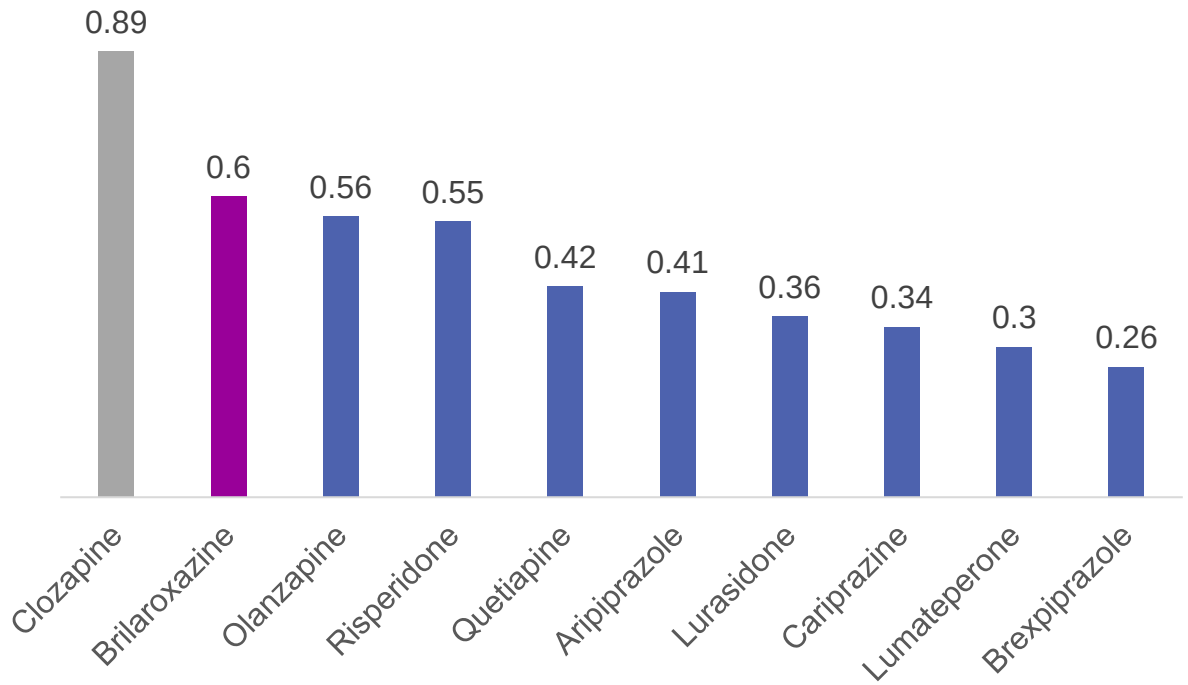
Key Metrics	PHASE 3 RECOVER (N=411 | 4-wk) NCT05184335	PHASE 2 REFRESH (N=234 | 4-wk) NCT01490086
Primary Endpoint (Brilaroxazine 50 mg vs Placebo)		
PANSS Total Score	-10.1 P<0.001 (Effect Size, 0.6)	-10.7 P<0.01
Secondary Endpoint (Brilaroxazine 50 mg vs Placebo)		
PANSS Positive Score	-2.8 P<0.001 (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	-0.5 P<0.001 (Effect Size, 0.5) Improvement ≥ 1, 78%	-0.5 P=0.02 Improvement ≥ 1, 72%
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)

(1) Reviva press release on Phase 3 RECOVER trial results on October 30, 2023 (https://revivapharma.com/press-releases/).
(2) Bhat, et al. J Neurol Neuromed 2018, 3(5): 39-50. (3) Cantillon, M. et al. Schizophrenia Research 2017, 189: 126-133

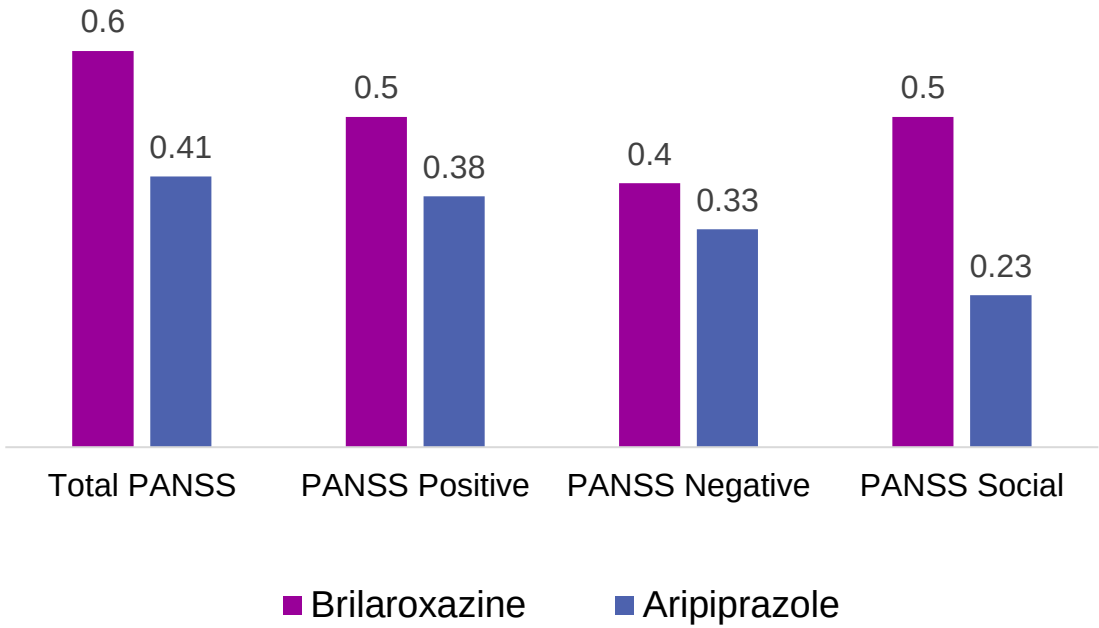
Comparison of Treatment Effect Size from Phase 3 Studies

Primary endpoints and major secondary efficacy endpoints

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



Brilaroxazine[1] vs Aripiprazole[2]



Source: (1) Brilaroxazine phase 3 topline results announced by Reviva; (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 efficacy schizophrenia symptom domains

Consistent, Wide-Spectrum Efficacy: Brilaroxazine demonstrated consistent efficacy, reducing multiple domains associated with schizophrenia including positive, negative, agitation, and social cognitive symptoms, and improving measures of functioning and quality of life.

Well-Conducted Trial, High-Quality Data: Data quality was continuously monitored for the duration of the trial by WCG Inc., utilizing validated methods to reduce error and placebo response with standardized training & calibration of the Positive and Negative Syndrome Scale (PANSS) and blinded monitoring of clinician and site performance.

Strong Efficacy/Side-Effect Ratio: Compared to historical data reported for marketed drugs, brilaroxazine shows significant wide-spectrum efficacy across primary as well as secondary endpoints, with a side effect profile and discontinuation rate comparable to or better than placebo.

Potential to Significantly Impact Unmet Needs: Brilaroxazine has the potential to address many unmet needs in the treatment of schizophrenia during acute and chronic phases. Further studies will help elucidate both efficacy and effectiveness of brilaroxazine in promoting remission of symptoms and functional recovery across the lifespan.

Brilaroxazine Phase 3 Study (RECOVER)
Safety, Tolerability and Compliance

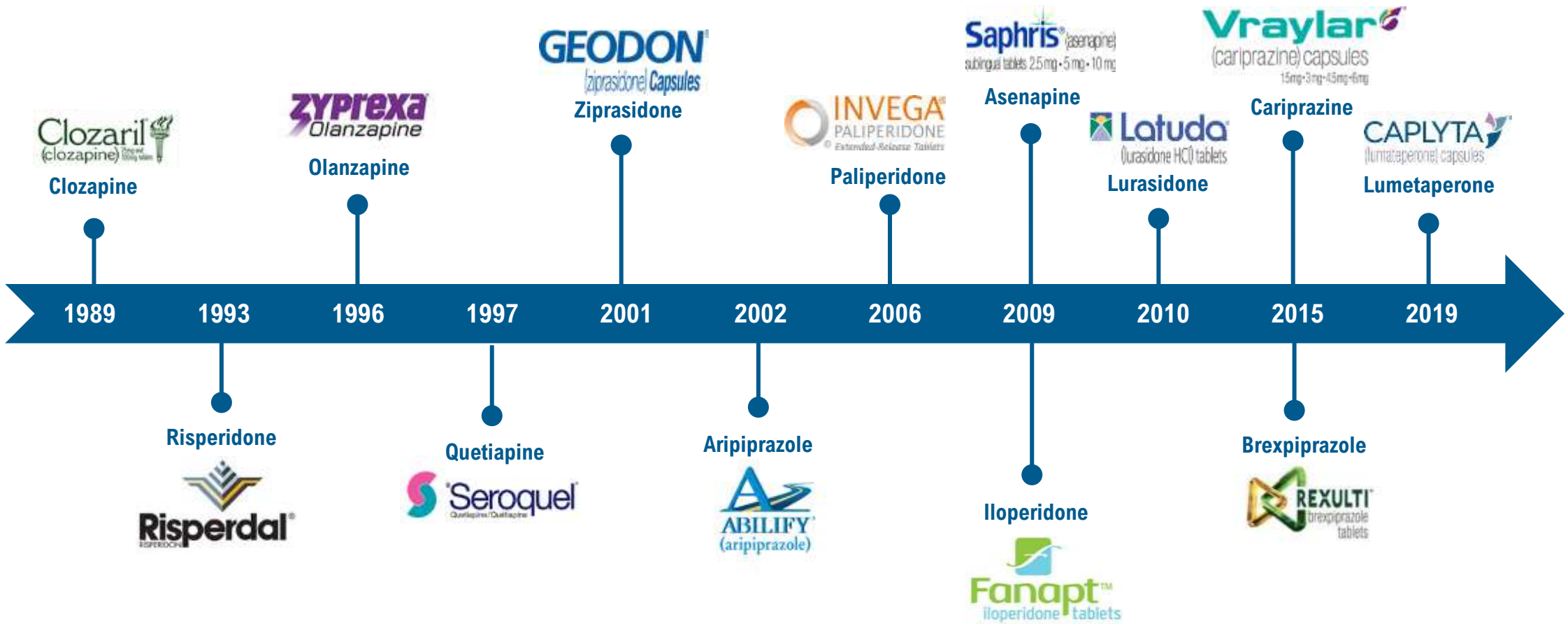
Dr. Larry Ereshefsky, PharmD, BCPP, FCCP

Retired Professor of Psychiatry, Pharmacology and Psychiatry, The University of Texas

Chief Scientific Officer, Owner

Follow the Molecule LLC

New Antipsychotics Approved Over Last 40 Years

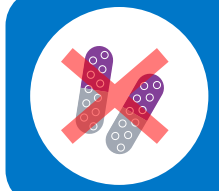


Source: H.C. Wainwright, Equity Research (RVPH), January 24, 2022

Symptoms of Disease and Side Effects of Treatments Impose a Burden

Suboptimal Efficacy[1]

+



Poor Tolerability/ Side Effects[1]

High Discontinuation/ Non-Compliance[1]

Estimated treatment discontinuation rates[1]:

30-50% in short-term treatment of acute patients and 42-74% in long-term treatment of stable patients

77% Reported medication side effects[2]

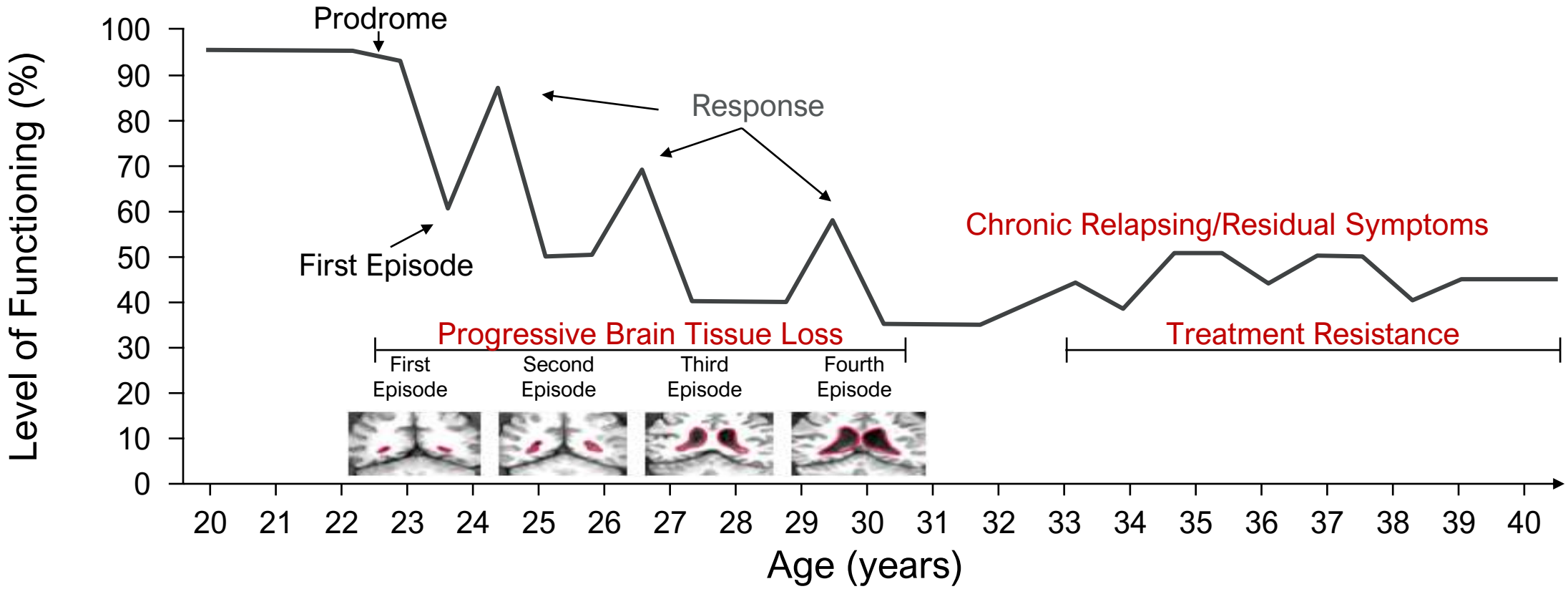
61% Reported impairment in their daily life as a result of medication side effects[2]

30% Reported moderate or severe impairment in their daily life as a result of medication side effects[2]

Study of 1825 participants with psychosis[2]

1. Torres-Gonzalez F et al, Neuropsychiatric Disease and Treatment 2014, 10:97-110 ; Stroup T S and Gray N, World Psychiatry 2018, 17:341-356; Bhat L et al, J Neurology and Neuromedicine 2018, 3(5): 39-50; Levin, S.Z. et al., Schizophrenia Research 2015, 164:122-126; Ermakov EA. et al., Frontiers in neuroscience 2022, 13:880568..
2. Morgan VA, et al. Aust N Z J Psychiatry. 2012;46(8):735-752. Awad AG, et al. Acta Psychiatr Scand Suppl. 1994;380:27-32. Barnes TR; Schizophrenia Consensus Group of British Association for Psychopharmacology. J Psychopharmacol. 2011;25(5):567-620.

With Every Relapse, In the Early Years of Illness, Patients are at Risk for Increased Brain Atrophy and Lifetime Functional Impairment



Lin D et al. Front Psych 2021, 12:695672; Alphs L et al. Int Clin Psychopharmacol 2016, 31:202-209; Emsley R et al . BMC Psychiatry 2013, 13:50;

Reflecting on the Past to Guide the Future

The need: better efficacy with fewer side effects

- Recovery or Remission are a rarity
- Sub-optimal efficacy as illustrated in acute schizophrenia clinical trials where a 20-30% reduction in Positive and Negative Symptom Scale (PANSS) Scores vs placebo are ‘successful’ outcomes
- Relapse prevention is less than 50% by the second year

Major Symptoms		
Positive symptoms	**Negative symptoms**	**Mood Symptoms**
Cognition Impairment	**Impaired function**	

Major Side Effects of Standard of Care

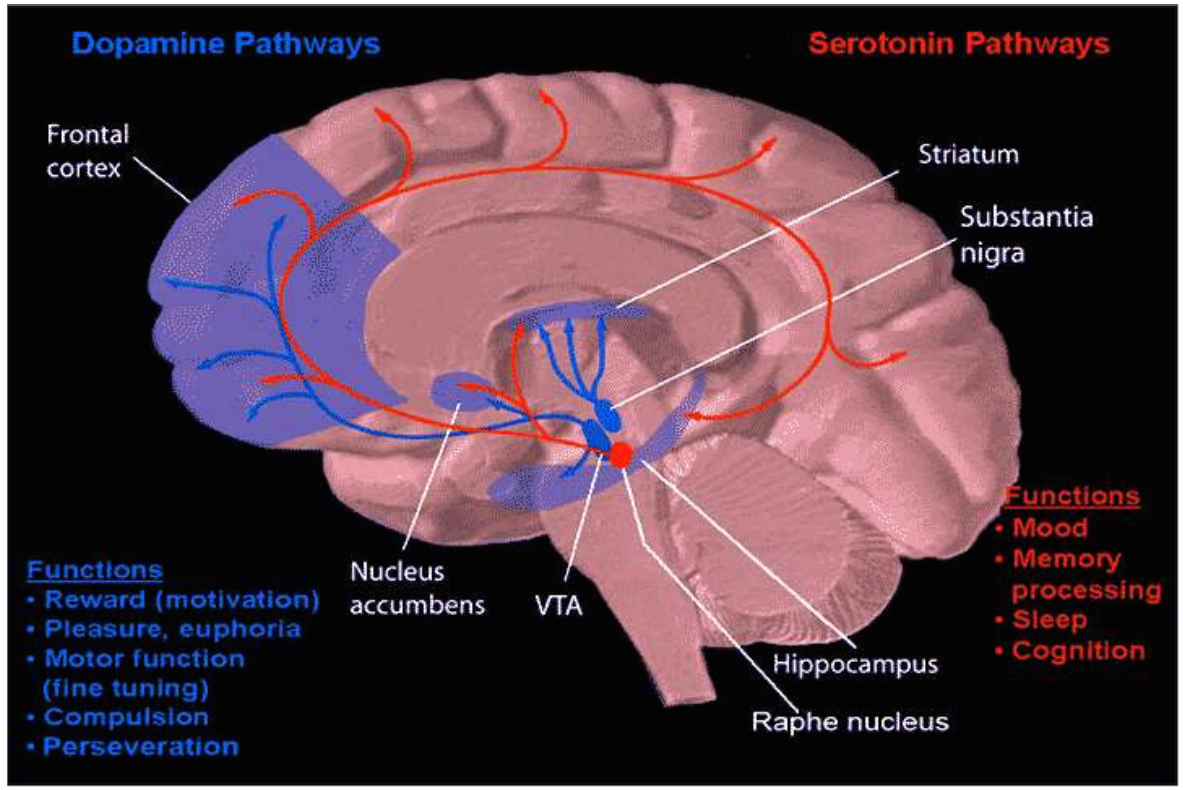
- **Metabolic Side effects** ➔ Weight gain, Diabetes, Dyslipidemia
- **Endocrine Side Effects** ➔ Hormone changes, sexual side effects
- **Neuroleptic Side Effects** ➔ EPS, Akathisia, Tardive Dyskinesia
- **Autonomic Side Effects** ➔ Anticholinergic, Cardiovascular

Emerging role for neuroinflammation: Associated with negative sx (anhedonia, apathy) and cognitive impairment

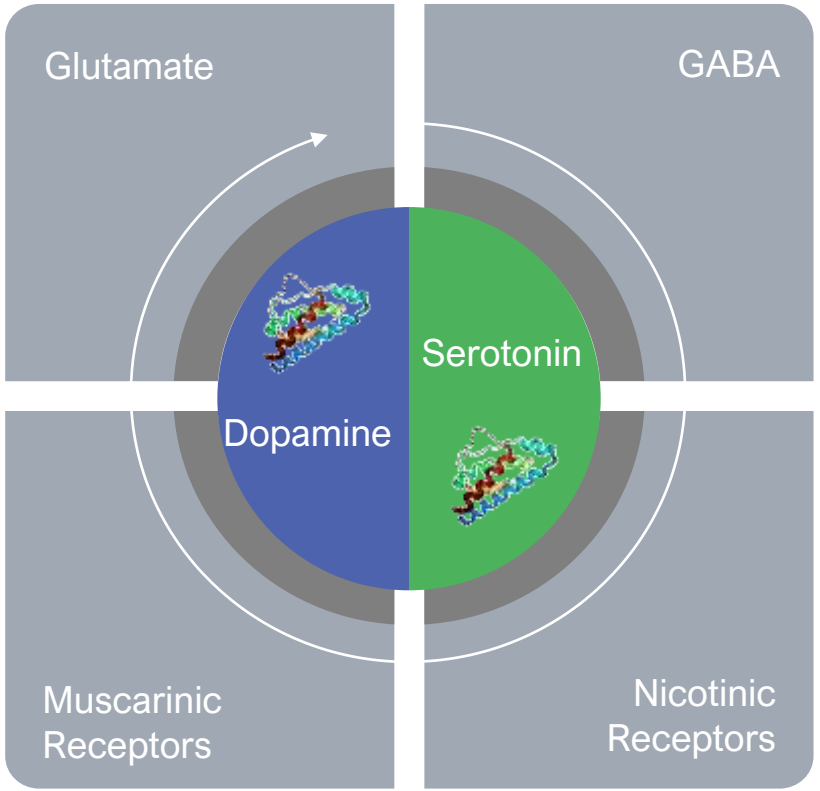
Müller N, et al. The role of inflammation in schizophrenia. Front Neurosci. 2015;9(OCT). doi:10.3389/fnins.2015.00372; Goldsmith DR et al. Inflammation and Negative Symptoms of Schizophrenia: Implications for Reward Processing and Motivational Deficits; Front Psychiatry. 2020;11. doi:10.3389/fpsyt.2020.00046; Wang D et al. Differences in inflammatory marker profiles and cognitive functioning between deficit and nondeficit schizophrenia. Front Immunol. 2022;13. doi:10.3389/fimmu.2022.958972

Pathobiology: Psychiatric Disorders are Primarily Driven by Dysfunctional Serotonin and Dopamine Signaling

Targeting serotonin and dopamine receptors can treat schizophrenia and comorbid symptoms



Source: American Society for Pharmacology and Experimental Therapeutics



Stepnicki P et al. Molecules 2018, 23:2087.

Serotonin and dopamine signaling drive pathobiology and symptom domains in schizophrenia, bipolar disorder, and play a major role in major depressive disorder, and attention/deficit hyperactivity disorder. Dynamic relationship between different neurotransmitters including a role for cholinergic, glutamatergic, and GABA-ergic modulation

Unique and Convergent Mechanisms Of Action Potentially Differentiate Brilaroxazine

'Traditional' activity at D2 (partial antagonist/agonist) and 5HT2 antagonist

NE and DA increases in mPFC

5-HT1A partial agonist

D4 partial antagonists

Direct/orthosteric activities lead to indirect and allosteric effects in glutamate, GABA, and cholinergic receptors

Multifaceted pharmacologic profile potentially converges on disease and neurocircuitry targets of illness

Effects mediate inhibition of pro-inflammatory and increasing anti-inflammatory cytokines and chemokines (BDNF, IL-6, IFN-γ IP-10, and MIP-1)

5-HT2B antagonist

5-HT7 antagonist

RECOVER Trial Safety and Tolerability Results: Brilaroxazine vs Placebo (ITT)

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
- No serious adverse events (SAEs) related to the study drug brilaroxazine
- No incidence of suicidal ideation
- No significant change in bodyweight, and blood glucose levels vs placebo
- Clinically significant decrease in cholesterol, LDL and increase in HDL vs placebo
- Common brilaroxazine TEAEs were headache (<6%) and somnolence (≤7.5%) generally transient in nature

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

- Metabolic Side Effects:
  - Weight gain N=3 (2.1%) in 15 mg and N=8 (5.9%) in 50 mg brilaroxazine and N=4 (2.9%) in placebo
  - Elevated LDL level none in brilaroxazine and N=4 (2.9%) in placebo
  - Low HDL level N=1 (0.7%) in 15 mg, N=2 (1.4%) in 50 mg brilaroxazine and N=2 (1.4%) in placebo
- Neuroleptic Side Effects:
  - Akathisia N=1 (0.7%) and EPS N=1 (0.7%) in 50 mg brilaroxazine and none in 15 mg and placebo
- Endocrine Side effects:
  - Clinically significant decrease in prolactin and directional improvement in thyroid levels compared placebo

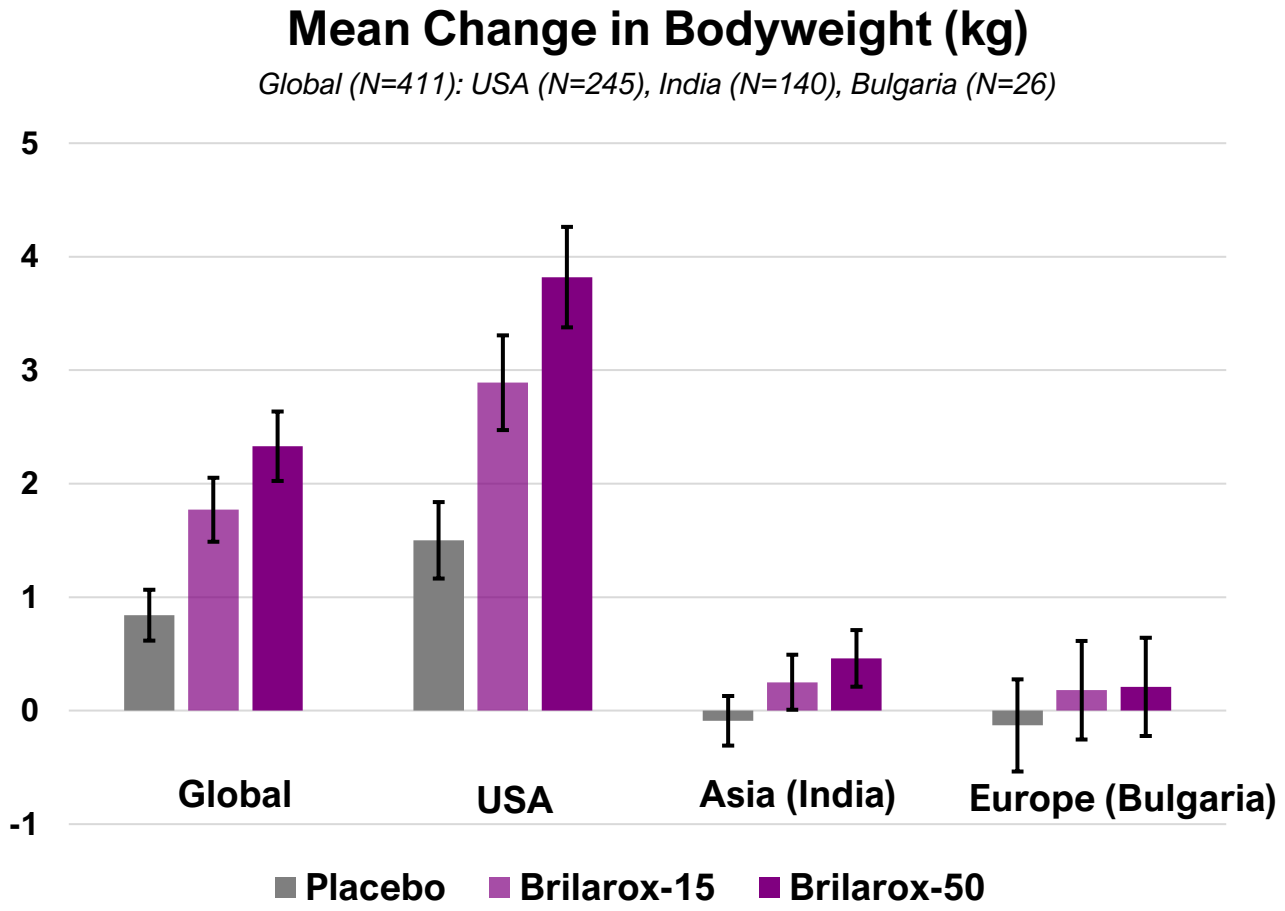
TEAE: Treatment-emergent adverse events; LDL: Low-density lipoprotein

Brilaroxazine Phase 3 Study: Change in Bodyweight at Week 4

Global and regional analysis of change in bodyweight in brilaroxazine vs placebo

Change in Bodyweight (kg)

- No clinically significant weight gain in brilaroxazine vs placebo
- Subjects from USA reported higher weight gain compared to subjects from ex-USA (Bulgaria/India)
- Weight gain AESI reported in 15 subjects: N=3 (2.1%) in 15 mg and N=8 (5.9%) in 50 mg brilaroxazine and N=4 (2.9%) in placebo
- Among AESI weight gain (N=15) reported in this study, 13 are in the USA and 2 are from ex-USA

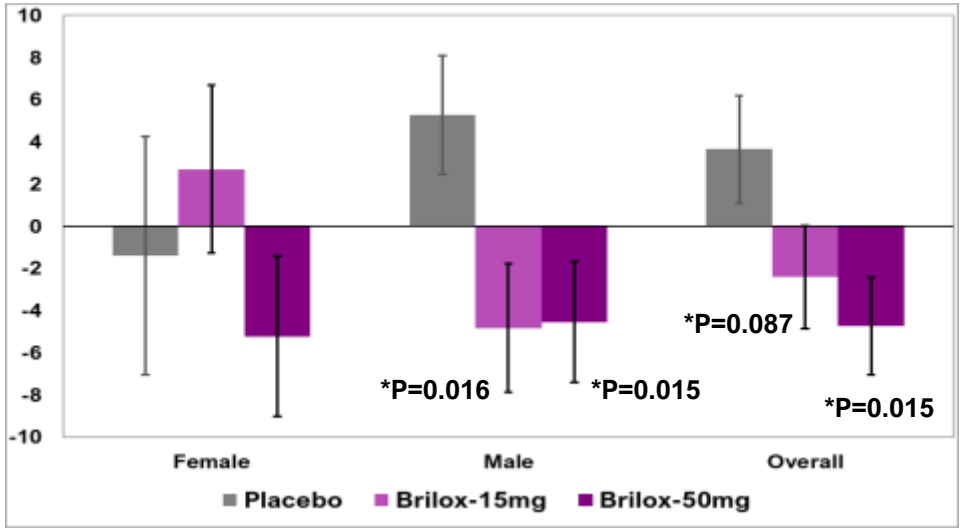


AESI = Adverse Events of Special Interest

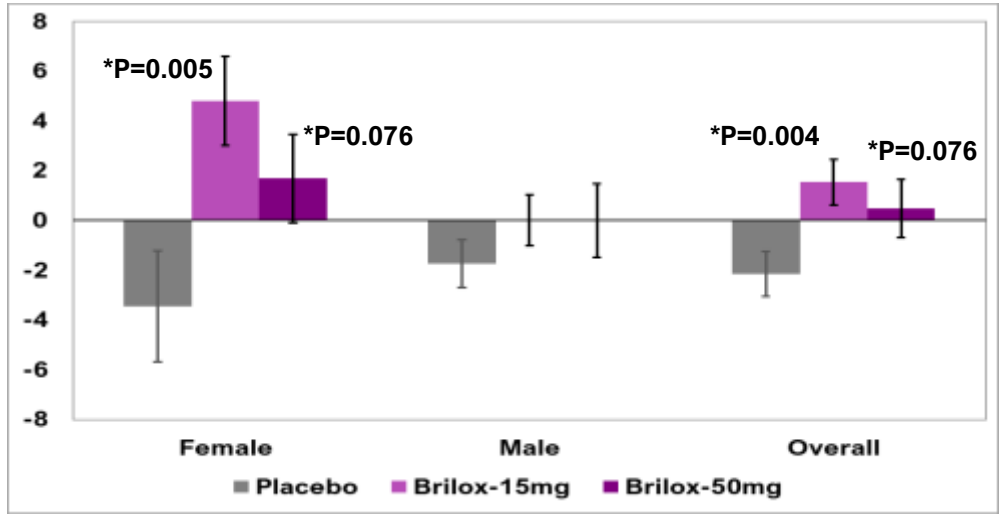
Brilaroxazine Phase 3 Study: Change in Lipids at Week 4

Clinically significant decrease in Cholesterol, LDL, and Increase in HDL in Brilaroxazine vs Placebo

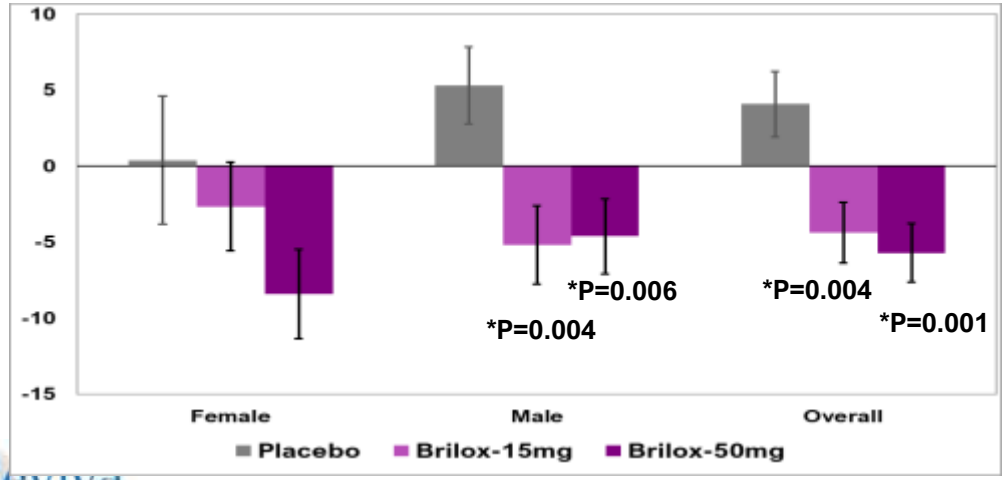
Decrease in total Cholesterol (mg/dL)



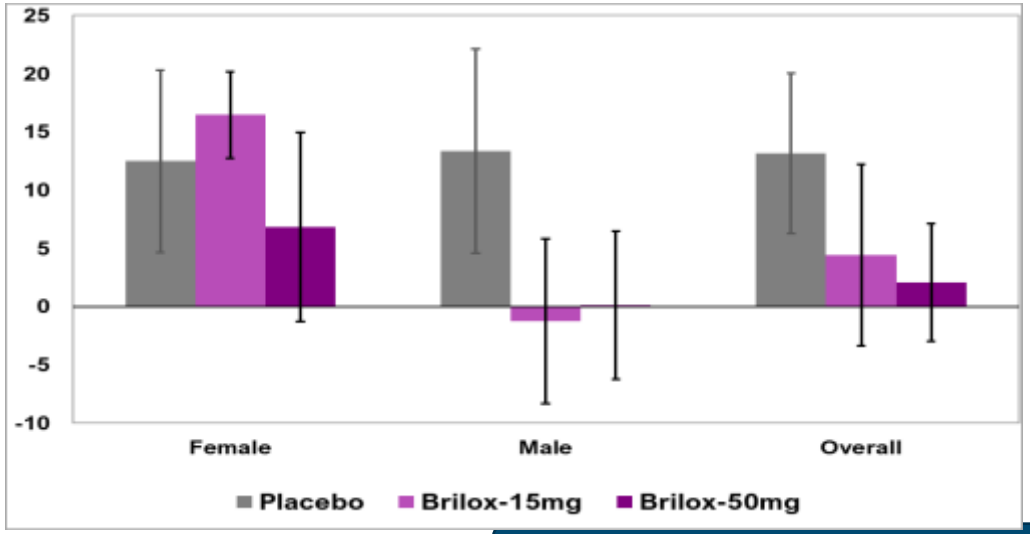
Increase in HDL (mg/dL)



Decrease in LDL (mg/dL)



Decrease in Triglycerides (mg/dL)



Brilaroxazine Phase 3 Study: Change in Prolactin Hormone at Week 4

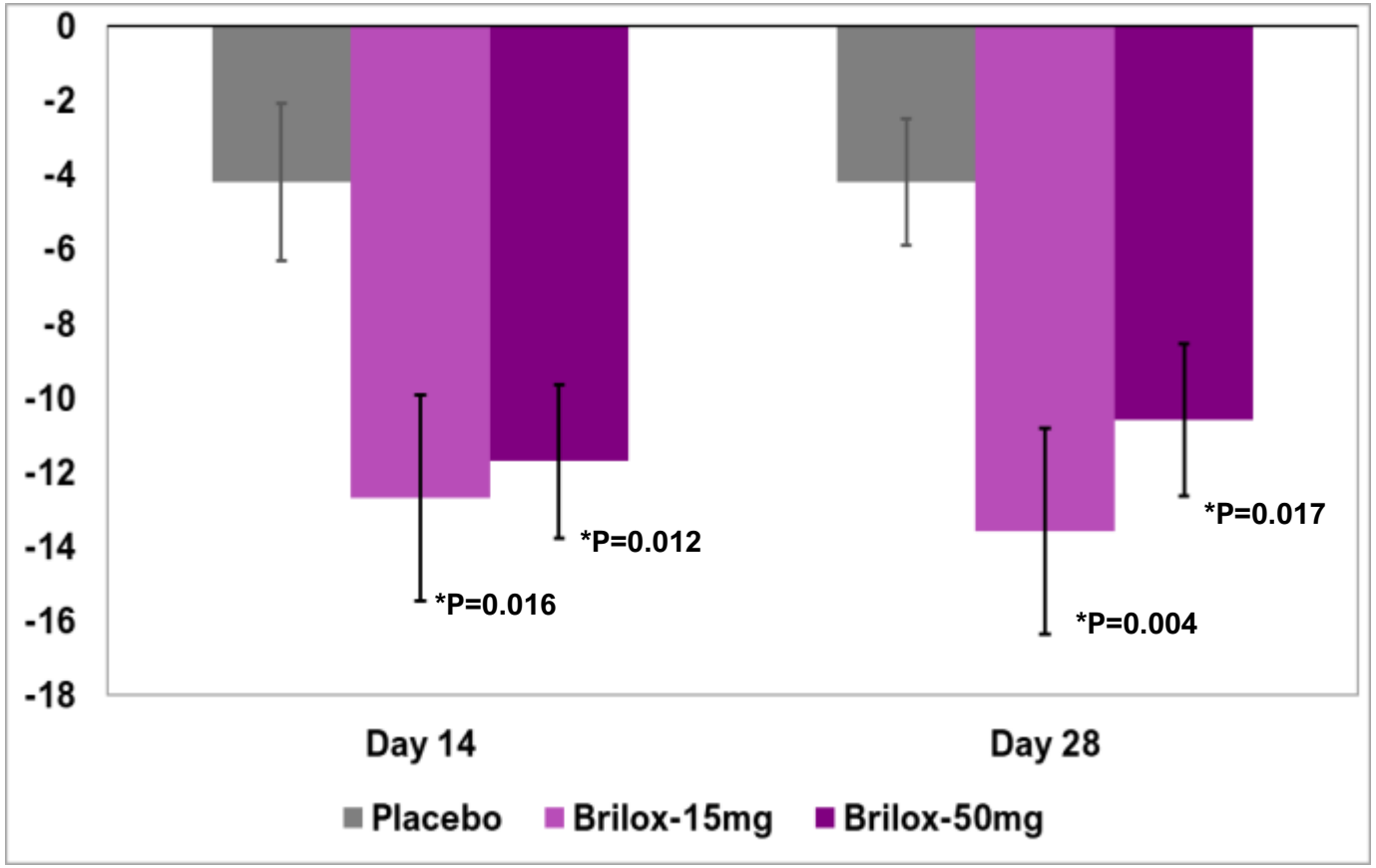
Clinically significant decrease in prolactin hormone levels in brilaroxazine (15 and 50mg) vs placebo

Decrease in Prolactin

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

---

- Hyperprolactinemia is common condition in patients with schizophrenia / psychiatric disorders
- Hyperprolactinemia is associate 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.



Borba VV et al. Front Immunol. 2028, 9:73; Rajkumar RP. Schizophrenia Research & Treatment 2014:175360.

Brilaroxazine Phase 3 Study: Change in Thyroid Hormones at Week 4

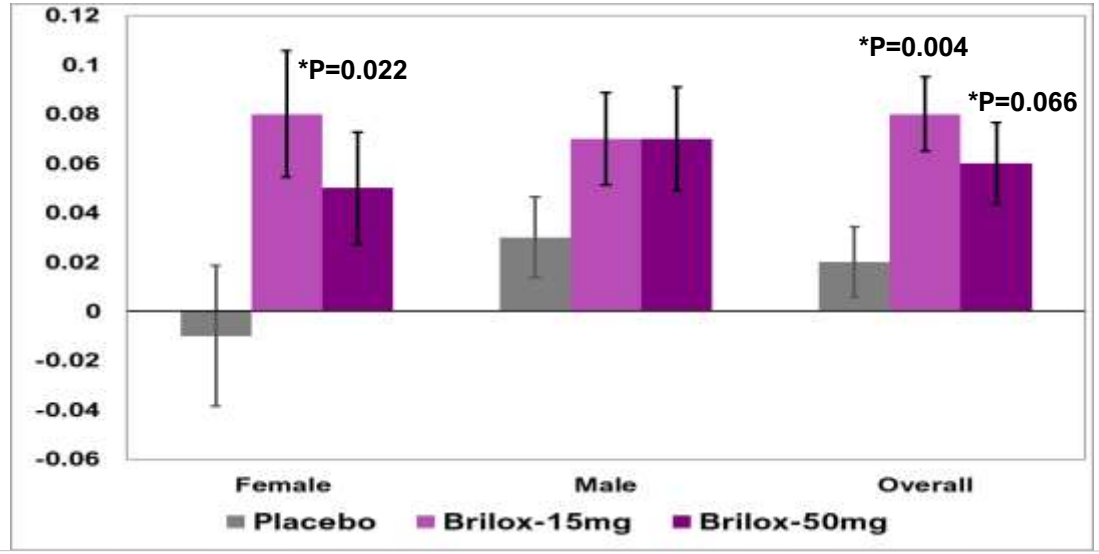
Clinically significant improvement in thyroid hormone T3 in brilaroxazine vs placebo

Changes in T3 and T4

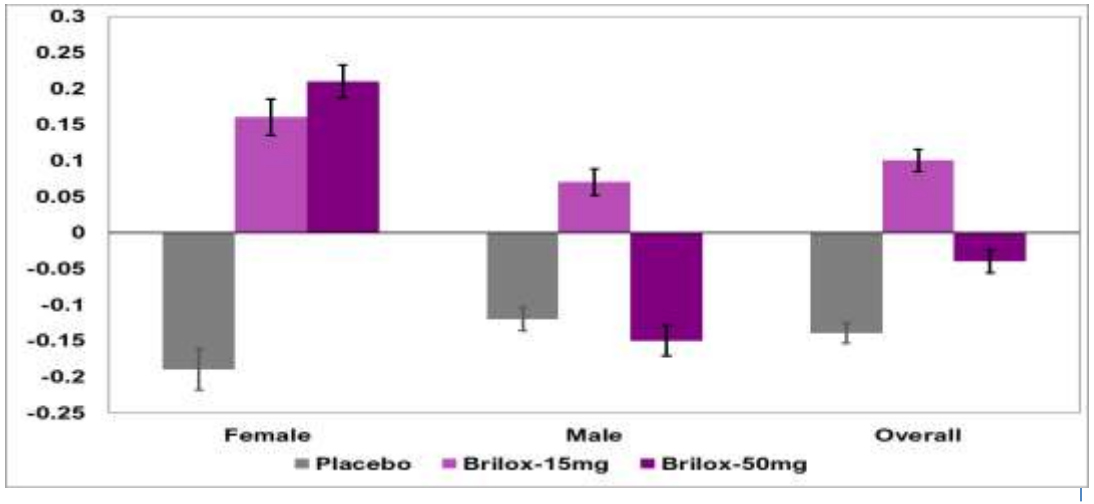
- Clinically significant improvement in T3 in brilaroxazine vs placebo
- Directional improvement in T4 in brilaroxazine vs placebo

- Schizophrenia patients show decreased levels of thyroid hormones T3 and T4
- Thyroid hormones are important for modulation of dopaminergic, serotonergic, glutamatergic, and GABAergic neurotransmitter system
- Hypothyroidism linked to negative symptoms, mood symptoms, cognitive deficits and metabolic syndrome
- Hypothyroidism linked to neuroinflammation and immune disorders
- A significant number of psychiatric patients suffer from immune disorders

Change in Thyroid Hormone T3 (ng/mL)



Change in Thyroid Hormone T4 (ng/mL)



Misiak B et al. Prog Neuropsychopharm & Biol Psych 2021, 111:110402; Santos NC et al. J Thyroid Res. 2012:569147

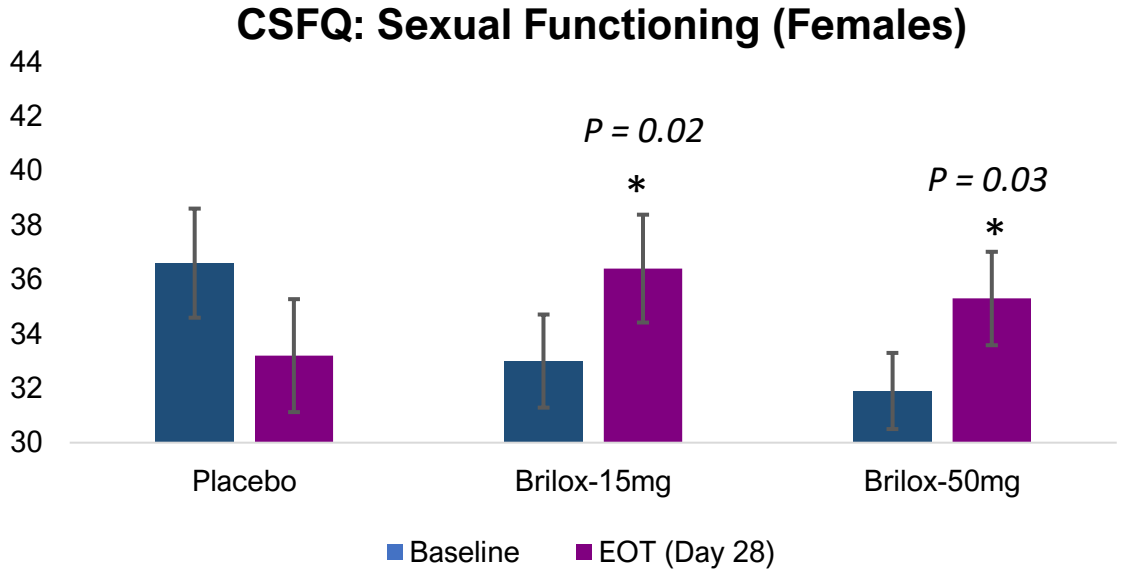
Sexual Functioning: CSFQ Score Changes in Phase 3 Trial at Week 4

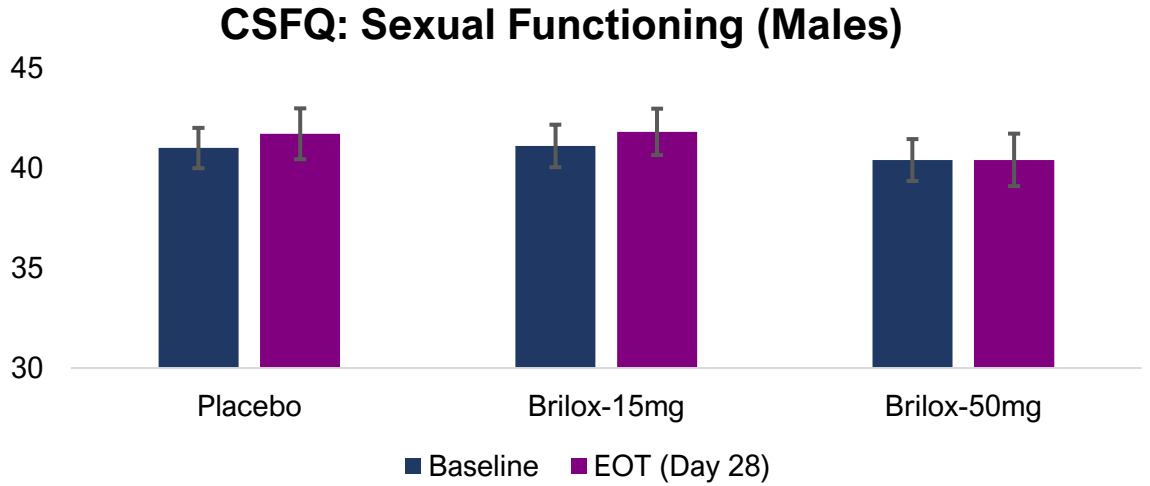
Significant Improvement in sexual functioning with Brilaroxazine vs Placebo (Females)

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;

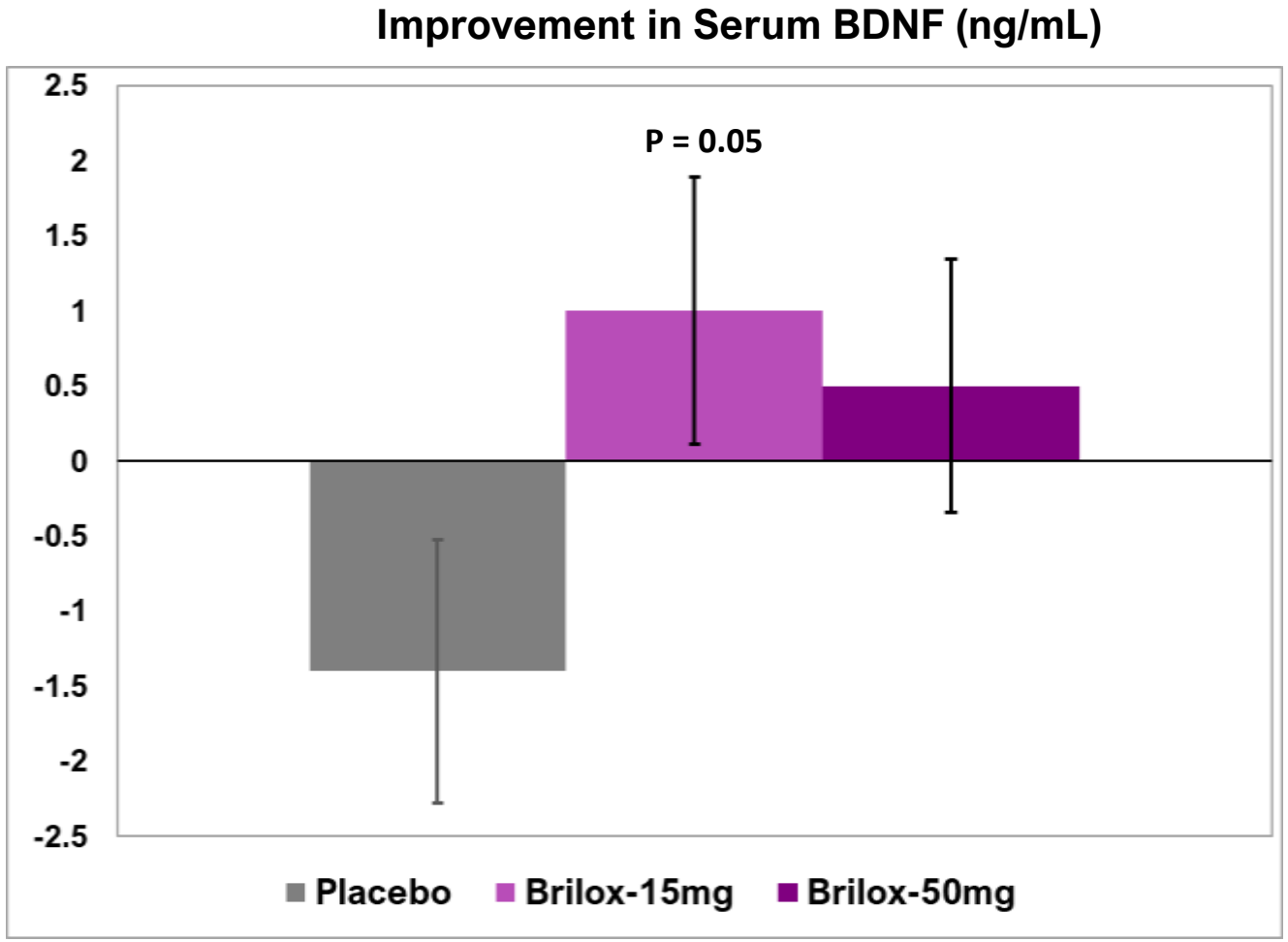
Brilaroxazine Phase 3 Study: Biomarker BDNF Changes at Week 4

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

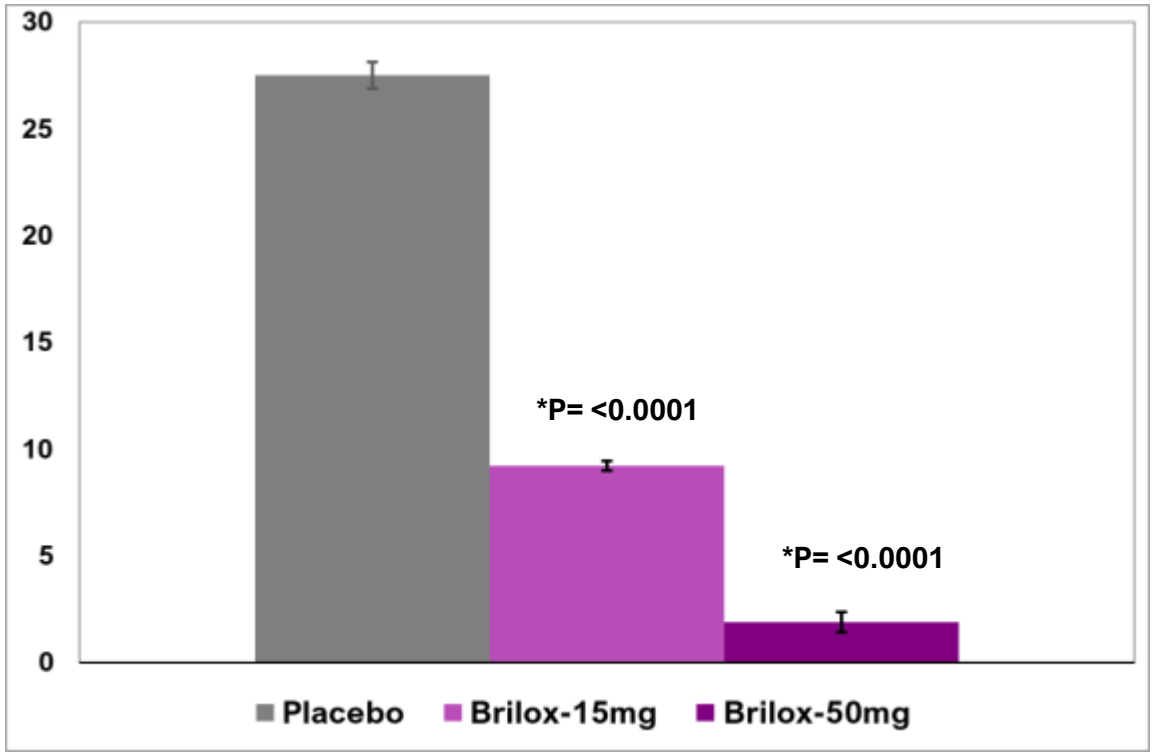


BDNF: Brain Derived Neurotrophic Factor. Nieto RR et al. Front Psychiatry 2021, 12: 662407; Xu H et al. Psychoneuroendocrinology 2019, 125:105121

Brilaroxazine Phase 3 Study: Change in Serum Cytokines at Week 4

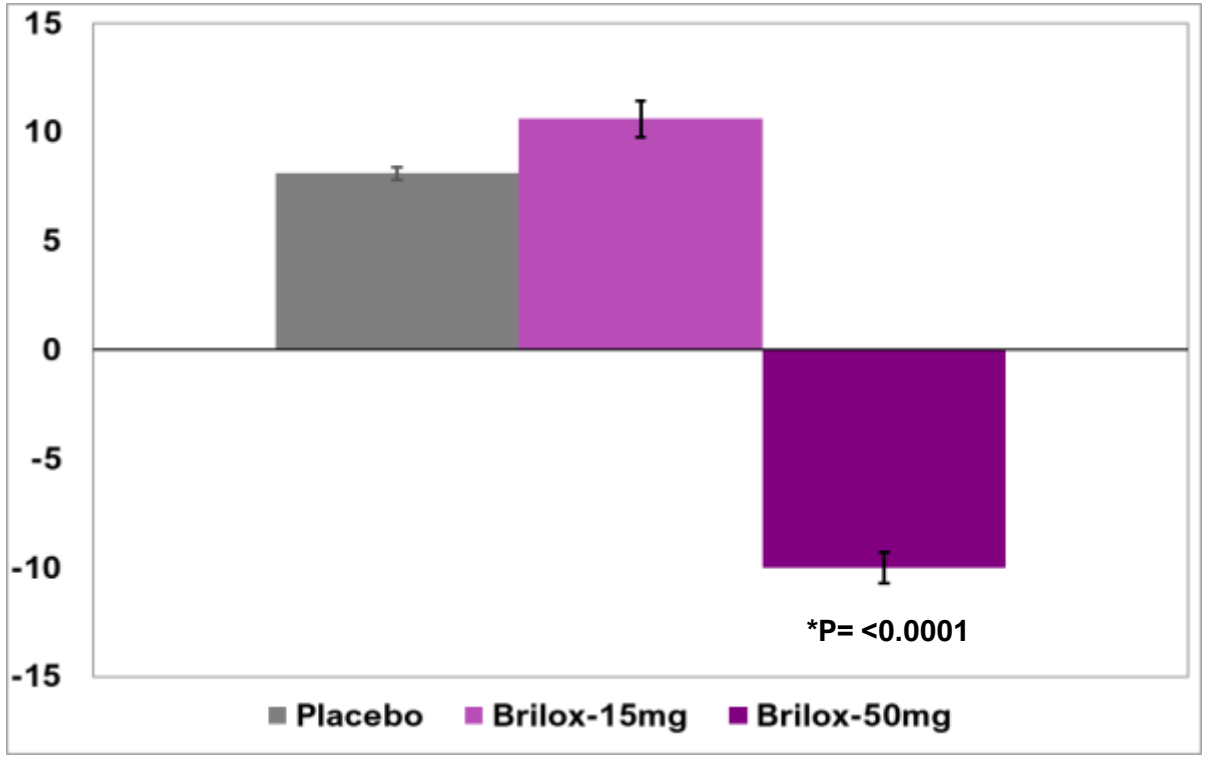
Clinically significant decrease in IL-8 and IFN-γ-IP-10 in Brilaroxazine 50 mg vs Placebo

Decrease in Proinflammatory Cytokine IL-8 (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)

Change in Proinflammatory Cytokine IFN-γ IP-10 (ng/mL)



- Interferon gamma (IFN-γ) inducible protein, IP-10 is a proinflammatory cytokine. IFN-γ has also been considered a target for cytokine-based immunotherapy in schizophrenic patients (Reale M et al. Front Psychiatry 2021, 12:536257)

Brilaroxazine Phase 3 Study: Change in Serum Chemokines at Week 4

Clinically significant decrease in MIP-1 in Brilaroxazine vs Placebo

Chemokine MIP-1

- Significant decrease in pro-inflammatory chemokine macrophage inflammatory protein MIP-1 in brilaroxazine (15mg, 50 mg) vs placebo.

- Elevated level of MIP-1 found in schizophrenia patients

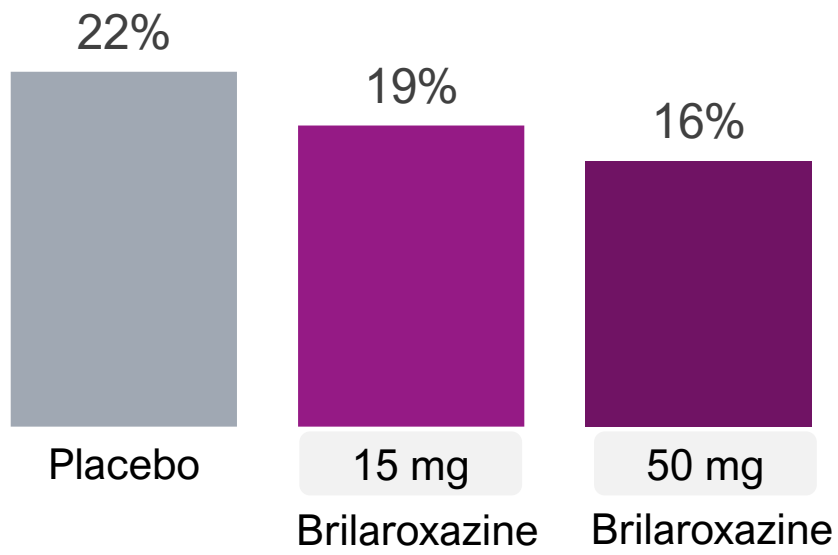
Decrease in Proinflammatory Chemokine MIP-1 (ng/mL)

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

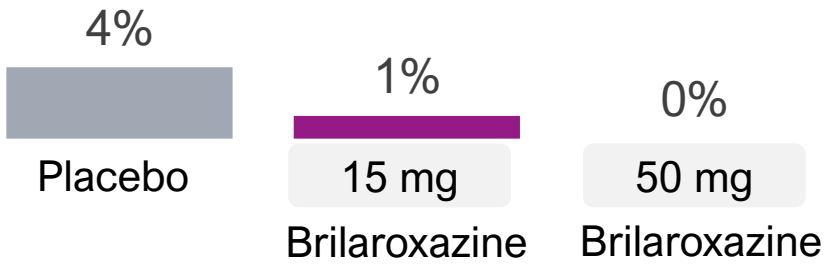
RECOVER Trial Discontinuation Rates: Brilaroxazine Vs. Placebo

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

Discontinuation Rate



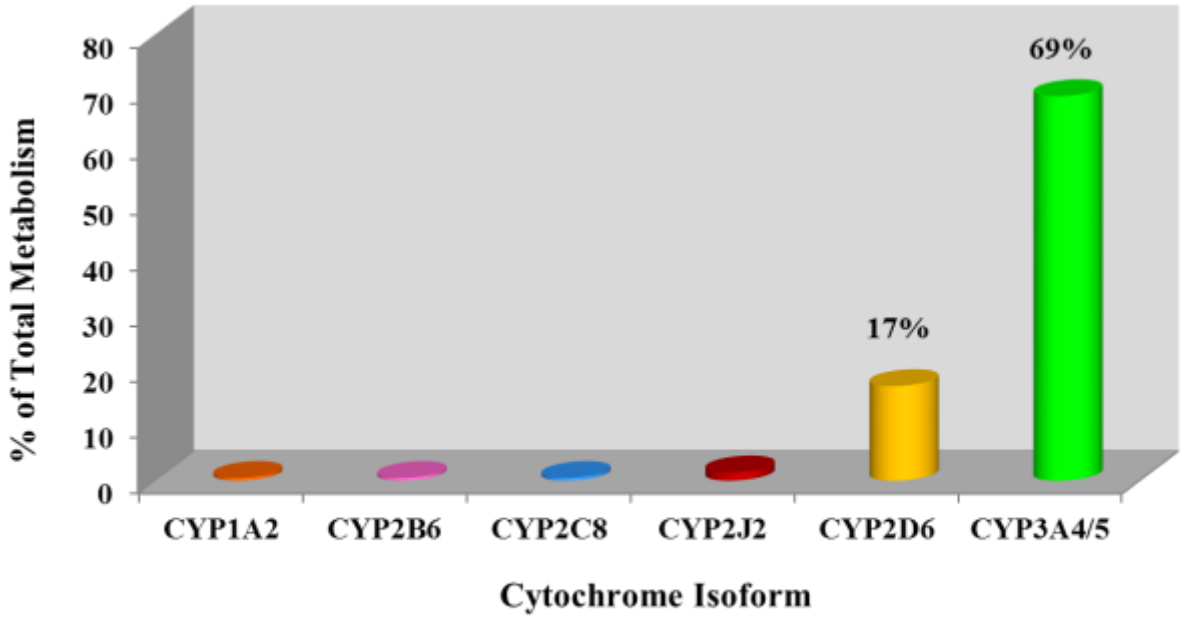
Discontinuation Due to Side Effects



ADME-PK Profiles: Brilaroxazine (RP5063) vs Approved Antipsychotics

Drug	Metabolism Major Path	Metabolite Activity (T1/2)
Brilaroxazine[1] In clinical development	CYP3A4/A5	Inactive
Aripiprazole	CYP2D6	Active (120h)
Lurasidone	CYP3A4	Active (7.5h)
Olanzapine	CYP1A2	Inactive
Risperidone	CYP2D6	Active (20h)
Quetiapine	CYP3A4	Active (12h)
Cariprazine	CYP3A4	Active (2-3 weeks)
Brexpiprazole	CYP3A4	Active (86h)
Clozapine	CYP1A2	Active (22h)

Brilaroxazine In vitro Metabolism Profile



- FDA has indicated no DDI studies for CYP2D6 are necessary

(1) Bhat L. et al, CYP3A inhibition and induction exert limited effects on brilaroxazine pharmacokinetics, ASPET Conference in May 18-21, 2023, Poster: #376,

Lower Drug-Drug Interactions (DDIs) with Brilaroxazine vs. Standards of Care

DDIs and polypharmacy alter plasma drug concentrations, and can impact efficacy and side effect profiles of a drug[11]

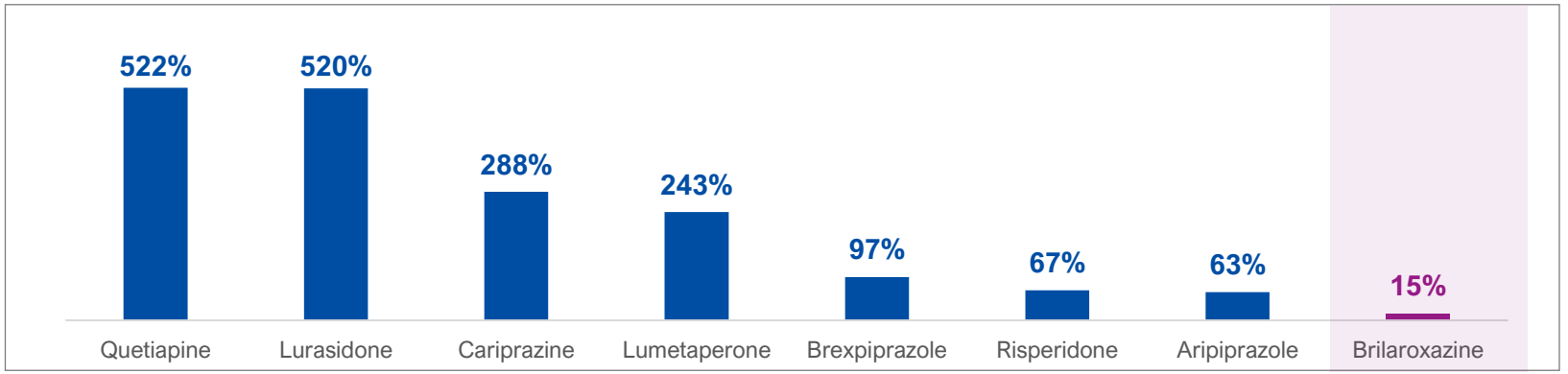
~50% of prescribed drugs and over 25% of approved antipsychotics are known to cause drug interactions in the presence of a strong CYP3A4 inhibitor drug

Change in drug concentration with a CYP3A4 Inhibitor

Antipsychotic	Fold increase vs brilaroxazine
Brilaroxazine	--
Aripiprazole	4.2x
Risperidone	4.5x
Brexpiprazole	6.5x
Lumetaperone	16.2x
Cariprazine	19.2x
Lurasidone	34.7x
Quetiapine	34.8x

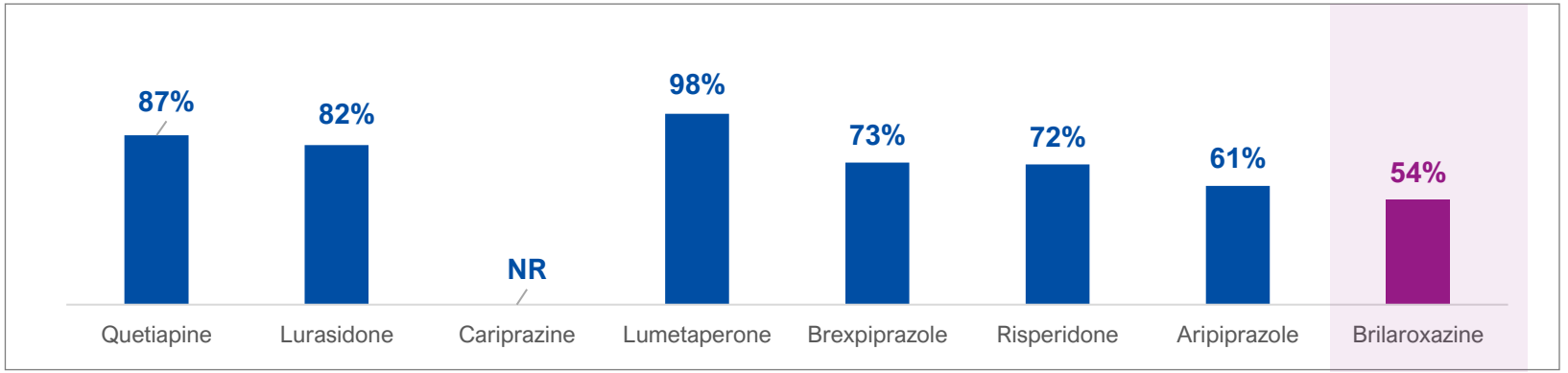
*Olanzapine[9] not evaluated; metabolized by CYP1A2[10]

% Increase in drug concentration (AUC) with a **CYP3A4 Inhibitor**



Lower is better

% Decrease in drug concentration (AUC) with a **CYP3A4 Inducer**



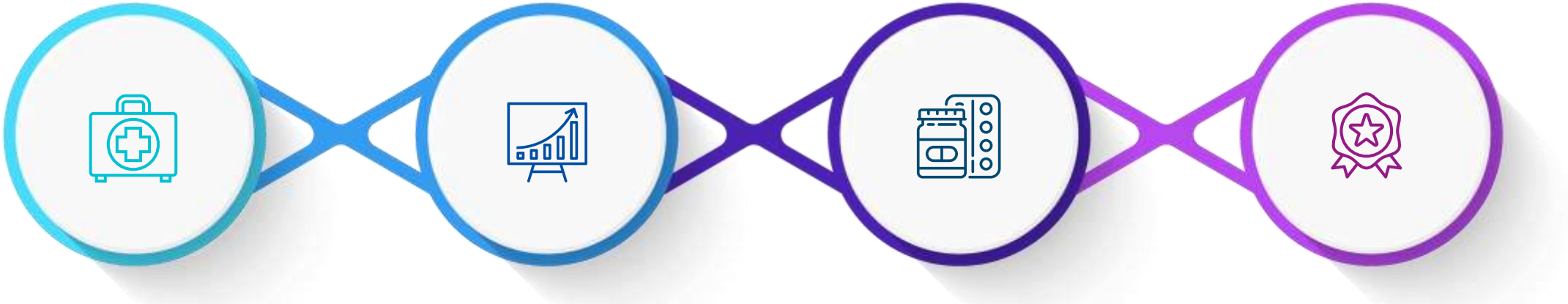
(1) Bhat L et al, ASPET 2023 (poster #376); (2) Aripiprazole (Abilify) NDA document, 2001; (3) Mahatthanatrakul et al, J Clin Pharm Thera 2007, 32(2):161-167 ; (4) Brexpiprazole (Rexulti) NDA document, 2014; (5) Lumetaperone (Caplyta) NDA document, 2018; (6) Cariprazine (Vraylar) NDA document 2014; (7) Pharmaceuticals 2020; (8) Quetiapine (Seroquel); Grim et al., Brit J Clin Pharm 2005, 61(1):58-69; (9) Olanzapine NDA document; (10) Vilckova et al., Onco Lett 2023, 25:85; (11) Bole B et al, Medicina 2023, 59:284. NR: not reported

RECOVER Trial Conclusion: Safety, Tolerability and Compliance

- Brilaroxazine is well tolerated with TEAs roughly comparable to placebo rates
  - Discontinuation rates due to side effects at both doses were lower than placebo
- Lipid profile moves in 'healthy direction': decreases in cholesterol, LDL and triglycerides and increase in HDL
- Thyroid T3 and T4 increase[1]; prolactin levels significantly decrease
  - Potentially contributing to improved sexual function in women
- Weight gain was not significantly different than placebo
- USA reported higher weight gain than Asia/Europe: Possible differences in healthcare/social systems and institutional feeding practices might contribute to modest weight increase
  - ~ zero weight gain in India and Bulgaria
- Longer term outpatient studies will better estimate brilaroxazine's effects on weight, lipids, and thyroid
- Remarkably low neuroleptic side effects <1% akathisia and <1 % EPS
- Preliminary evidence of anti-inflammatory action and potential for neurotrophic effects in schizophrenia
- No meaningful interactions with CYP2D6 and CYP3A4 inhibitors

[1]no statistically significant difference

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

Reviva Clinical Development Pipeline

Program		Prioritized Target Indications*	Development Phase: Discovery	Preclinical	Phase I	Phase II	Phase III
Brilaroxazine – Serotonin/ dopamine modulator (NCE)	Neuropsychiatric	Schizophrenia					
		Bipolar Disorder					
		Major Depressive Disorder					
		Attention Deficit Hyperactivity Disorder					
	Inflammatory	Pulmonary Arterial Hypertension					
		Idiopathic Pulmonary Fibrosis					
		Psoriasis (topical gel)					
RP1208 – Triple reuptake inhibitor (NCE)		Depression					
		Obesity					

*Opportunity to expand into other indications including Parkinson's Psychosis and Alzheimer's (Psychosis/agitation)

Reviva Pharmaceuticals Holdings, Inc.

General Inquiries

info@Revivapharma.com

Business Inquiries

busdev.rp@Revivapharma.com

Investor Relations Contact

IR@Revivapharma.com

Q&A