REVIVA PHARMACEUTICALS HOLDINGS, INC. (NASDAQ: RVPH)

Corporate Presentation, December 2024

Reviva PHARMACEUTICALS

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 planned 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 and expenses, planned or intended additional trials and the timing thereof, planned or intended regulatory submissions and the timing thereof, the timing of availability of additional data or initiation of additional trials, 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, 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.

Late-stage Clinical Program with Differentiated Profile in Schizophrenia

Brilaroxazine – A once-daily, serotonin-dopamine signaling modulator with potential to reduce neuroinflammation

De-risked Program with Multiple Successful Trials

Positive Phase 3 trial in N = 411 schizophrenia patients

Positive Phase 2 trial in N = 234 schizophrenia patients

Completed most non-clinical activities supporting NDA

Compelling Topline Phase 3 RECOVER-1 Data

Primary Endpoint: 10.1-point reduction in PANSS total score in brilaroxazine 50 mg vs placebo

Statistically significant results on all secondary endpoints including reduction in positive symptoms, negative symptoms, and social cognition deficits

Near-term Registration Pathway

Long-term clinical safety trial topline readout in December 2024

RECOVER-2; Registrational Ph3

- Expected initiation in Q1 2025
- Topline readout expected in Q1 2026

Potential NDA filing in Q2 2026

NDA: New Drug Application

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)

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

(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

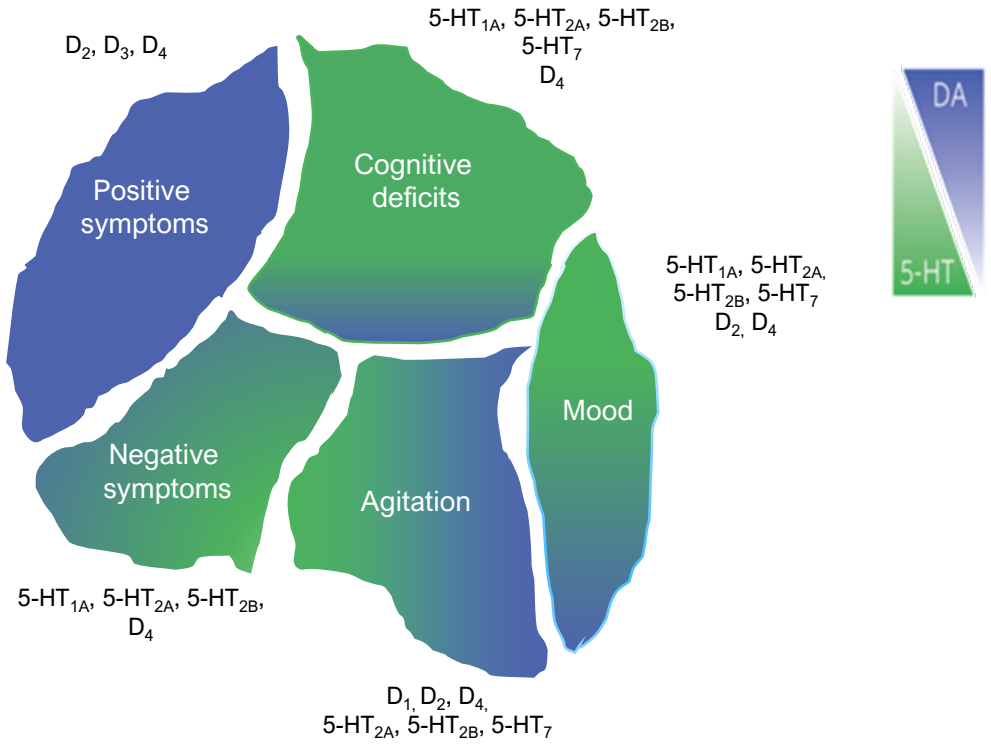
Schizophrenia: Common Psychiatric Condition With Multiple Symptom Domains

Primarily driven by dysfunctional serotonin and dopamine signaling

- Affects ~1.1% of the world's population
  - ~ 24 million people globally
  - ~ 3.5 million people in USA
- Schizophrenia is not a single disease rather a mix of heterogenous psychotic symptoms with varying degrees of severity
- Most patients requires lifelong treatment
- ~30% of patients are treatment refractory
- Neuroinflammation is implicated as major contributing factor to schizophrenia
- Negative symptoms and nonadherence to treatment are the top unmet needs

Major Symptom Domains of Schizophrenia

Primary target receptors implicated in the pathophysiology

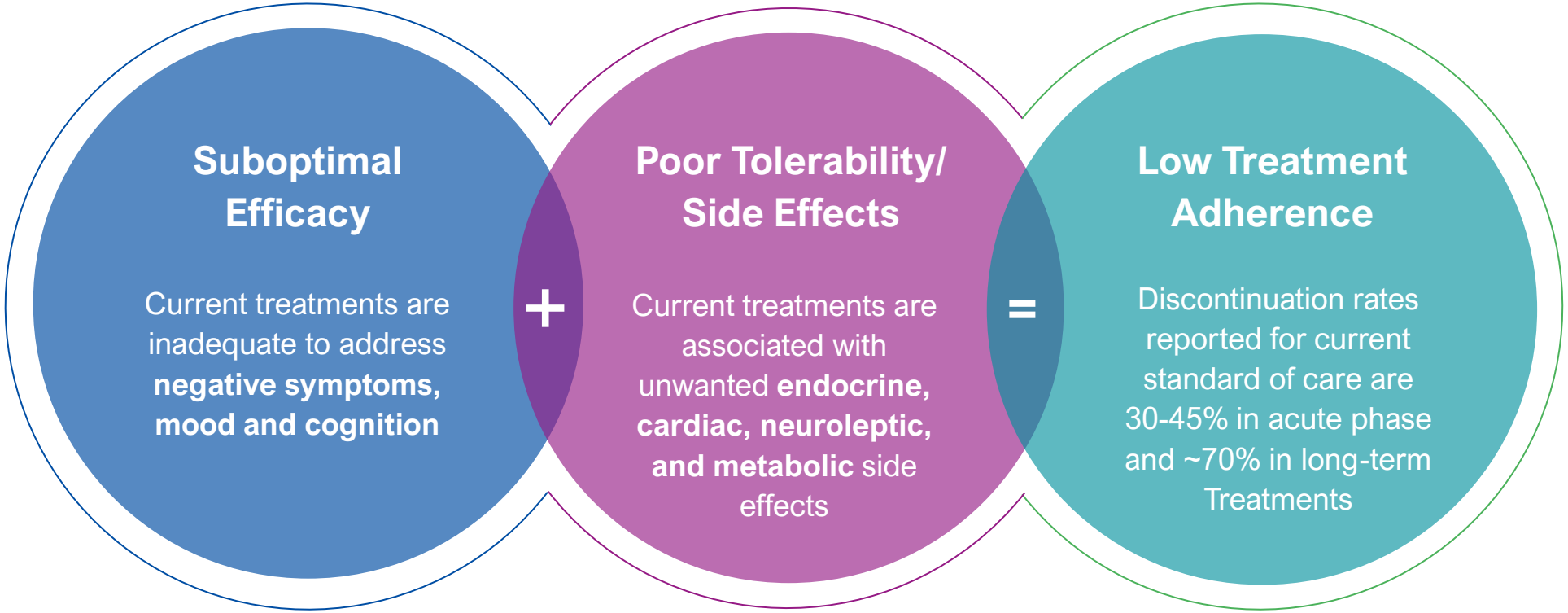


Negative symptoms include social withdrawal, avolition, alogia, anhedonia, disorganized behavior, and poor self-care.

Source: Delveinsight Market Research 2023; 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..

No Current Therapies Address all Needs of Patients with Schizophrenia

Suboptimal efficacy and side effects limit long-term use due to high rates of discontinuation and non-compliance



Brilaroxazine Differentiation

Statistically significant results on positive symptoms, negative symptoms and cognition factor

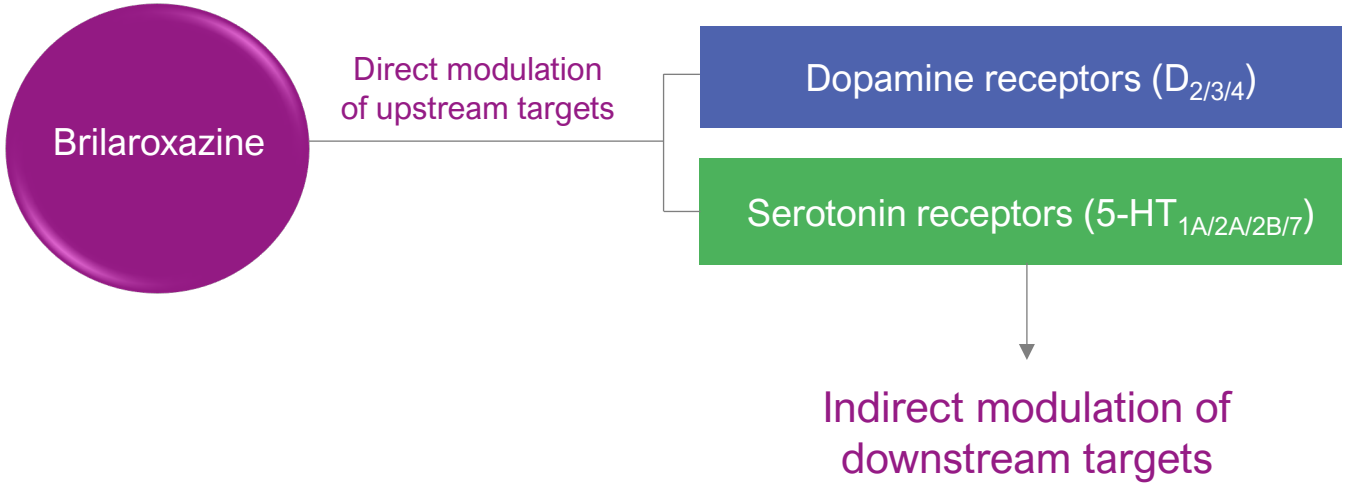
No significant change in body weight & blood glucose levels; improvement in lipid levels, or endocrine hormones

Discontinuation rate of 12-16% (lower than placebo) in acute phase treatment trials

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

Brilaroxazine: Novel Serotonin Dopamine Signaling Modulator

Multi-faceted direct and indirect activities on critical pathways implicated in schizophrenia



Brilaroxazine Receptor Activities		
High (Ki, nM)* **($5\text{-}HT_{2B} > D_2$)**	Dopamine D_2	0.4
	Dopamine D_3	3.7
	Dopamine D_4	6
	Serotonin 5-HT_{1A}	1.5
	Serotonin 5-HT_{2A}	2.5
	Serotonin 5-HT_{2B}	0.19
	Serotonin 5-HT_7	2.7
Moderate (Ki, nM)	Nicotine $\alpha_4\beta_2$	36.3
	Serotonin 5-HT_6	51
Weak or no significant activity	No significant activities at therapeutic dose for off-targets 5-HT_{2C}, $\alpha_{1,2,}$ and $M_{1\text{-}4}$ implicated in cardiometabolic, metabolic, or GI side effects	

Inflammatory cytokines

Implicated in neuroinflammation

Nicotinic receptors

Implicated in positive symptoms and cognition

NMDA/Glycine receptors

Implicated in negative symptoms and cognition

GABA receptors

Implicated in mood

**partial agonists for $D_{2,3,4}$ and 5-$HT_{1A/2A}$ receptors*

Bhat L, et al. Medical Research Archives 2023, 11(4):3834; Rajagopal et al, Behavioral Brain Research 2017, 332;180-199

Clinical Trial Results

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 announced in December 2024	Expected initiation in Q1 2025; Topline readout expected in Q1-2026

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 NDA filing is planned for Q2 2026

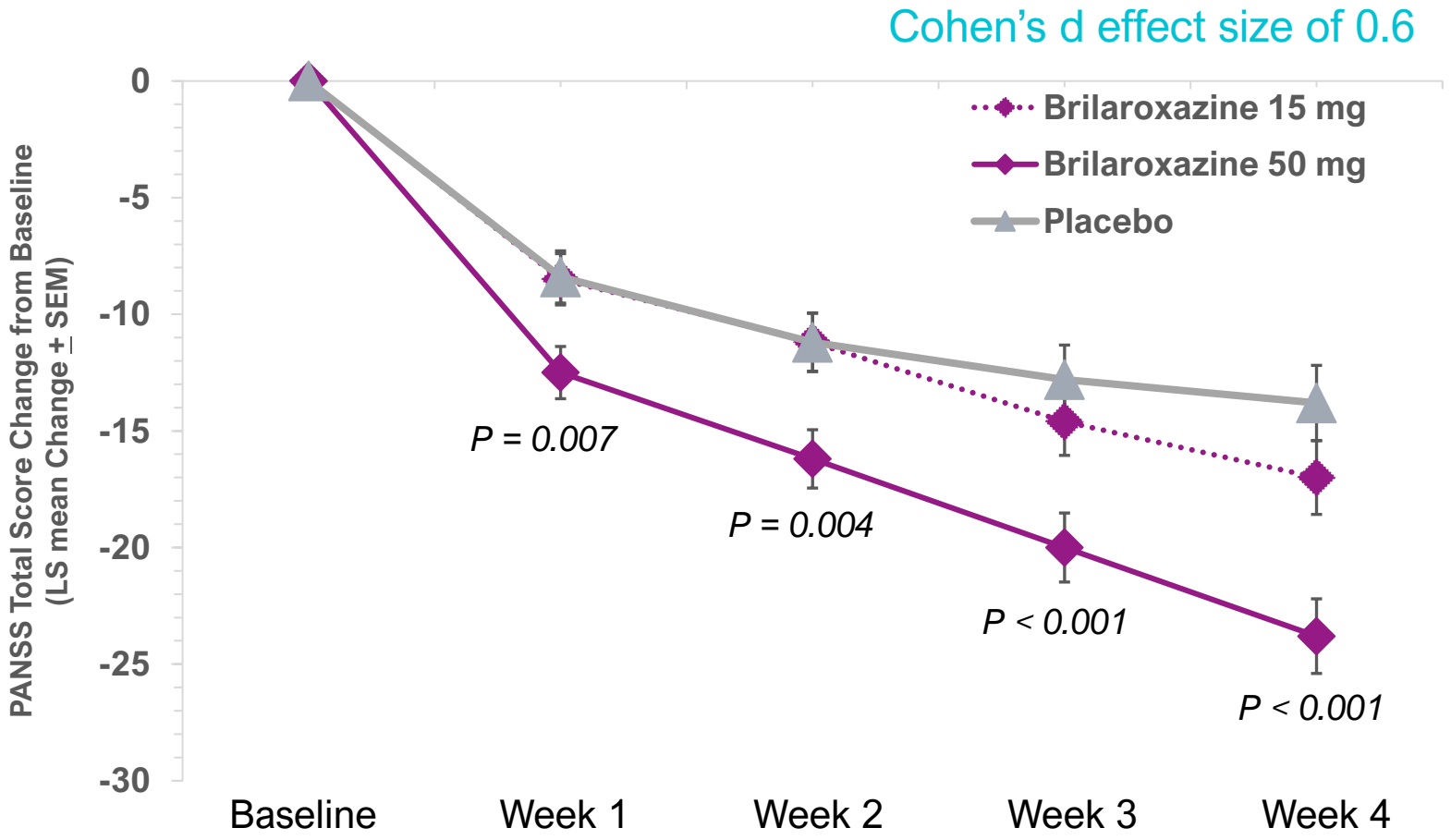
OLE: Open Label Extension

RECOVER-1 Trial Primary Endpoint: PANSS Total Score

10.1-point reduction in PANSS total score vs. placebo, 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
- Separation for brilaroxazine 50 mg from placebo within a week
- Brilaroxazine 15 mg numerically separated from placebo
- Results further supported by biomarker data



PANSS: Positive and Negative Syndrome Scale

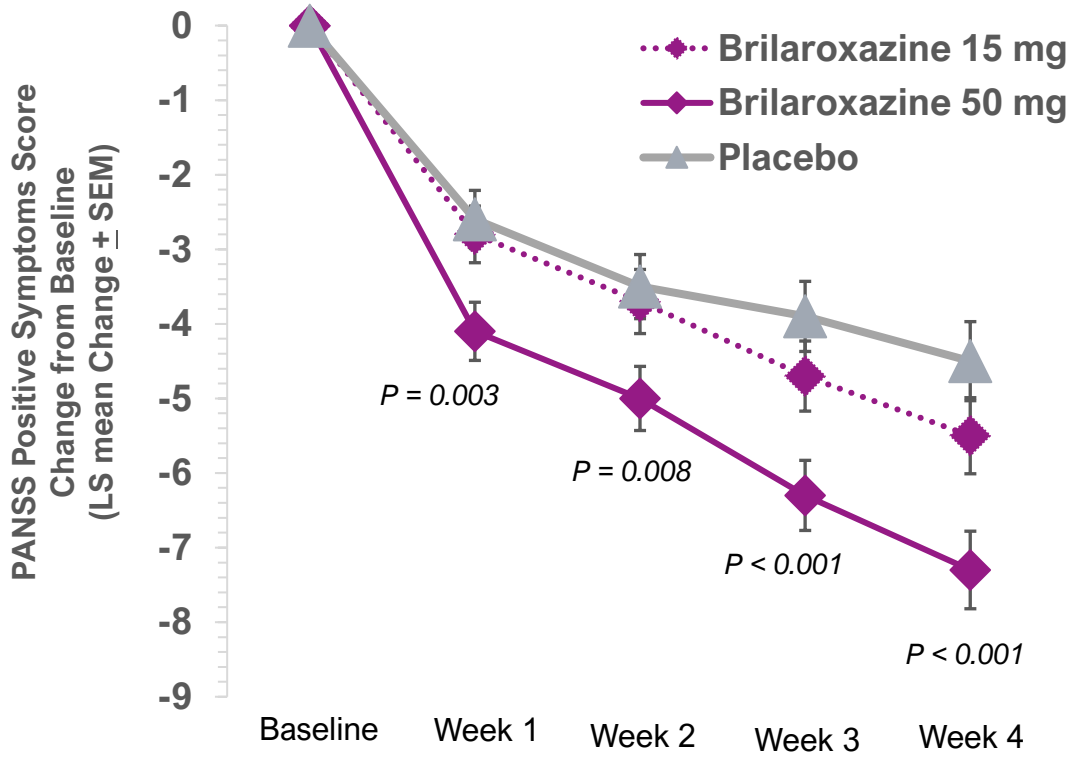
Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

RECOVER-1: Efficacy Endpoints Positive Symptoms and Agitation/Excitement

Significant decrease in positive symptoms & agitation/excitement in brilaroxazine 50 mg vs. placebo

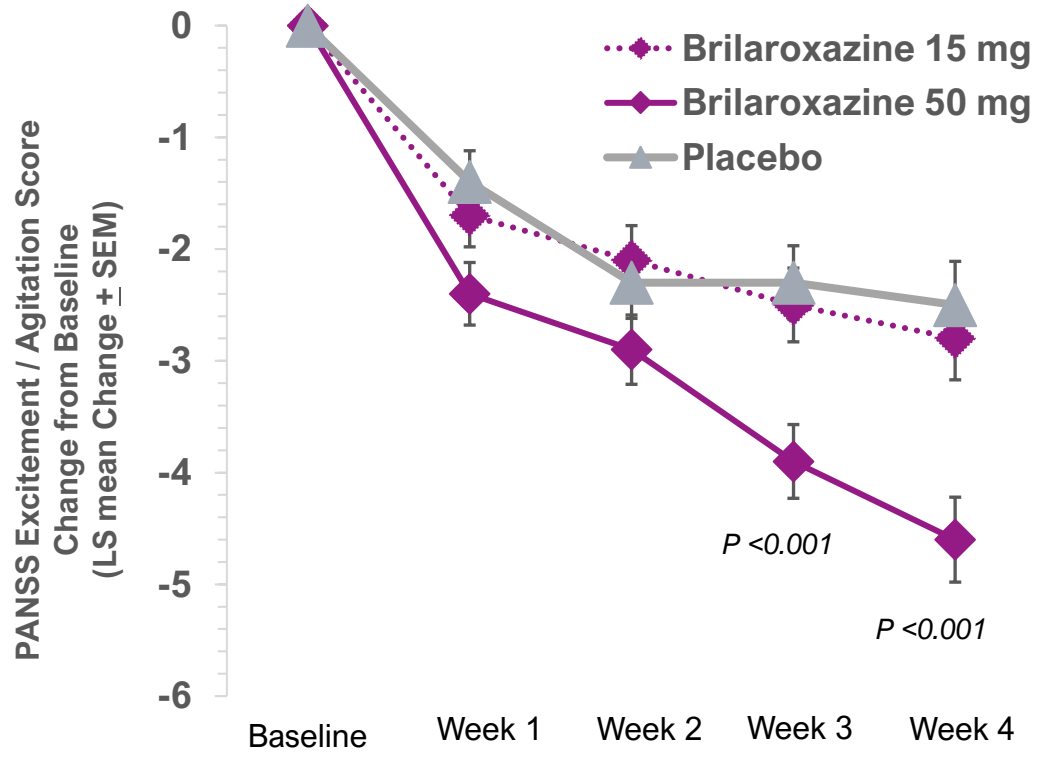
Decrease in Positive Symptoms

Cohen's d effect size of 0.5



Decrease in Agitation/Excitement Symptoms

Cohen's d effect size of 0.5



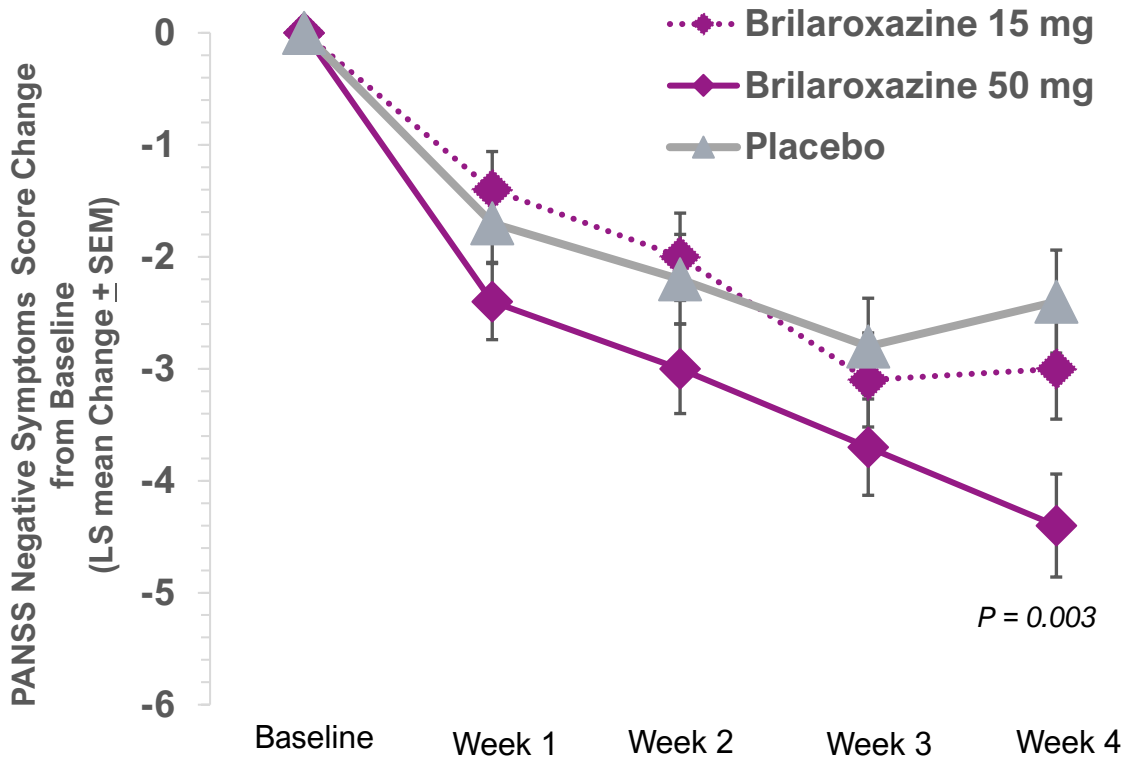
Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

RECOVER-1: Efficacy Endpoint Negative Symptoms

Significant reduction in negative symptoms in brilaroxazine 50 mg vs. placebo

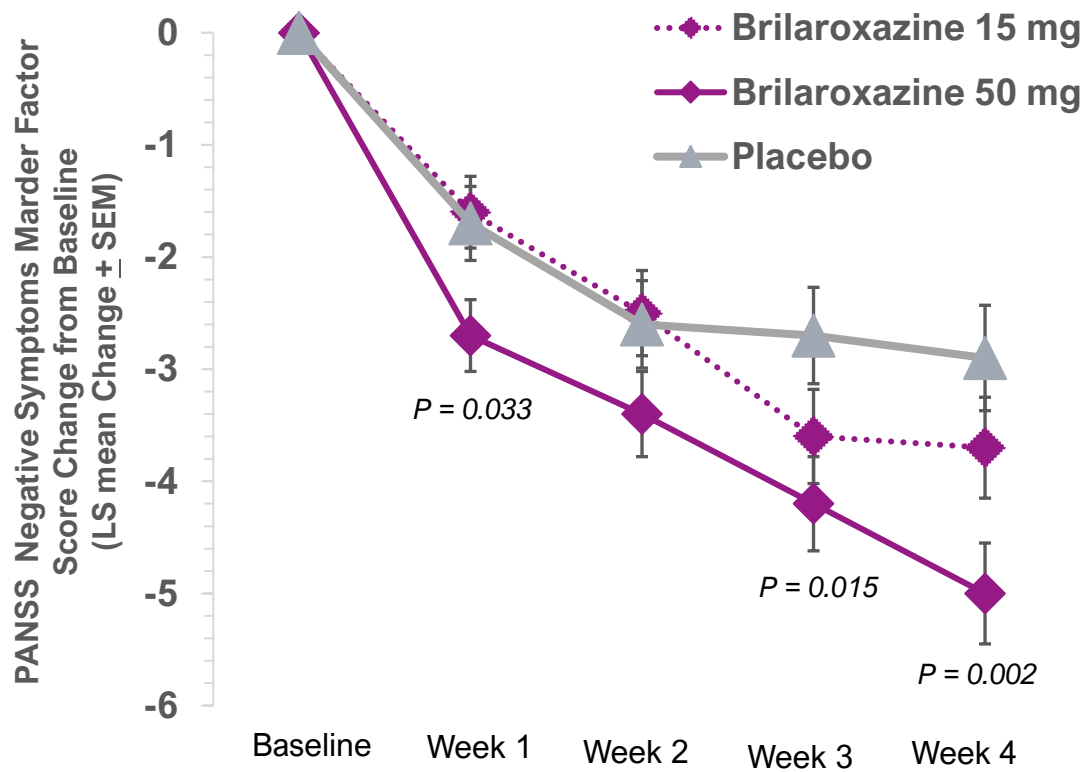
Decrease in Negative Symptoms

Cohen's d effect size of 0.4



Decrease in Negative Symptoms (Marder Factor)

Cohen's d effect size of 0.4



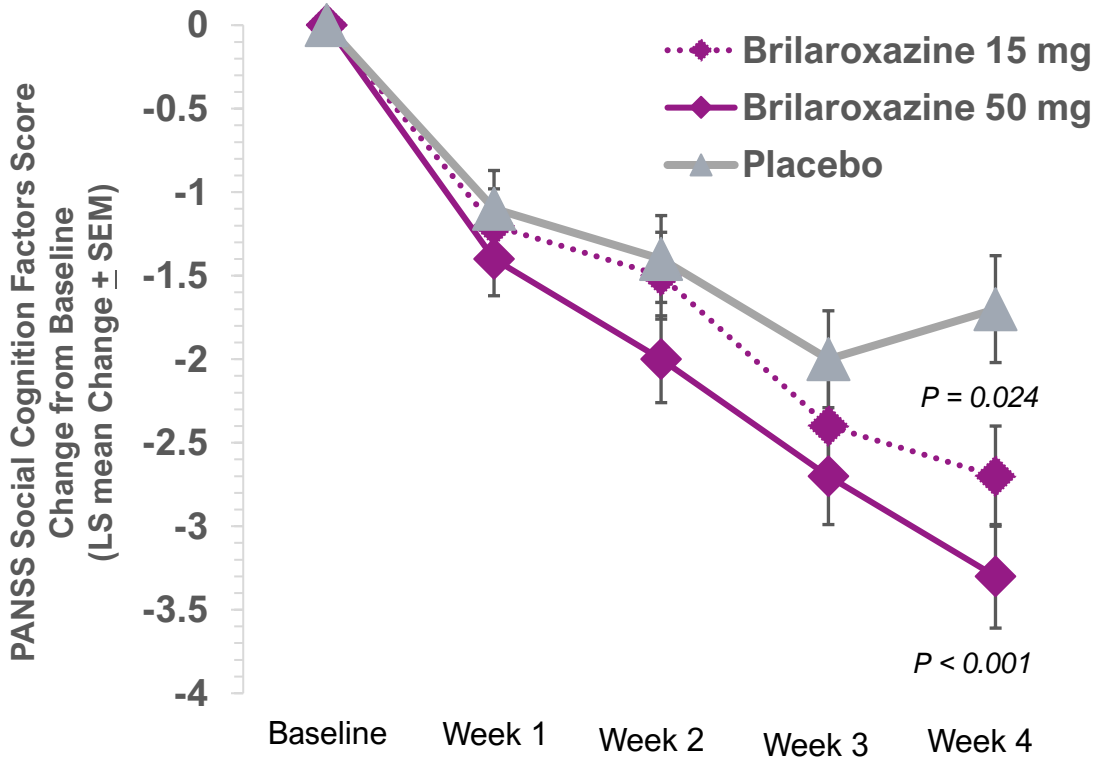
Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

RECOVER 1: Efficacy Endpoints Social Cognition and Social Functioning

Significant decrease in social cognition deficits and improvement in personal & social performance

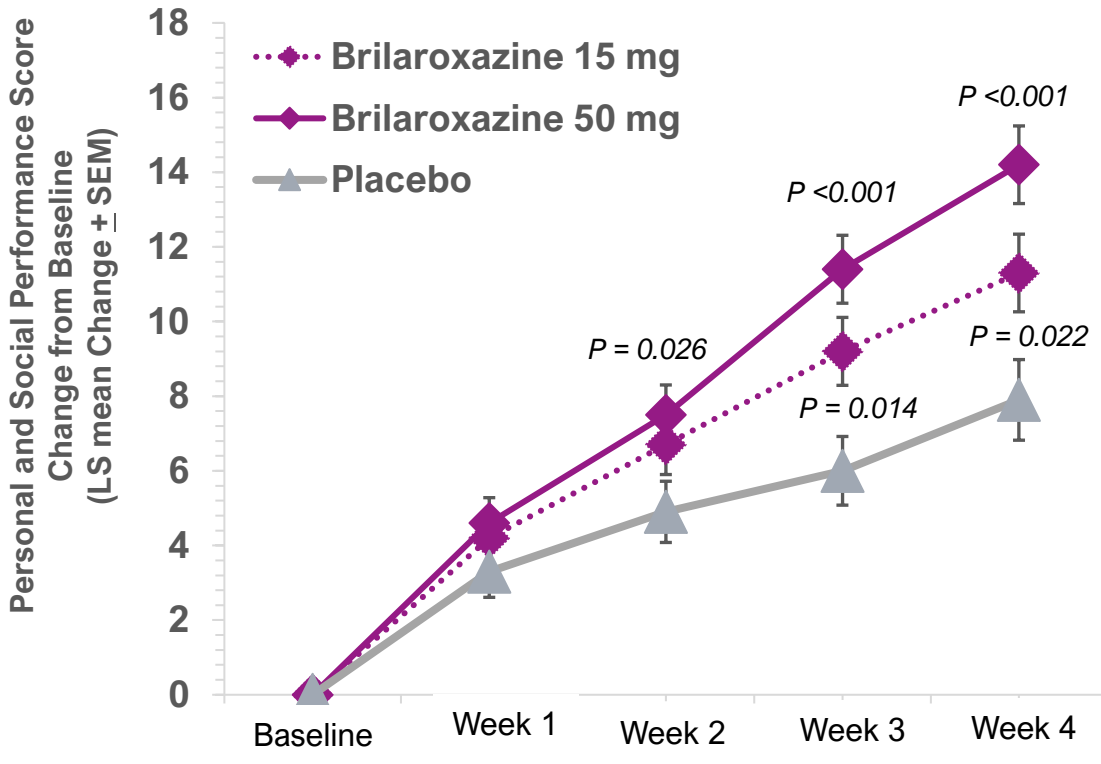
Decrease in Social Cognition Deficits

Cohen's d effect size of 0.5



Improvement in Personal & Social Performance

Cohen's d effect size of 0.5



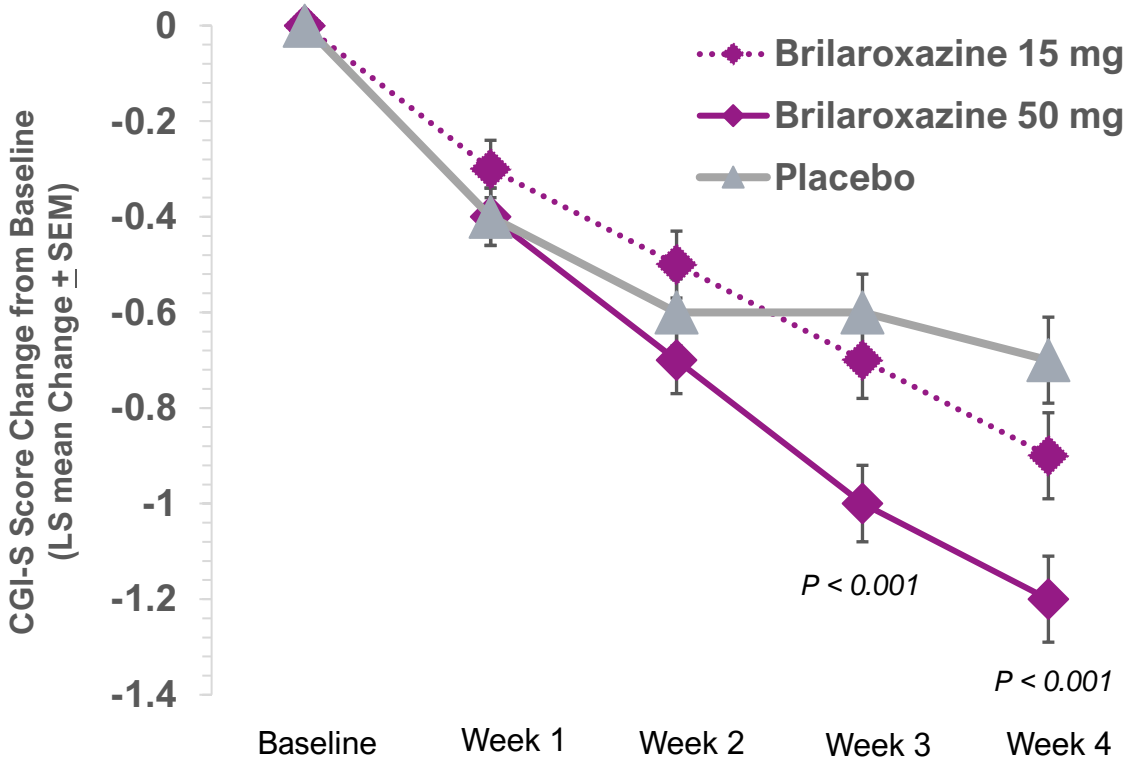
Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)

RECOVER-1: Efficacy Endpoint CGI-S Scores

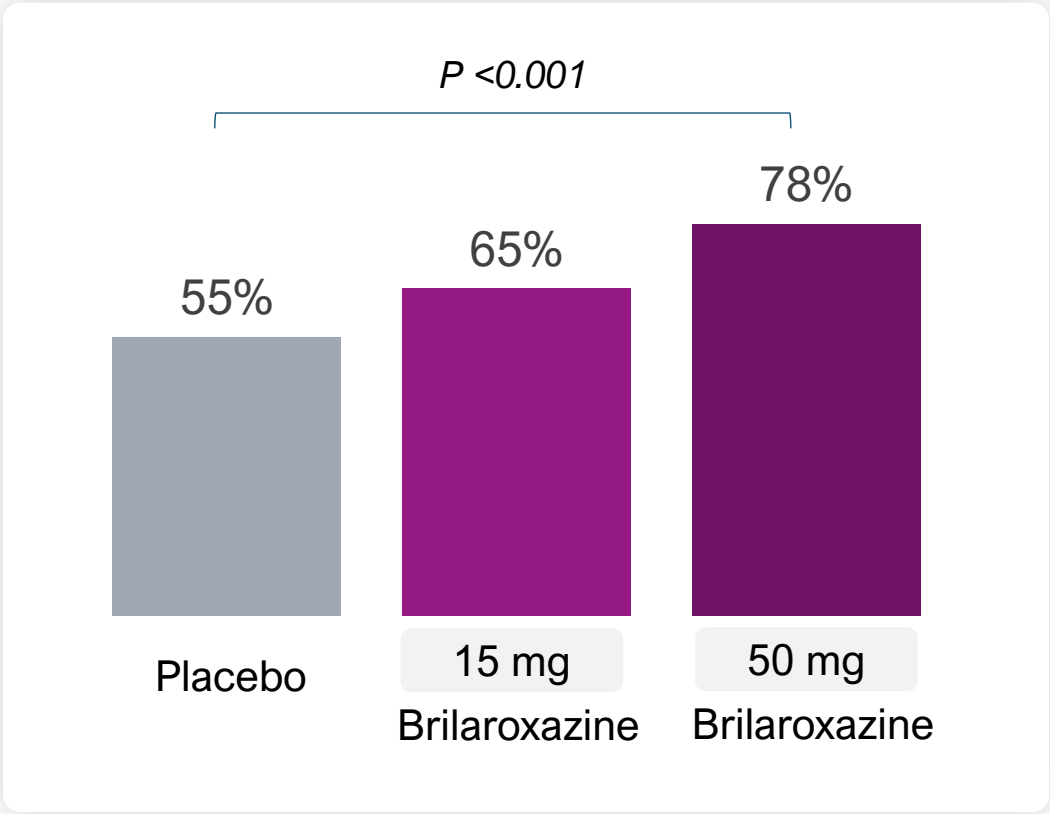
≥1-Point reduction in CGI-S score in brilaroxazine 50 mg vs. placebo

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)

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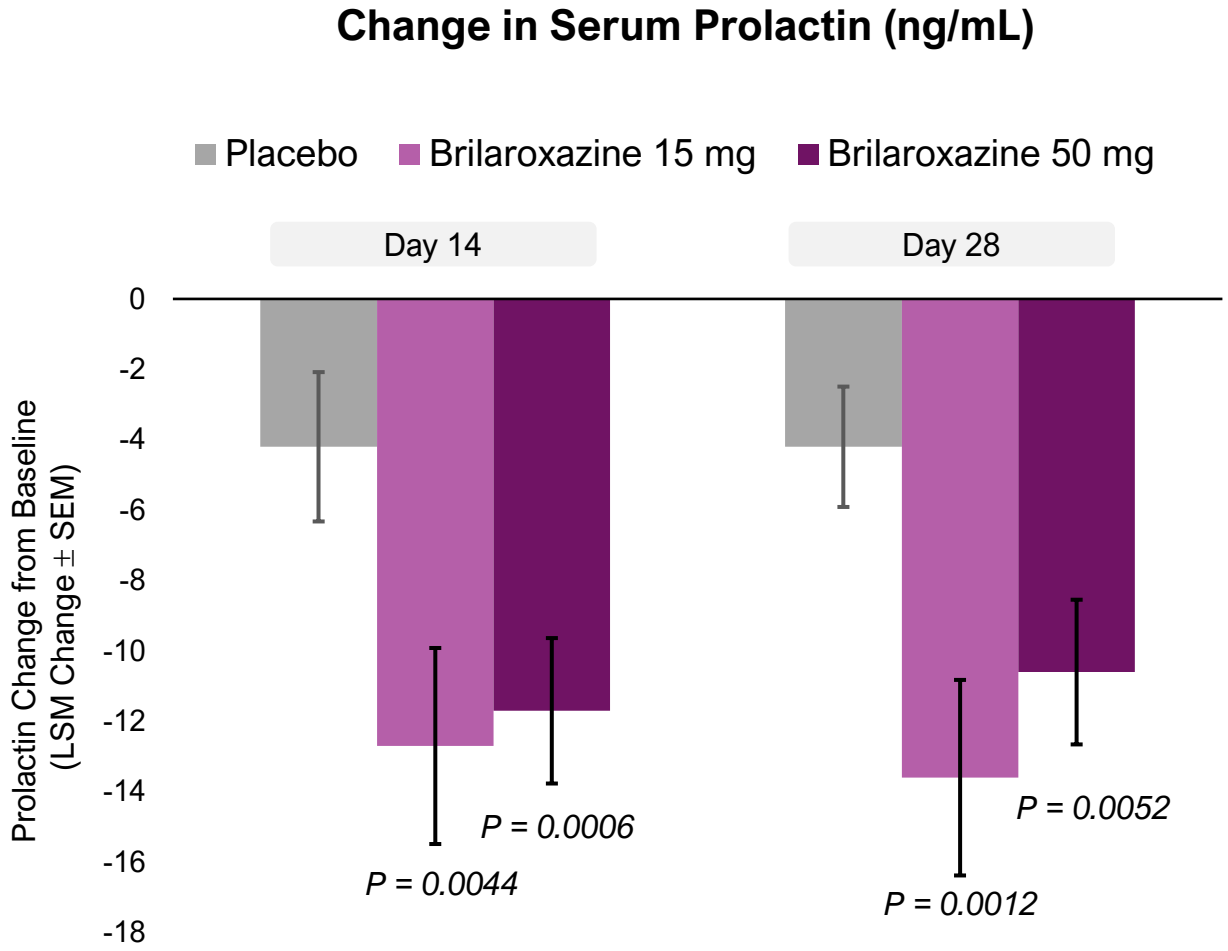
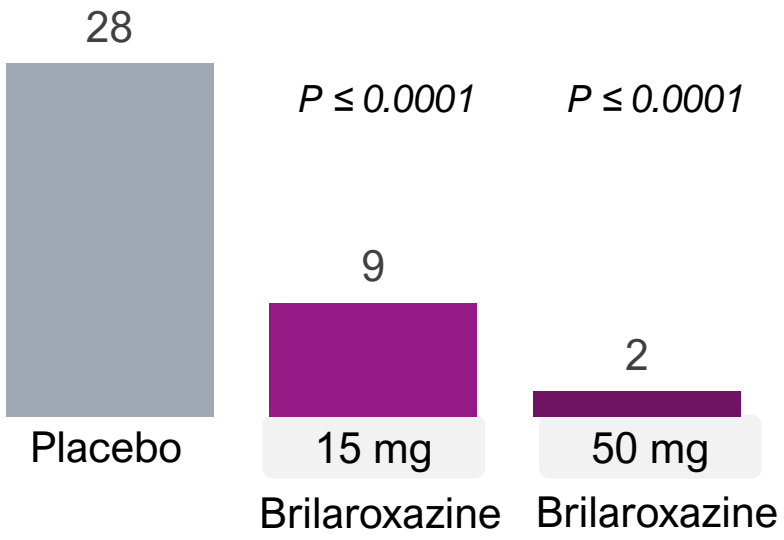
- Hyperprolactinemia is common condition in patients with schizophrenia / psychiatric disorders
- Hyperprolactinemia is associated with immune disorders / diseases and believed to play crucial role in their pathogenesis
- Hyperprolactinemia is associated with variety of adverse effects: weight gain,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



Efficacy & Safety Biomarkers: Change in Serum Cytokines & Chemokines

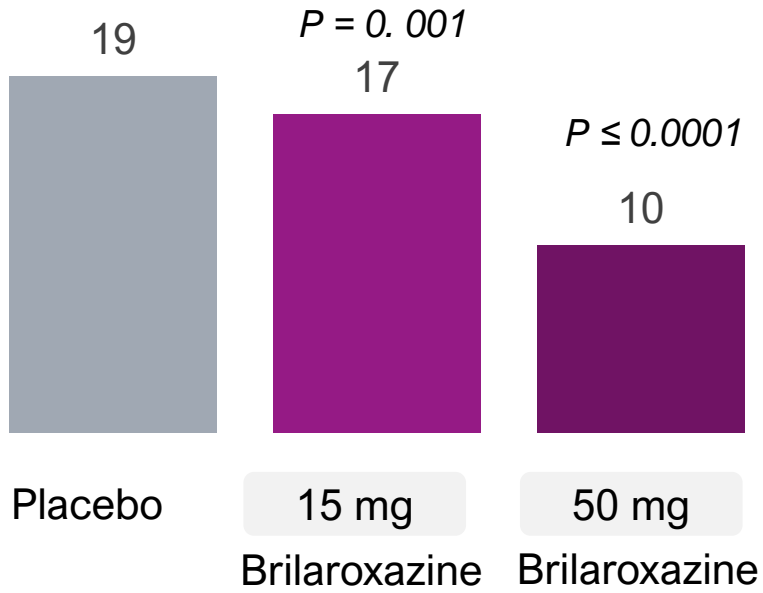
RECOVER-1: Significant decrease in cytokine IL-8 and chemokine MIP-1 in **b**rilaroxazine vs placebo

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 Chemokine MIP-1 (ng/mL)



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)

☞Brilaroxazine showed decrease in IL-6 and IFN-γ inducible protein IP-10, and increase in IL-10 versus placebo

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

Brilaroxazine Key Points of Clinical Differentiation Supported by Biomarkers

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

Significant Change in Blood Biomarkers Patients (N=411, ITT)

BDNF ↑

Hormones:

Prolactin ↓

Thyroid T3 ↑

Cytokines:

IL-8 ↓

IL-10 ↑

IP-10 ↓

MIP-1 ↓

Significant Treatment Effects on Major Symptom Domains & Unmet Needs in all Patients (N = 411, ITT)

Primary Endpoint:

10.1-point (ES: 0.6) ↓ PANSS total score

Secondary Endpoints:

2.8-point (ES: 0.5) ↓ Positive symptoms

2-point (ES: 0.4) ↓ Negative symptoms

2.1-point (ES:0.4) ↓ Negative symp, Marder

1.6-point (ES: 0.5) ↑ Social cognition

6.1-point (ES:0.5) ↑ Personal & Social Performance

2.1-point (ES: 0.5) ↓ Agitation/excitement

≥1-point (ES: 0.5) ↓ CGI score in 78% patients

Treatment Adherence

16% Discontinuation in brilaroxazine vs 22% in placebo

Digital Biomarker, VBM Prominent Negative Symptoms Patients (N=220, VBM Positive)

Primary Endpoint*:

15-point (ES: 0.9) ↓ in PANSS total score

Secondary Endpoints*:

3.5-point (ES: 0.8) ↓ Positive symptoms

3.7-point (ES: 0.6) ↓ Negative, Marder

3.8-point (ES: 0.8) ↑ Social cognition

≥1-point (ES: 0.7) ↓ CGI-S score

***Greater effect size and statistically improvements in efficacy outcomes**

↓ = Reduction / Decrease, ↑ = Increase

Brilaroxazine Phase 3 RECOVER Trial Double-blind Trial (4-week)

Safety, Tolerability and Compliance

Variables	Brilaroxazine 15 mg (N=140)	Brilaroxazine 50 mg (N=134)	Placebo (N=137)
Any Treatment Emergent Adverse Event (TEAE)	104 (34.5%)	107 (35.5%)	90 (29.9%)
Discontinuation[1], n (%)	26 (18.6%)	22 (16.4%)	30 (21.9%)
TEAE occurring in >5% participants			
Somnolence	4 (2.9%)	10 (7.5%)	3 (2.2%)
Headache	8 (5.7%)	7 (5.2%)	3 (2.2%)
Metabolic Changes (weight and lipids), TEAE			
Body Weight Change in kg, Least Square Mean (SE)	1.91 (0.30)	2.41 (0.30)	0.82 (0.30)
≥7% Increase in Body Weight, n (%)	4 (2.8)	9 (6.7)	4 (2.9)
Cholesterol change in mg/dl, Mean (SD)	-2.4 (27.99)	-4.73 (26.13)	3.65 (28.47)
LDL change in mg/dL, Mean (SD)	-4.38 (22.63)	-5.71 (22.06)	4.07 (24.07)
HDL change in mg/dL, Mean (SD)	1.54 (10.46)	0.48 (13.27)	-2.16 (10.18)
Extrapyramidal Symptoms, TEAE			
Barnes Akathisia Rating Scale Score, Mean (SD)	0.0 (0.13)	0.0 (0.19)	0.1 (0.35)
Abnormal Involuntary Movement Scale Score, Mean (SD)	-0.0 (0.41)	-0.0 (0.28)	0.0 (0.48)
Simpson-Angus Scale Score, Mean (SD)	0.1 (0.42)	0.2 (0.48)	0.3 (0.71)

(1) Brilarox-15 mg had 1 (0.71%) TEAE related discontinuation;

Positive Topline Phase 3 RECOVER 1-Year Open-Label Extension Results

Strengthen the safety, efficacy and adherence findings of the Phase 3 RECOVER double-blind study (4-week)

Enrollment Metrics for OLE

- 435 patients total enrolled across 3 dose groups:
  - 139 in 15 mg brilaroxazine
  - 155 in 30mg brilaroxazine
  - 141 in 50mg brilaroxazine
- 156 (35.86%) rollover participants from the double-blind Phase 3 trial
- 279 (64.13%) de novo participants enrolled in the trial

Safety and Tolerability Over 1-year

- 15.2% reported at least one TRAE, which were mostly mild (12.2%) or moderate (3%) in severity and transient in nature
- Most common TRAEs ≥1% were weight increase (3.2%), insomnia (1.8%) and somnolence (1.6%)
- Not associated with any clinically meaningful changes in movement disorder scales
- No drug related SAEs observed or major safety concerns; 3 SAEs were reported and none were related to brilaroxazine treatment

Compliance / Treatment Adherence Over 1-year

- 35% treatment discontinuation rate primarily due to:
  - withdrawal of consent (22%)
  - participant lost to follow up (7%)
  - TRAE (1.6%)

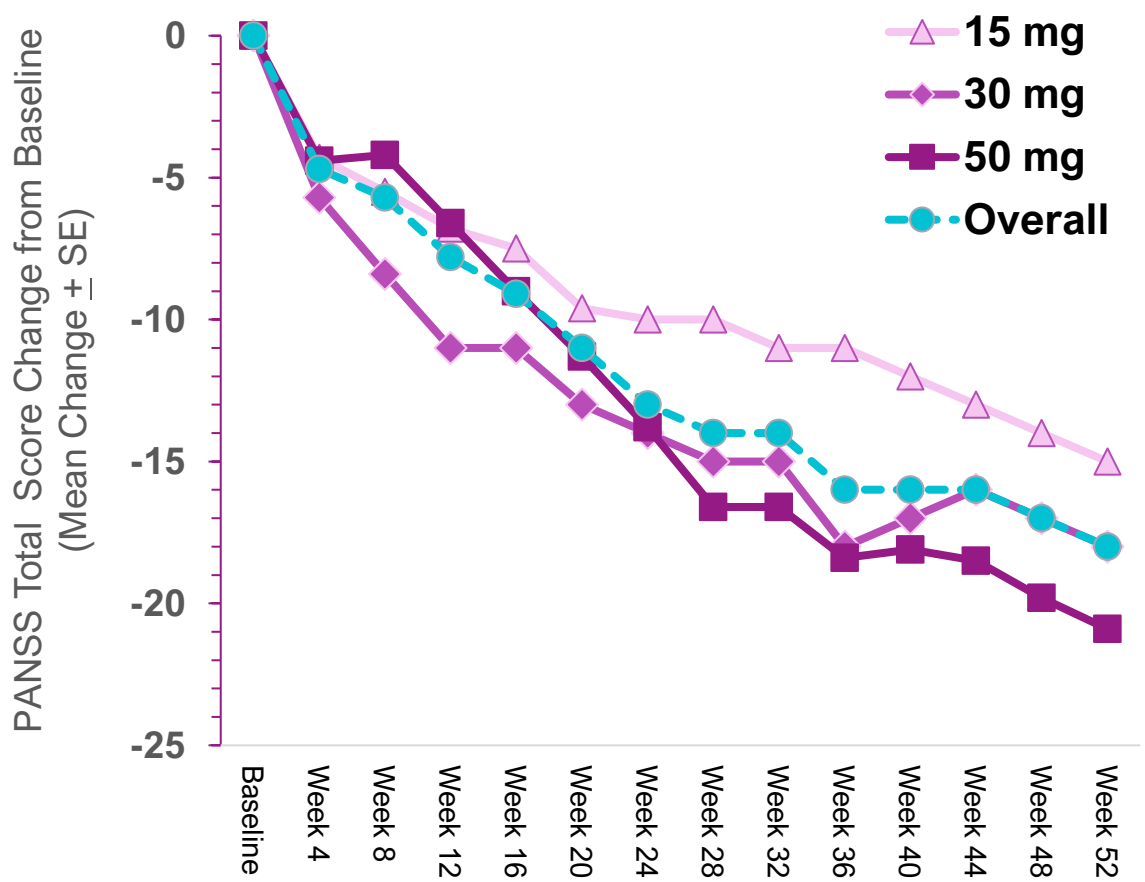
TRAE: treatment-related adverse event ; SAE: serious adverse event

Brilaroxazine Phase 3 RECOVER Open-label Trial Topline Efficacy Results

Robust broad-spectrum efficacy sustained over 1-year for PANSS total, PANSS positive and PANSS negative symptoms vs. baseline ($p \leq 0.0001$)

- Brilaroxazine 15, 30, and 50 mg showed dose dependent efficacy with decrease in PANSS total scores -15.2, -18.6 and -20.8 points, respectively, from baseline to Week-52 (1-year)
- Pooled analysis of brilaroxazine 15, 30, and 50mg doses demonstrated clinically meaningful and sustained long-term (1-year) efficacy with a significant decrease in PANSS total scores, PANSS positive symptoms and PANSS negative symptoms vs. baseline ($p \leq 0.0001$):
  - PANSS Total scores: 18.6-point decrease (71.6 → 53)
  - PANSS Positive: 5.2-point decrease (17.7 → 12.5)
  - PANSS Negative: 4.5-point decrease (19.5 → 15.0)
- Strong sustained efficacy from acute through maintenance treatment over 1-year treatment
- Decrease in PANSS total score in rollover patients from the double-blind trial:
  - ≥30-point in 86.76% of patients
  - ≥40-point in 64.70% of patients
  - ≥50-point in 33.82% of patients

Change in PANSS Total Scores (N=113, 1-Year)



PANSS: Positive and Negative Syndrome Scale

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]

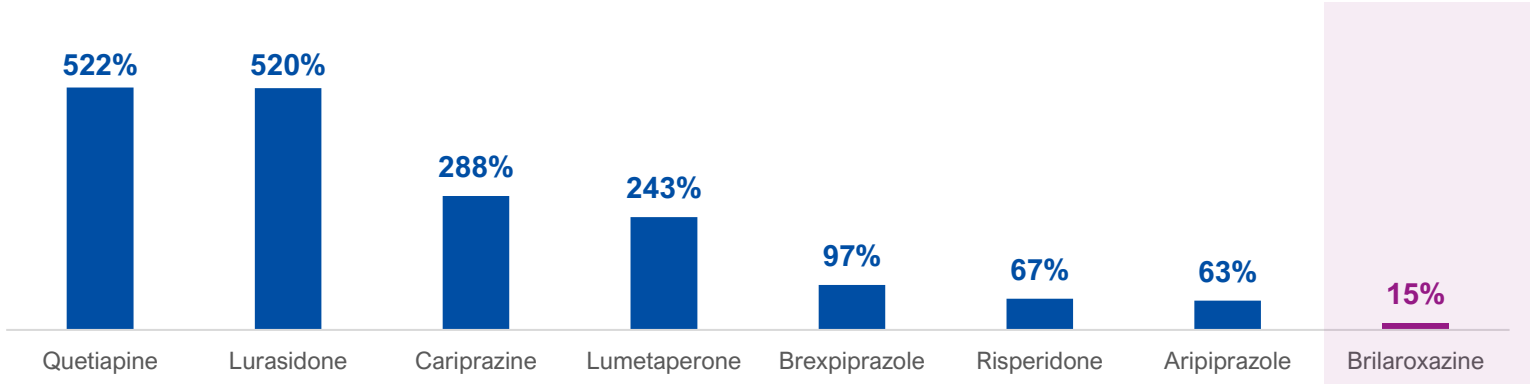
~50% of prescribed drugs and over 25% of approved antipsychotics are known to cause drug interactions in the presence of a strong CYP3A4 inhibitor drug

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

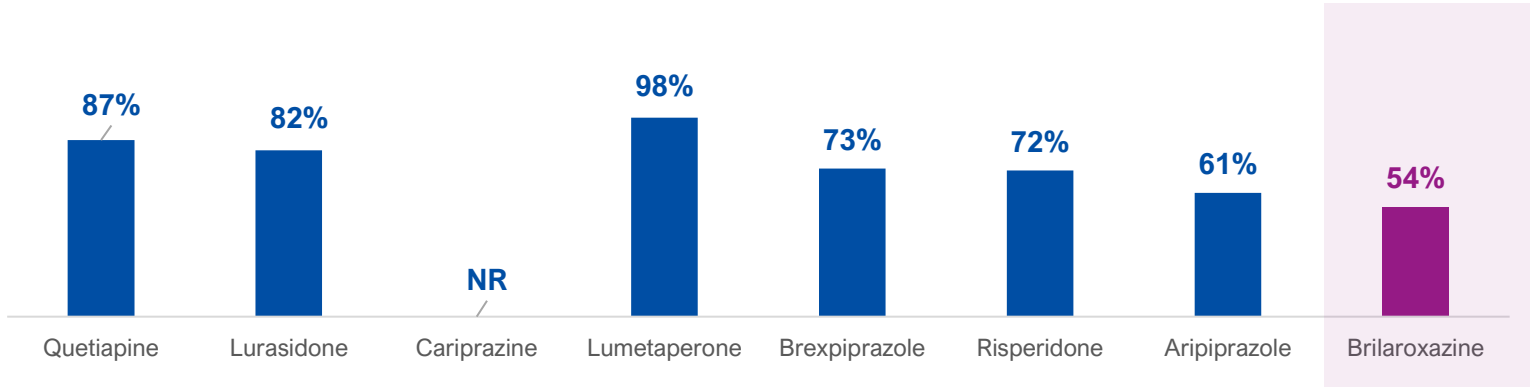
*Olanzapine[9] not evaluated; metabolized by CYP1A2[10]

% 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

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

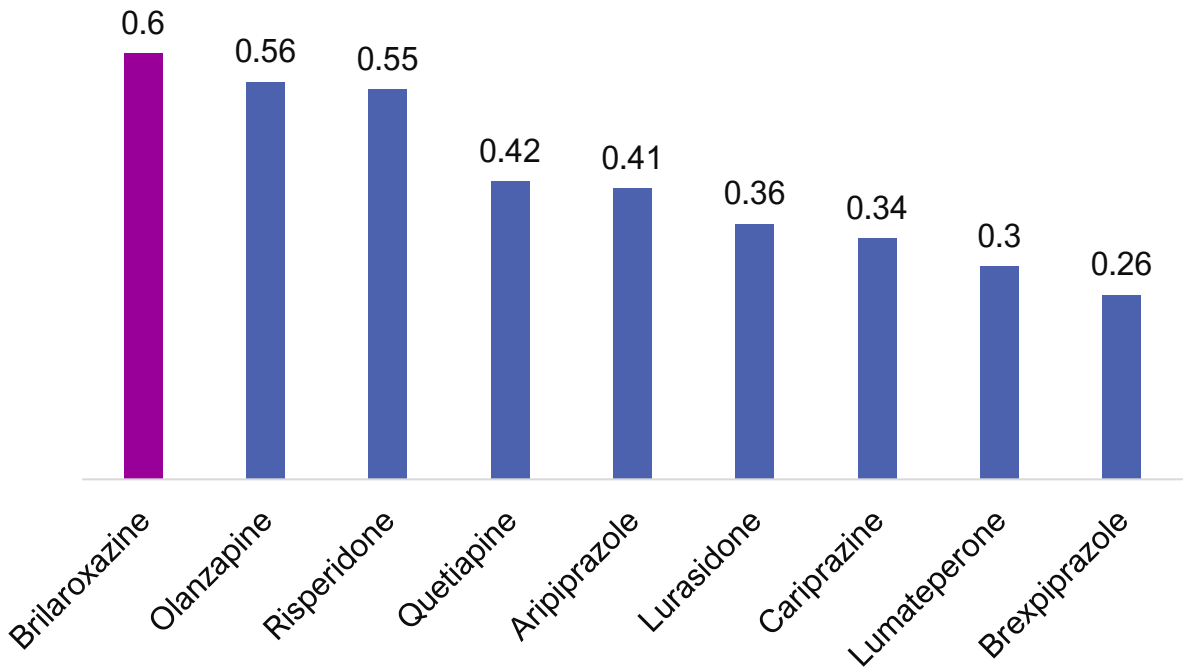
Key Metrics	PHASE 3 RECOVER (N=411 | 4-wk) NCT05184335	PHASE 2 REFRESH (N=234 | 4-wk) NCT01490086
Primary Endpoint (Brilaroxazine 50 mg vs Placebo)		
PANSS Total Score	-10.1 P<0.001 (Effect Size, 0.6)	-10.7 P<0.01
Secondary Endpoint (Brilaroxazine 50 mg vs Placebo)		
PANSS Positive Score	-2.8 P<0.001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

(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

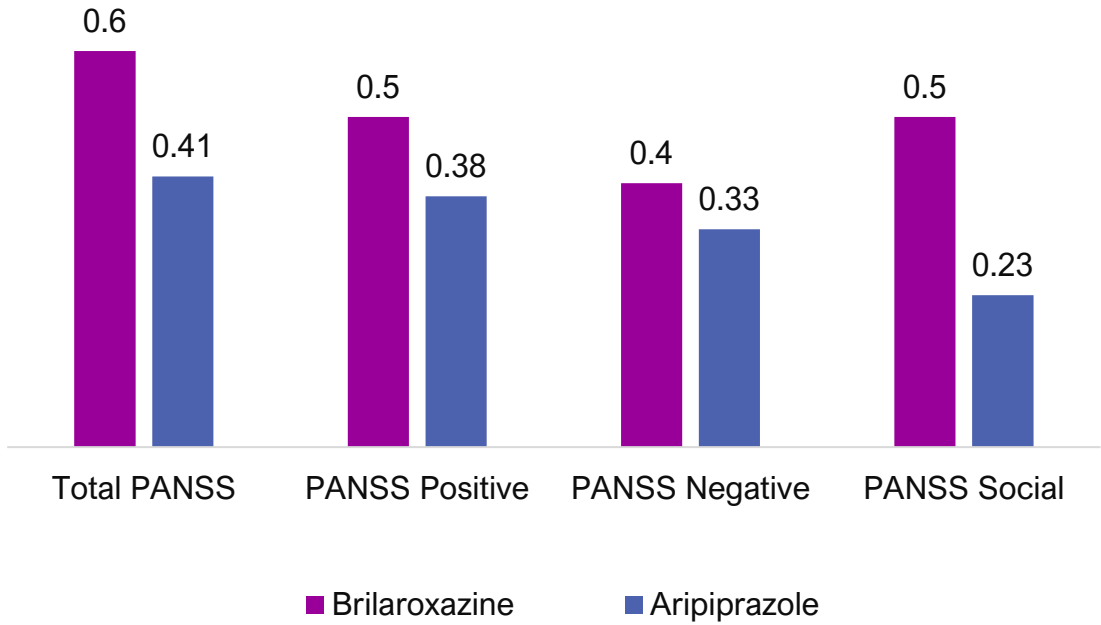
Comparison of Treatment Effect Size from Phase 3 Studies

Primary endpoints and major secondary efficacy endpoints

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



Brilaroxazine[1] vs Aripiprazole[2]



Source: (1) 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

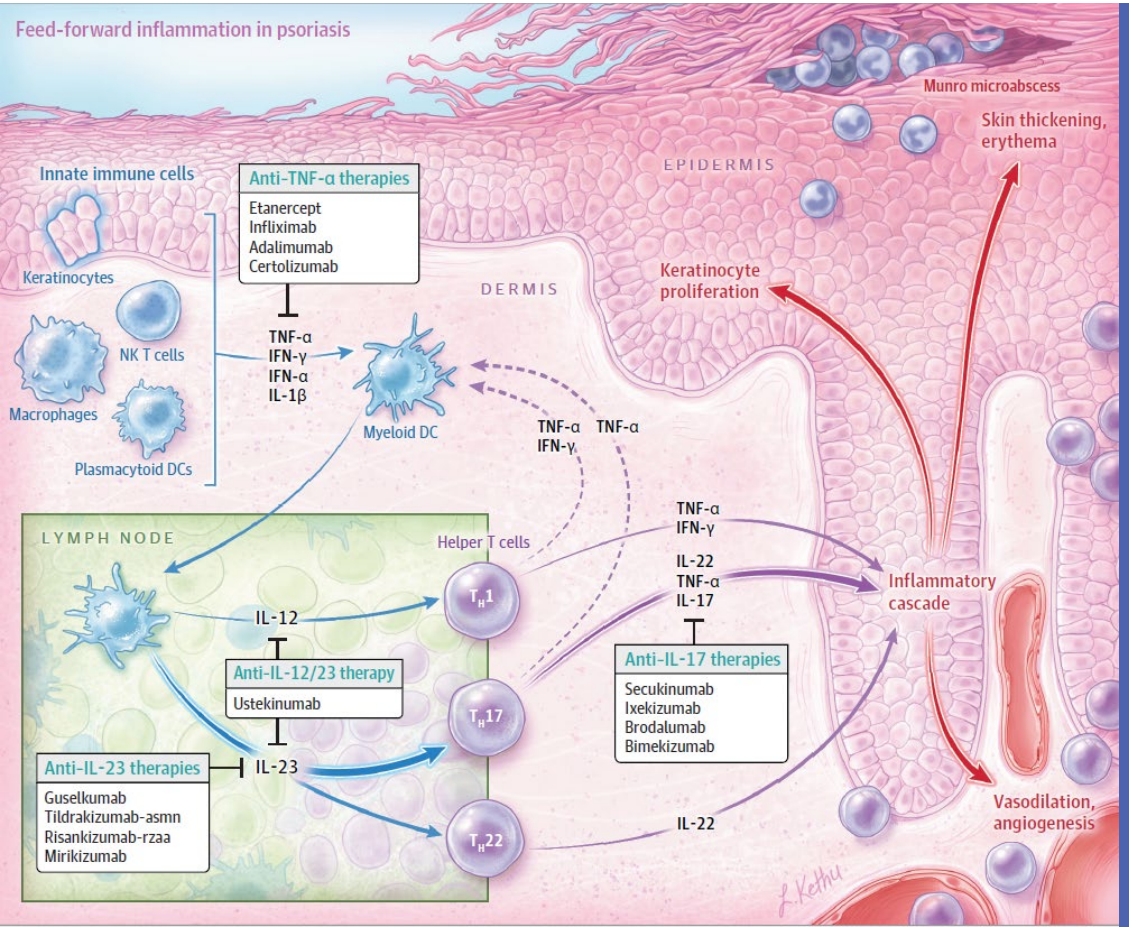
Reviva PHARMACEUTICALS

Inflammatory / Immune Disease Programs

Psoriasis | Pulmonary Arterial Hypertension (PAH) | Idiopathic Pulmonary Fibrosis (IPF)

Brilaroxazine has Potential to Treat Psoriasis

Inflammatory skin disease driven by dysfunctional serotonin-dopamine signaling



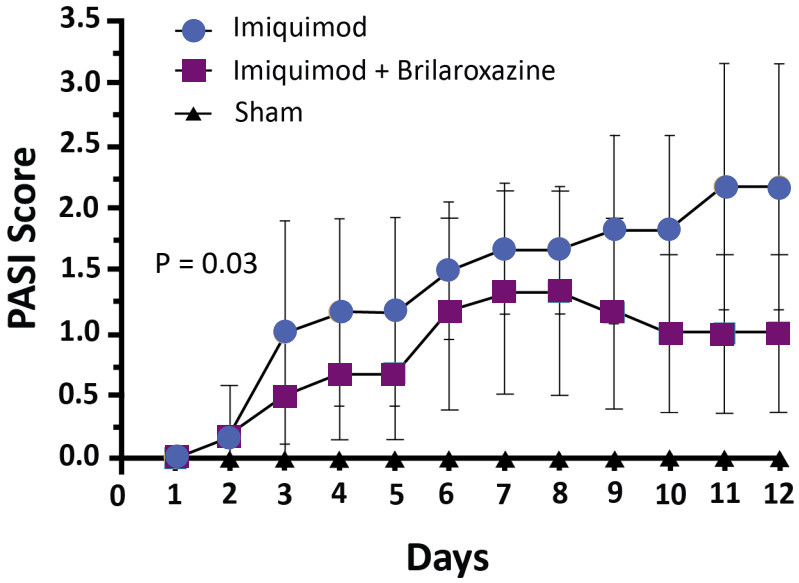
- Approx 3% of the US population and an estimated 125 million people worldwide suffer from psoriasis
- An estimated one-third of neuropsychiatric and neurodegenerative disease patients suffer from psoriasis
- Currently there is no cure for psoriasis
  - Topical corticosteroids therapies remain the cornerstone for treating mild psoriasis
  - Biologics that inhibit cytokines TNF-α, p40IL-12/13, IL-17, and p19Il-23, and oral PDE-4 inhibitor for moderate to severe plaque psoriasis

Armstrong AW. Pathobiology, clinical presentation, and Treatment of psoriasis, JAMA 2020, 323(19):1945-1960; Bhat L, et al. ISID 2023, Poster #LB1745; www.revivapharma.com/ISID-2023-Poster

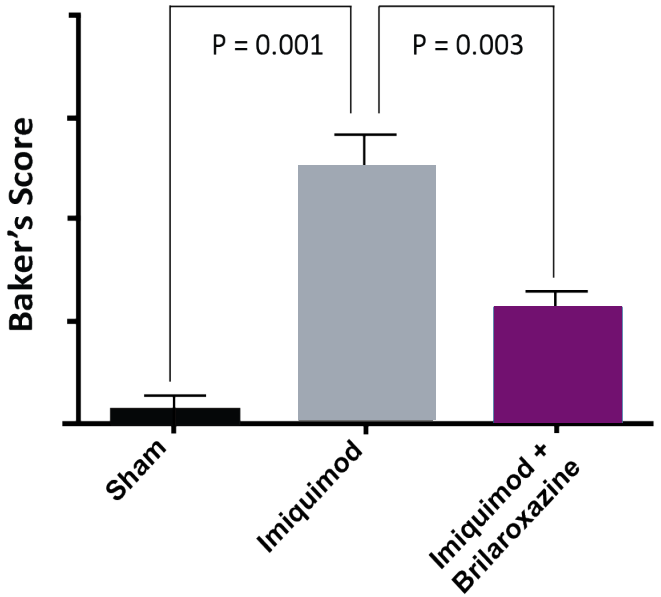
Brilaroxazine Demonstrated Encouraging Preclinical Efficacy

In an imiquimod induced mouse model of psoriasis

Psoriasis Area Severity Index (PASI)



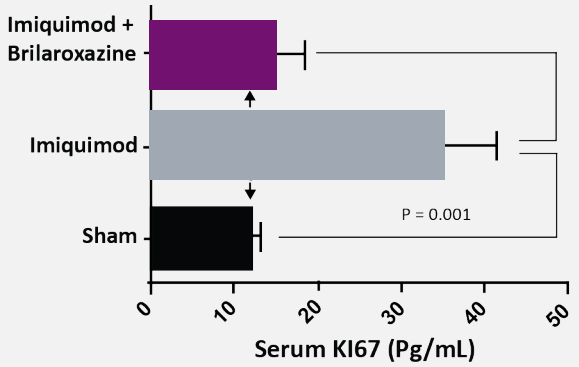
Psoriasis Severity by Baker Score

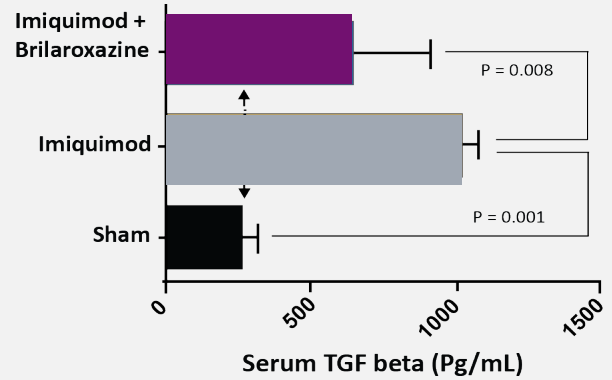


Brilaroxazine topical liposomal gel significantly decreased

- Psoriasis area severity index (P= 0.03)
- Clinical severity of psoriasis, Baker score (p=0.003)
- Proinflammatory and proliferation cytokine, KI67 (P=0.001)
- Profibrotic chemokine, TGF-β (P=0.001)

Decrease in anti-inflammatory and proliferation cytokine (KI67) and profibrotic chemokine (TGF-β)



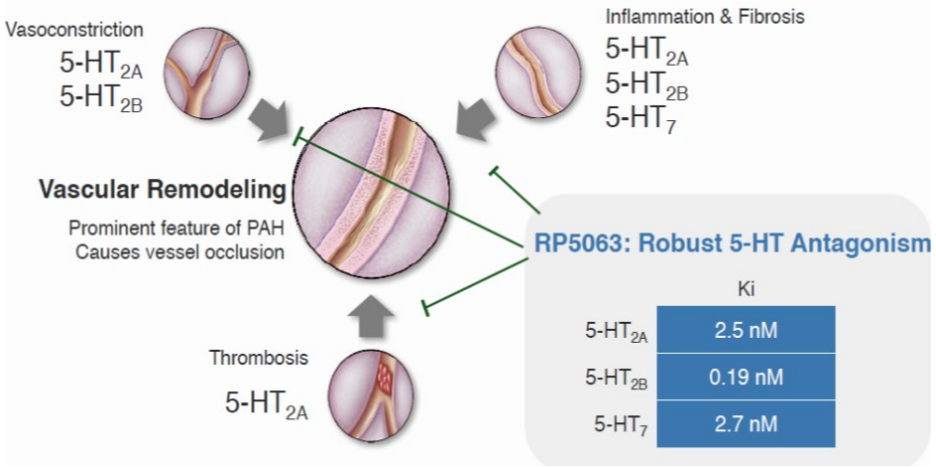


Bhat L, et al. Brilaroxazine lipogel displays psoriasis activity in imiquimod-induced mouse model. *Skin Res Technol*. 2024;e13606. https://doi.org/10.1111/srt.13606

Brilaroxazine: Potential to Delay PAH and IPF Disease Progression

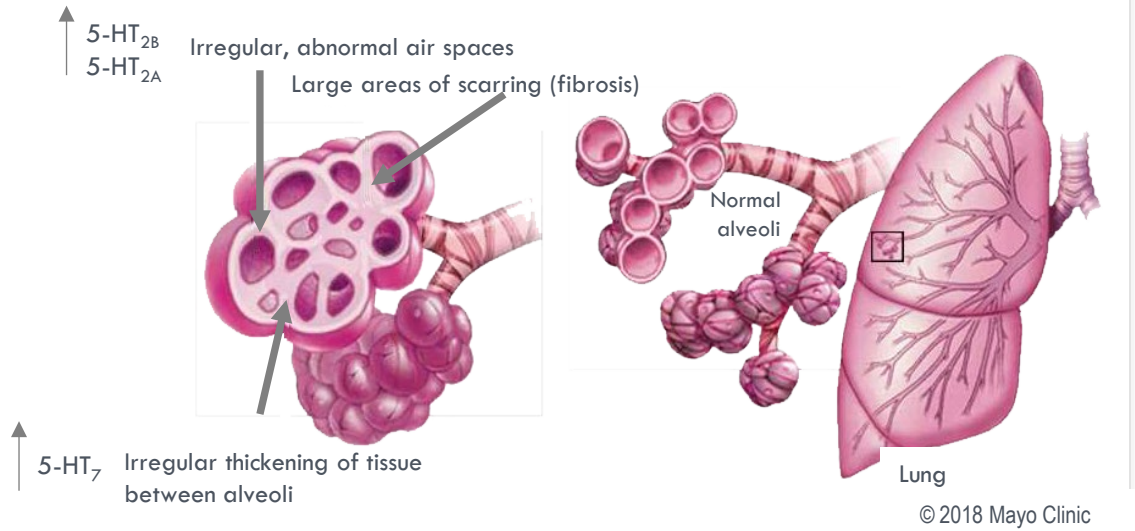
PAH and IPF are Orphan Diseases that involve dysfunctional serotonin signaling

Lung Vascular Remodeling in PAH



- PAH and IPF are rare, chronic, and debilitating conditions
- No therapies significantly delay disease progression
- Patients experience elevated plasma serotonin (5-HT) levels, increased expression of 5-$HT_{2A/2B/7}$ receptors & inflammatory cytokines in lungs

Lung Alveoli Remodeling in IPF



- Lung vascular/alveoli remodeling occurs due to inflammation, fibrosis, and pulmonary hypertension
- Brilaroxazine has robust antagonism against serotonin receptors involved in vasoconstriction, fibrosis, blood clots, and inflammation

Bhat L, et al. Medical Research Archives 2023, 11(4):3837; Bhat et al., Eur J Pharmacol 2018, 827:159-166; Lofdahl et al, Am J Pathobiology 2018, 188(5): 1113-1119; Tawfik and Makary, European J Pharmacology 2017, 814: 114-123; Pulmonary fibrosis image adapted from https://tinyurl.com/y9r6ld48

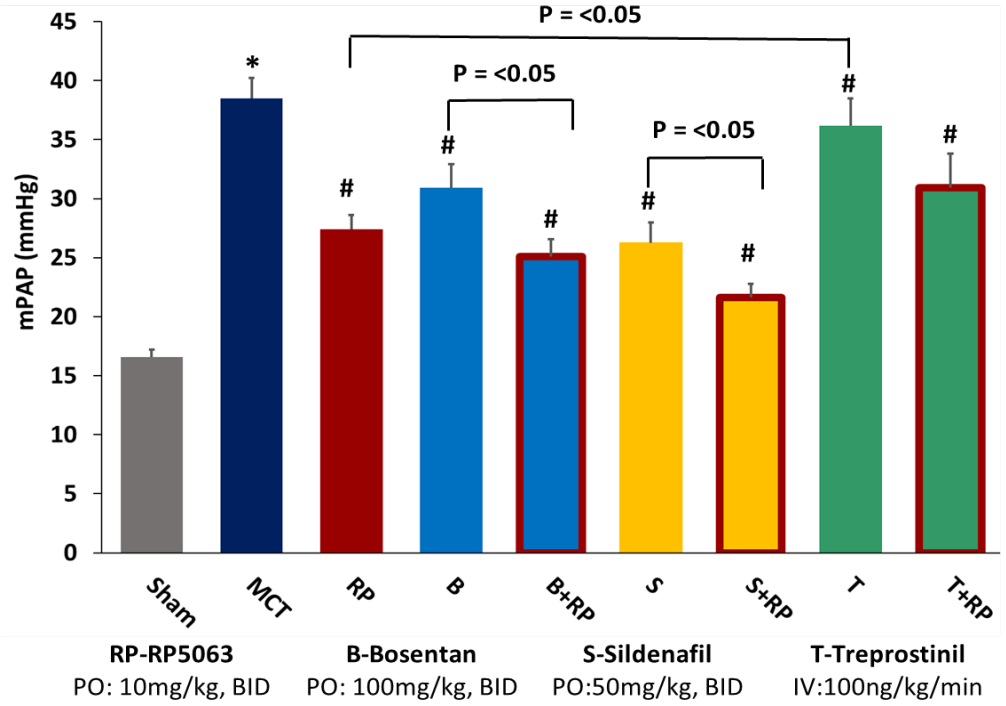
Brilaroxazine: Encouraging Results in PAH Translational Rodent Models

Potential for Improved Treatment Effect Compared to Standard of Care

Brilaroxazine alone and co-administered with standard of care for PAH

- Mitigated PAH in MCT and Sugen-Hypoxia rodent models
- Decreased respiratory resistance and restored blood oxygen saturation
- Decreased vascular remodeling and fibrosis in the small vessels
- Mitigated inflammation & reduced small vessel thickness
- Significantly reduced inflammatory cytokines TNFα, IL-β, IL-6, and chemokine LTB4

Brilaroxazine mitigates pulmonary hypertension and lung fibrosis/collagen



Bhat and Salvail, J Rare Dis Res Treat 2017, 2(5): 5-12. Bhat, et al. European J Pharmacology 2017, 810:83-91 and 92-99.
Bhat, et al. European J Pharmacology 2018, 827: 159-166.

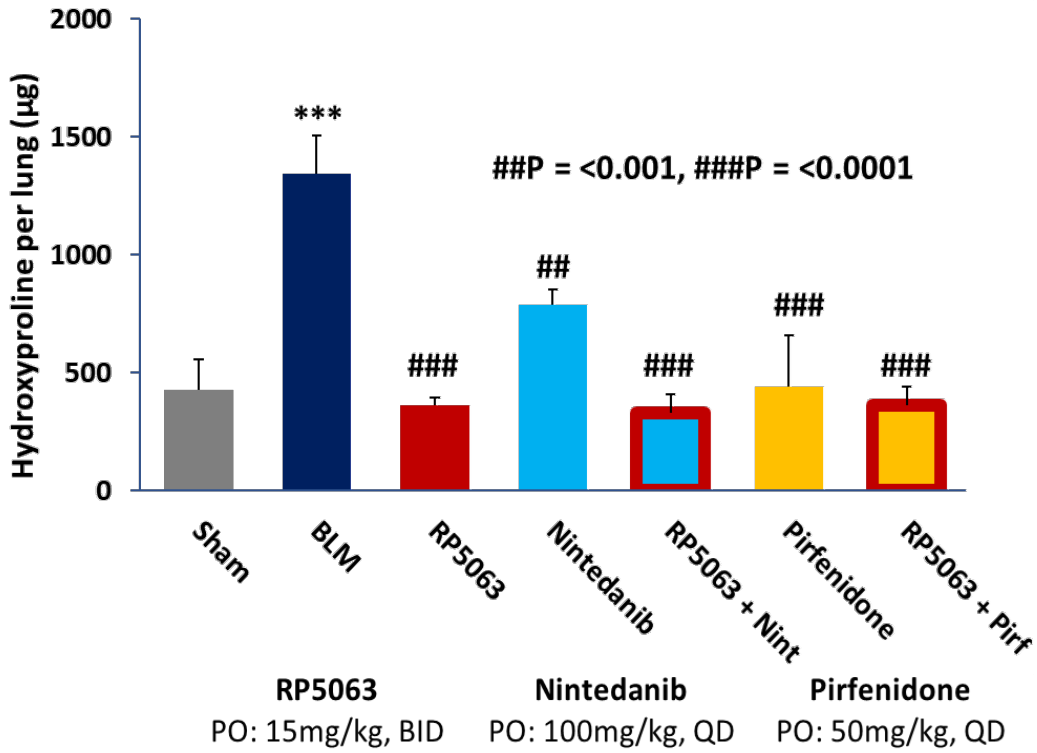
Brilaroxazine: Encouraging Results in Bleomycin-Induced IPF Rodent Model

Potential for Improved Treatment Effect Compared to Standard of Care

Brilaroxazine both alone and co-administered with standard of care for IPF

- Mitigated lung fibrosis and collagen deposits
- Decreased respiratory resistance & improved blood oxygen saturation
- Restored body weight and cardiac output
- Reduced the IPF biomarkers BALF cell counts, hydroxyproline, and blood lactate levels
- Decreased cytokines RANTES, IFNγ, MCP1, IL-6, and IL-17
- Improved survival rates

Brilaroxazine mitigates lung fibrosis / collagen (Decrease in Hydroxyproline)



Bhat L, et al. Medical Research Archives 2023, 11(4):3837

Brilaroxazine: Ready for Phase 2 Trials in PAH and IPF

FDA granted Orphan Drug Designation

Brilaroxazine Phase 2 trials in PAH and IPF

- Preclinical evidence supports the use of Brilaroxazine in PAH and IPF
- Generally well-tolerated in clinical studies for schizophrenia in >250 patients
- Completed long-term regulatory toxicology studies
- Manufactured API and drug products (clinical trial materials)
- Oral once daily dosing, potential to develop once daily inhaler for enhanced effect and convenience

Key regulatory milestones achieved

- FDA reviewed preclinical pharmacology, toxicology, CMC, and clinical Phase 1 safety data for initiating a Phase 2 study
- FDA reviewed and provided guidance on Phase 2/3 clinical development plan and a potential “Disease Modifying Agent” label claim
- FDA granted Orphan Drug Designation for the treatment of PAH and IPF

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