



(Nasdaq: RVPH)

Reviva Pharmaceuticals

Corporate Presentation | September 2025

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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						\$9.74 ⁽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) In 2025 per Bipolar Disorder Market by Towards Healthcare Report 2025. (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

Positive Registrational Trials for Brilaroxazine in Schizophrenia

- Completed required NDA-enabling safety pharmacology, toxicology & carcinogenicity studies, & CMC development
- In light of successful completion of the RECOVER double-blind study and OLE, Reviva is currently assessing appropriate next steps in Brilaroxazine's path to approval

PHASE 1A and 1B, Clin Pharm Studies (N≈150)	PHASE 2 REFRESH NCT01490086	PHASE 3 RECOVER DB NCT05184335	PHASE 3 RECOVER OLE NCT05184335
Phase 1A Healthy subjects, double-blind, safety and tolerability, pharmacokinetics (PK)	N = 234 (4-Week) Acute schizophrenia or schizoaffective disorder	N = 411 (4-Week) Acute schizophrenia	N = 446 (52-Week/1-Year) Stable schizophrenia
Phase 1B Stable schizophrenia patients, double-blind, POC efficacy, safety and tolerability, PK	Efficacy and safety of brilaroxazine vs placebo	Efficacy and safety of brilaroxazine vs placebo	Long-term safety/tolerability, efficacy and compliance of brilaroxazine
ADME & Bioavailability Once daily brilaroxazine, ~72% bioavailability	3:3:2 Randomized, 4-week, double-blind, placebo-controlled, multicenter	1:1:1 Randomized, 4-week, double-blind, placebo-controlled, multicenter	Open label, 1-year outpatient extension of RECOVER
Drug-Drug Interactions No clinically significant drug-drug interactions	Once daily brilaroxazine 15, 30, 50 mg	Once daily brilaroxazine 15, 50 mg	Once daily brilaroxazine 15, 30, 50 mg flexible dose
	Completed and met primary and multiple secondary endpoints	Completed and met primary and multiple secondary endpoints	Completed and met primary and multiple secondary endpoints

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)

(1) Reviva press release on Phase 3 RECOVER trial results on October 30, 2023 (<https://revivapharma.com/press-releases/>).

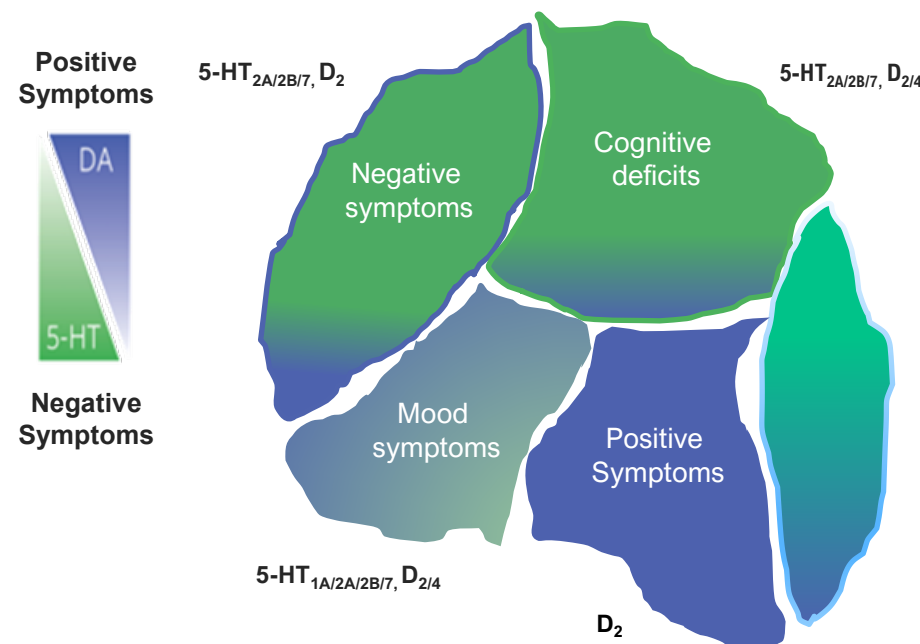
(2) Bhat, et al. J Neurol Neuromed 2018, 3(5): 39-50. (3) Cantillon, M. et al. Schizophrenia Research 2017, 189: 126-133

Schizophrenia: Common Psychiatric Condition With Multiple Symptom Domains

- Affects ~1.1% of the world's population
 - ~ 24 million people globally
 - ~ 3.5 million people in USA
- Mix of heterogenous psychotic symptoms with varying degrees of severity
- ~30% of patients are treatment refractory
- Most patients requires lifelong treatment
- High treatment discontinuation rate (30-74%)
- 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

Primarily driven by dysfunctional serotonin and dopamine signaling



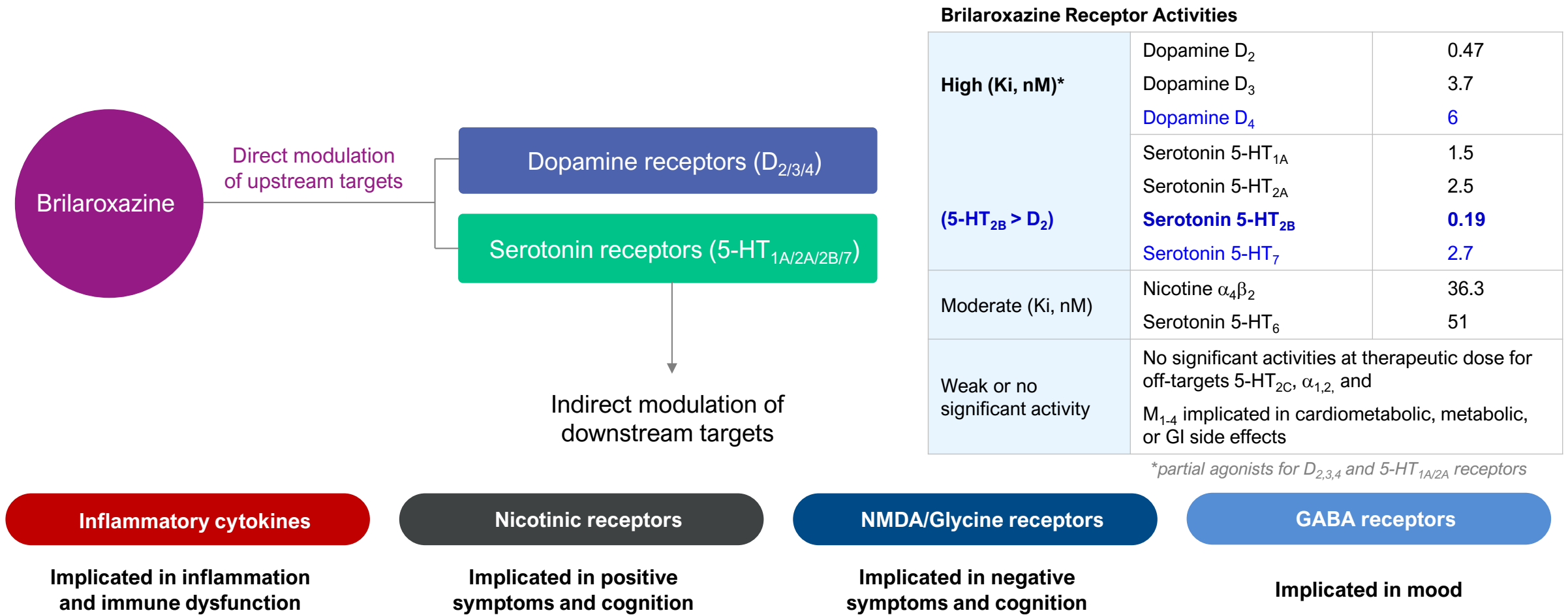
D = Dopamine signaling/ and 5-HT = Serotonin signaling

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://therehab.com/schizophrenia/statistics/>; <https://www.nimh.nih.gov/health/statistics/schizophrenia>; Kane JM et al. J Clin Psychology 2019, 80(2):18com12123..Divroye C et al. Neuropsychopharmacology 2016, 109:59068; peng I et al. Expert Review of Neurotherapeutics 2018, 18(5):435-442; Nikiforuk et al. CNS Drugs 2015, 29:265-275; Tan T et al. Schizophrenia Bulletin 2017, 45(5): 1012-1023. Bhat L, et al. Medical Research Archives 2023, 11(4):3834

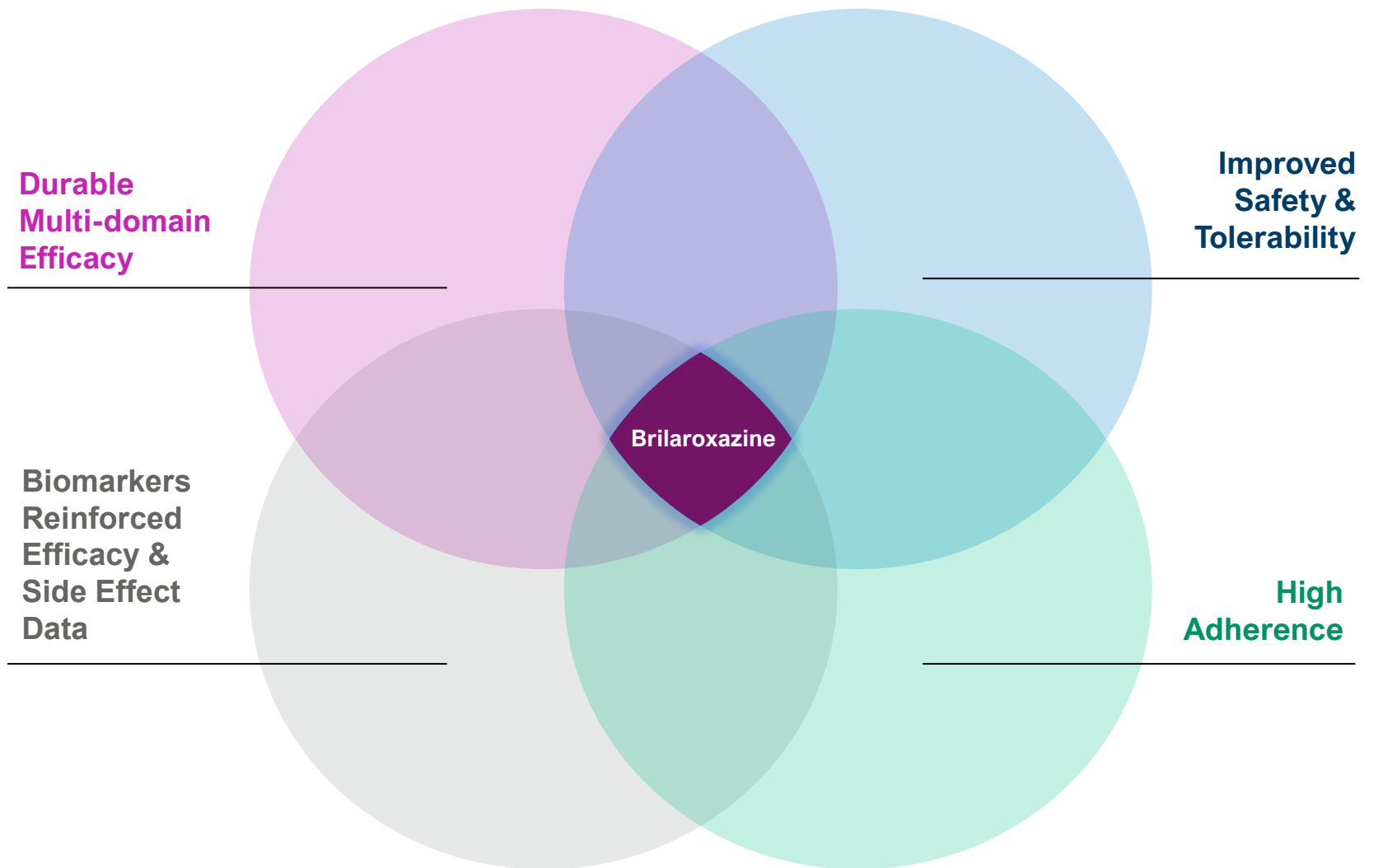
Brilaroxazine: Novel Serotonin-Dopamine & Neuroinflammatory Signaling Modulator

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



Brilaroxazine

Differentiated clinical profile with potential to address unmet needs across the treatment of schizophrenia



For KOL webinars on brilaroxazine phase 3 RECOVER trial results in schizophrenia, please visit: www.revivapharma.com

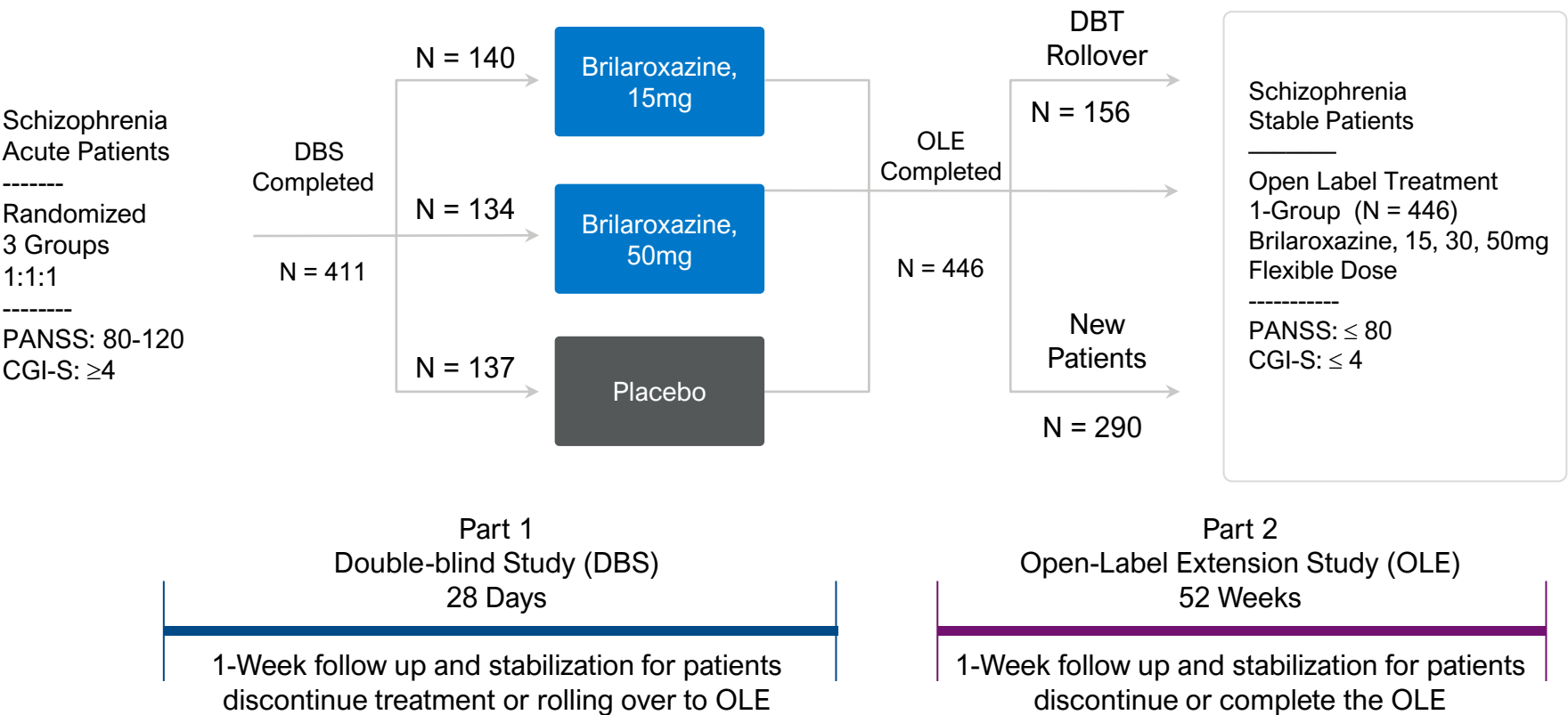
(1) [chrome-extension://efaidnbmnnnibpcajpcgclclefindmkaj/https://revivapharma.com/wp-content/uploads/2025/06/20250602-RS-Reviva-KOL-Webinar-Slide-Deck.pdf](https://efaidnbmnnnibpcajpcgclclefindmkaj/https://revivapharma.com/wp-content/uploads/2025/06/20250602-RS-Reviva-KOL-Webinar-Slide-Deck.pdf)

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(3) [chrome-extension://efaidnbmnnnibpcajpcgclclefindmkaj/https://revivapharma.com/wp-content/uploads/2023/10/Reviva-RECOVER-Topline-Results-Presentation_October-2023.pdf](https://efaidnbmnnnibpcajpcgclclefindmkaj/https://revivapharma.com/wp-content/uploads/2023/10/Reviva-RECOVER-Topline-Results-Presentation_October-2023.pdf)

Brilaroxazine Phase 3 RECOVER Trial For Schizophrenia

Phase 3, Randomized, 28 Days, Double-blind, Placebo-controlled, Multicenter Study to Assess the Safety and Efficacy of Brilaroxazine in Subjects with an Acute Exacerbation of Schizophrenia, Followed by a 52-Week Open-label Extension



Study Overview

Primary Endpoint (DBS):

Reduction in total PANSS at the end of treatment in a brilaroxazine arm from baseline versus placebo

Safety (DBS, OLE):

Clinical, labs, body weight, lipids, fasting glucose, prolactin

Pharmacokinetics:

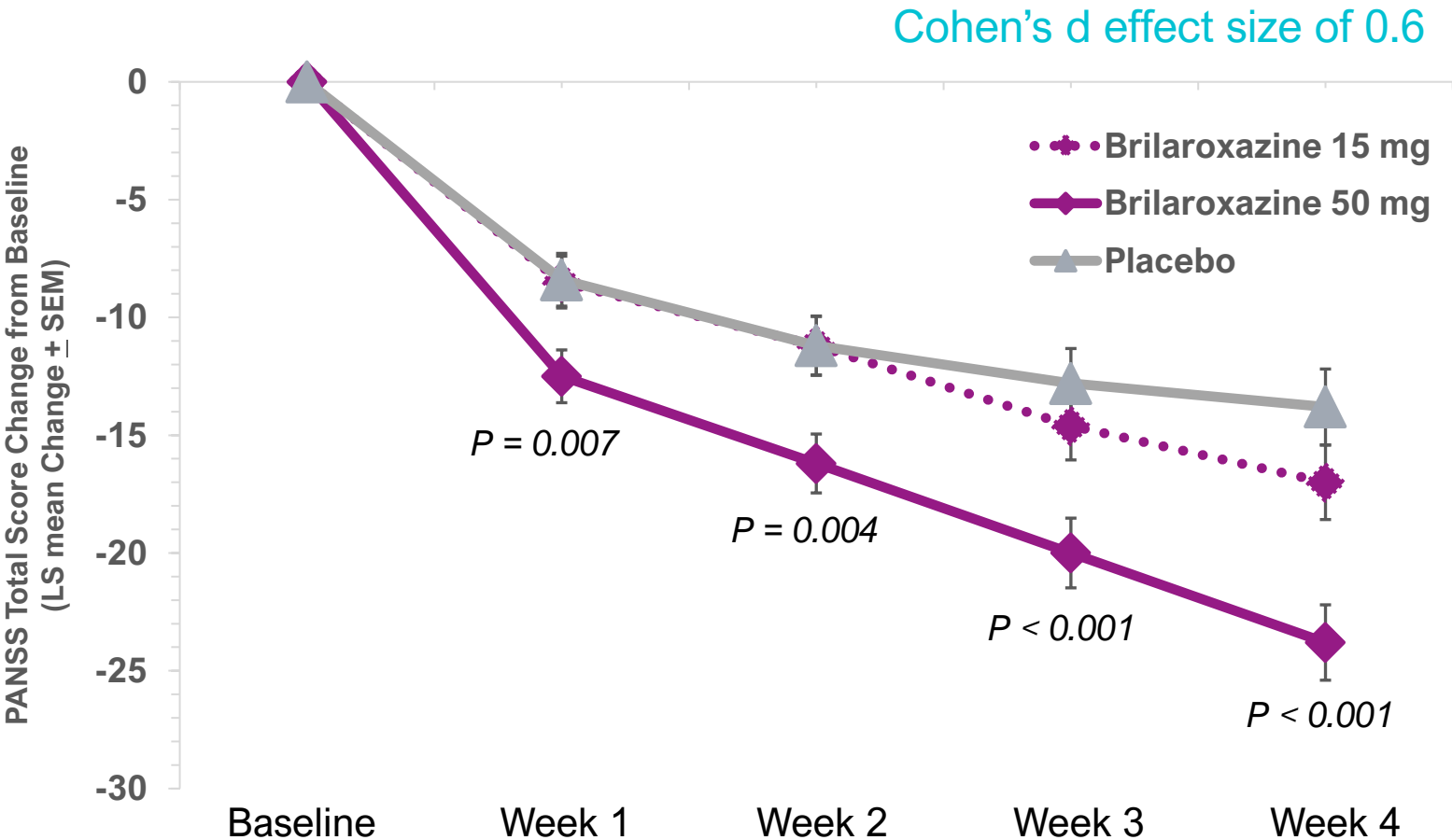
Population pharmacokinetics

Brilaroxazine Phase 3 RECOVER 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 vocal and blood biomarkers data



Brilaroxazine Phase 3 Trial: Favorable Efficacy, Safety & Discontinuation

Early onset of action with strong broad-spectrum efficacy further supported by vocal biomarker (VBM) & blood biomarkers

	Acute Schizophrenia Patients		Primary Negative Symptom Patients		Acute Patients	
Symptom Domains & Adherence	Brilaroxazine 50mg vs Placebo		Vocal Biomarker Positive Patients Brilaroxazine 50mg vs Placebo		Blood Biomarkers	
	Point Improvement	Cohen's d Effect Size	Point Improvement	Cohen's d Effect Size		
	PANSS Total Score	-10.1	0.6	-15	0.9	Neurotrophins* BDNF
	Positive Symptoms	-2.8	0.5	-3.5	0.8	Hormones* Prolactin Thyroid T3
	Negative Symptoms	-2.0	0.4	---	---	
	Negative Marder Factor	-2.1	0.4	-3.7	0.6	Cytokines IL-6 IL-8* IL-10 IFN-γ/IP-10* TNF-α MIP-1*
	PANSS Social Cognition	-1.6	0.5	-3.8	0.8	
	Personal & Social Performance	6.3	0.5	6.3	0.6	
	CGI-S score ≥1-point	-0.5	0.5	-0.7	0.7	
	PANSS Excitement/Agitation	-2.1	0.5			
	PANSS Gen Psychopathology	-5.3	0.6			
Treatment Discontinuation	16% Brilaroxazine	22% Placebo				

Bhat L et al ASCPT 2024 (Poster #LB008) and SIRS 2024 (Poster #T291)
Cohen et al CNS Summit 2024, ISCTM 2025

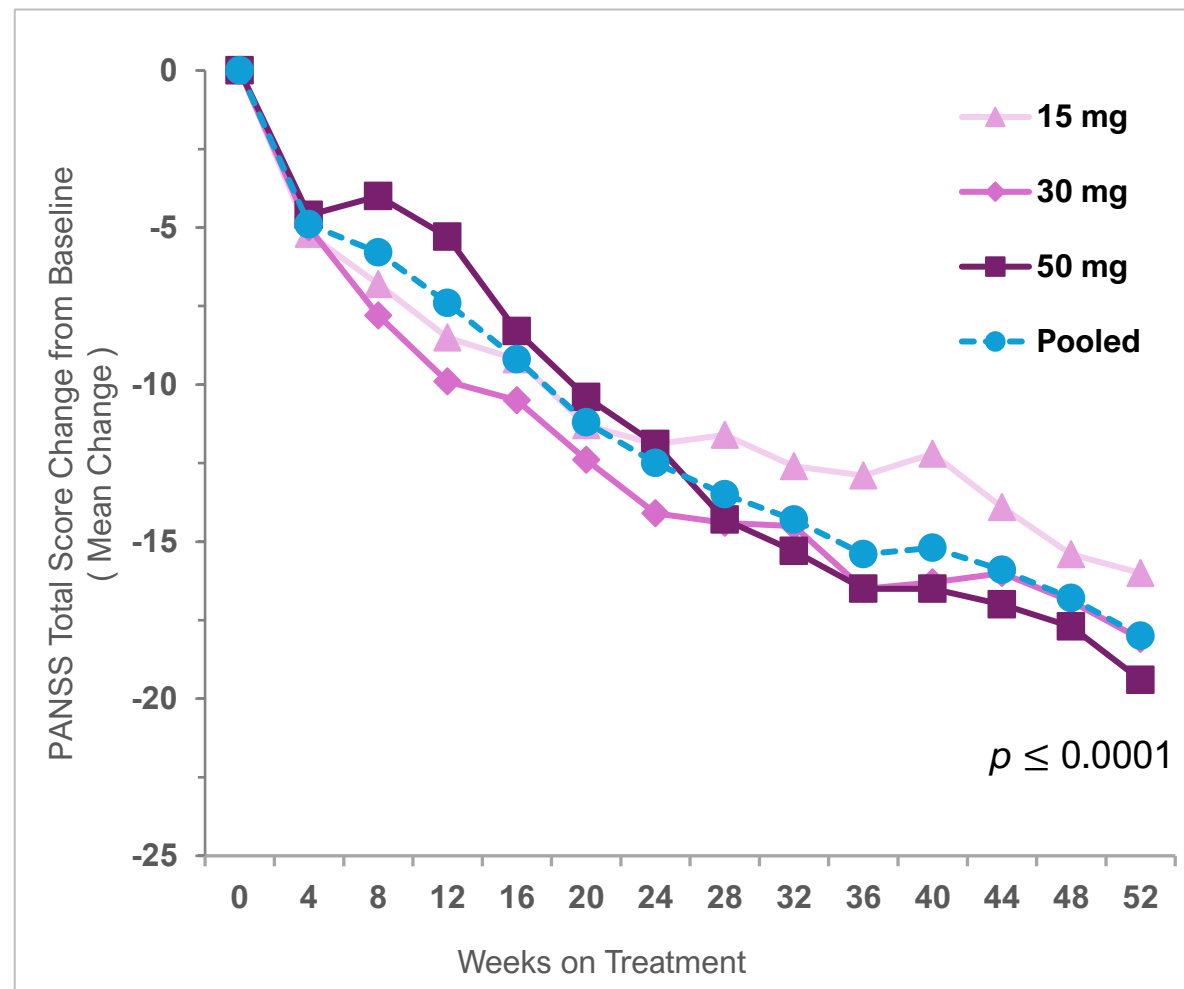
*Significant improvement, P≤0.05

PANSS Total Score: Robust Broad-Spectrum Efficacy Sustained Over 1-year

18-point decrease with brilaroxazine pooled (15, 30, and 50 mg) at Week-52 vs baseline ($p \leq 0.0001$; $n = 159$)

CHANGE IN PANSS TOTAL SCORE

- Dose dependent decrease from baseline to Week-52 (1-year)
 - 16.0-point decrease in 15 mg (61.2 → 45.2)
 - 18.0-point decrease in 30 mg (69.7 → 51.7)
 - 19.4-point decrease in 50 mg (75.6 → 56.2)
 - 18.1-point decrease in pooled (69.9 → 51.8)
- 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 to OLE over 1-year treatment (Baseline to Week-56):
 - 46.1-point decrease in 15 mg (94.4 → 51.3)
 - 49.6-point decrease in 50 mg (102.7 → 53.1)



Brilaroxazine Phase 3 Trial OLE: Favorable Efficacy & Discontinuation

Significant, consistent and sustained efficacy for major symptom domains across all three doses of brilaroxazine

Stable Schizophrenia Patients

Symptom Domains & Adherence

Brilaroxazine 15, 30 and 50mg (pooled)

	OLE Point Improvement* at 6M (N=303)	OLE Point Improvement* at 12 M (N=159)	Rollover Patients DB Trial to OLE Point Improvement* at 13 M (N= 50)
PANSS Total Score	-10.7	-18.1	-47.7
Positive Symptoms	-3.3	-5.0	-14.0
Negative Symptoms	-2.8	-4.4	-10.5
Negative Marder Factor	-3.0	-4.4	---
PANSS Social Cognition	-1.5	-2.9	---
Personal & Social Performance	4.5	11.3	32.7
CGI-S score >1-point	37.3%	58.5%	100%
PANSS Excitement/Agitation	-1.4	-3.5	---
PANSS Gen Psychopathology	-4.7	-8.7	-23.2

Treatment Discontinuation

35%

Blood Biomarkers

Neurotrophins*

BDNF

Hormones*

Prolactin

Thyroid T3

Cytokines*

IL-6

IL-8

IL-10

IFN- γ /IP-10

TNF- α

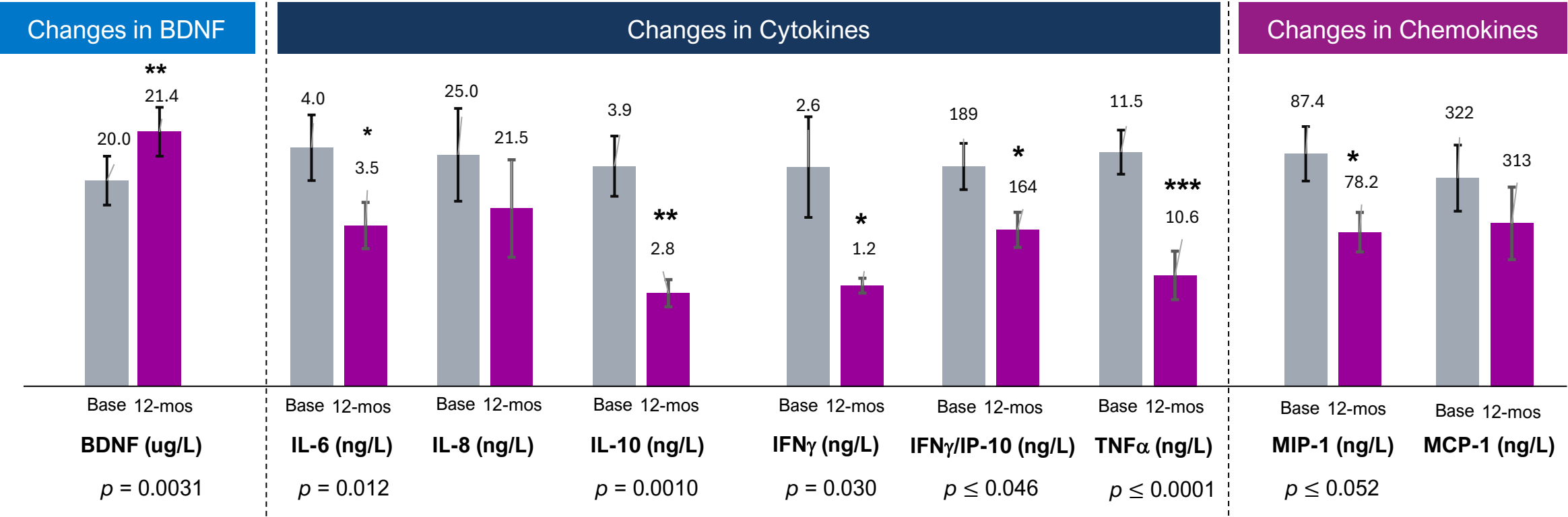
MIP-1

*Significant improvement, P= ≤ 0.05

*Baseline to EOT, P = ≤ 0.001 ; OLE: Open Label Extension

Brilaroxazine Phase 3 RECOVER OLE Trial Inflammatory Biomarker Data

A significant increase in BDNF & decrease in inflammatory cytokines and chemokines over 12 months



Individual treatment groups (15, 30 50 mg) also showed increase in BDNF and decrease proinflammatory cytokines and chemokines

Reduced BDNF implicated in cognitive and memory impairments in schizophrenia and depression

Elevated proinflammatory cytokines IL-6, IL-8, IL-10, IFN γ , and TNF α reported in schizophrenia, bipolar and depression patients

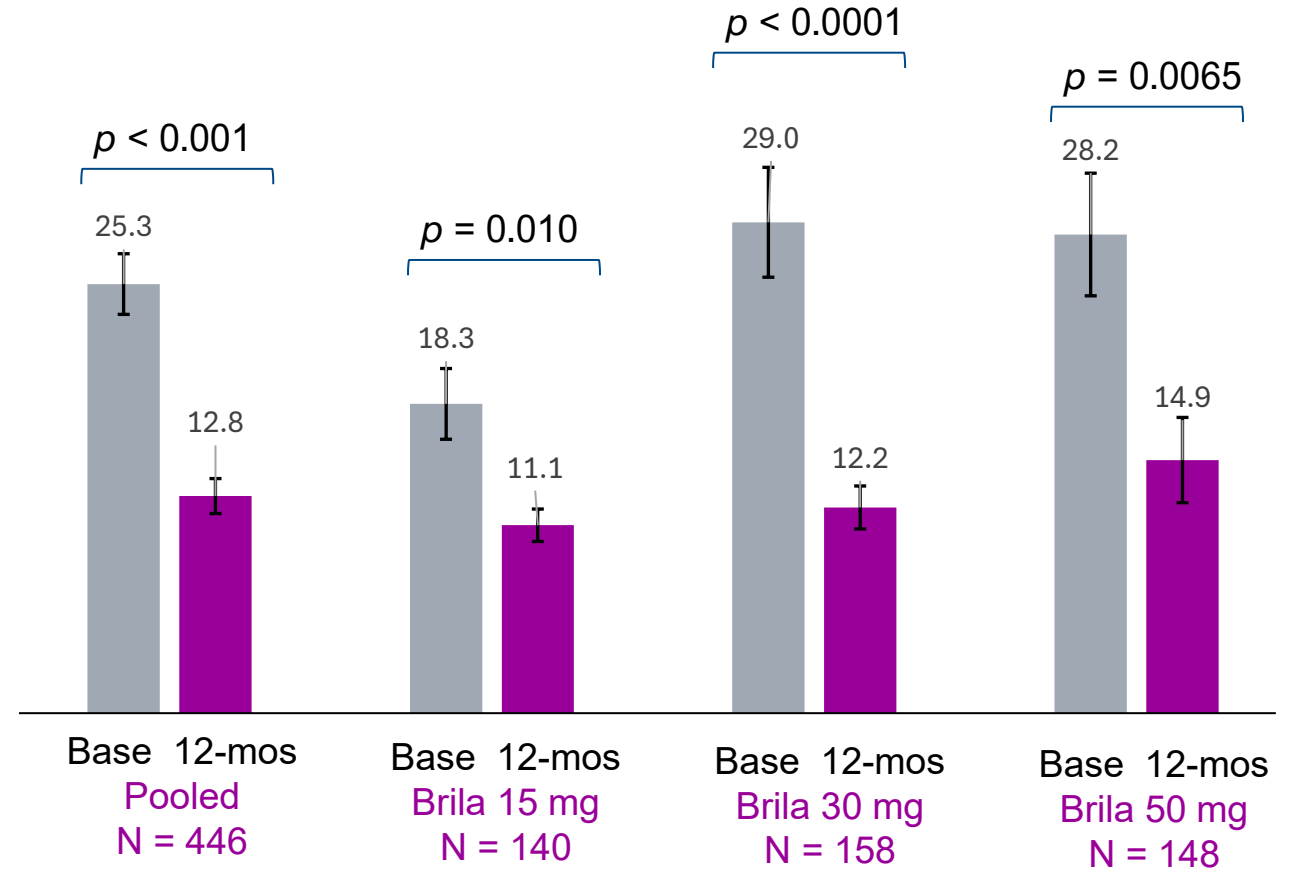
Chemokine dysregulation is associated with neuroinflammation in schizophrenia

Brilaroxazine Phase 3 OLE Trial: Change in Prolactin Hormone

Clinically significant decrease in prolactin levels across all doses of brilaroxazine over 12 months

DECREASE IN PROLACTIN

- Elevated serum prolactin levels reduced to normal across all doses of brilaroxazine from baseline to week-52/EOT ($p \leq 0.01$):
 - 7.14 $\mu\text{g/L}$ in 15mg, (18.26 $\rightarrow$ 11.12)
 - 16.79 $\mu\text{g/L}$ in 30mg, (28.95 $\rightarrow$ 12.16)
 - 13.30 $\mu\text{g/L}$ in 50 mg, (28.24 $\rightarrow$ 14.94)
 - 12.50 $\mu\text{g/L}$ Overall, (25.32 $\rightarrow$ 12.82)
- Hyperprolactinemia is common condition in patients with schizophrenia / psychiatric disorders
 - Associated with immune diseases (multiple sclerosis, systemic sclerosis etc)
 - Associated with variety of adverse effects: weight gain, type 2 diabetes, breast tenderness and enlargement, sexual dysfunction (lack of libido), and erectile dysfunction in men



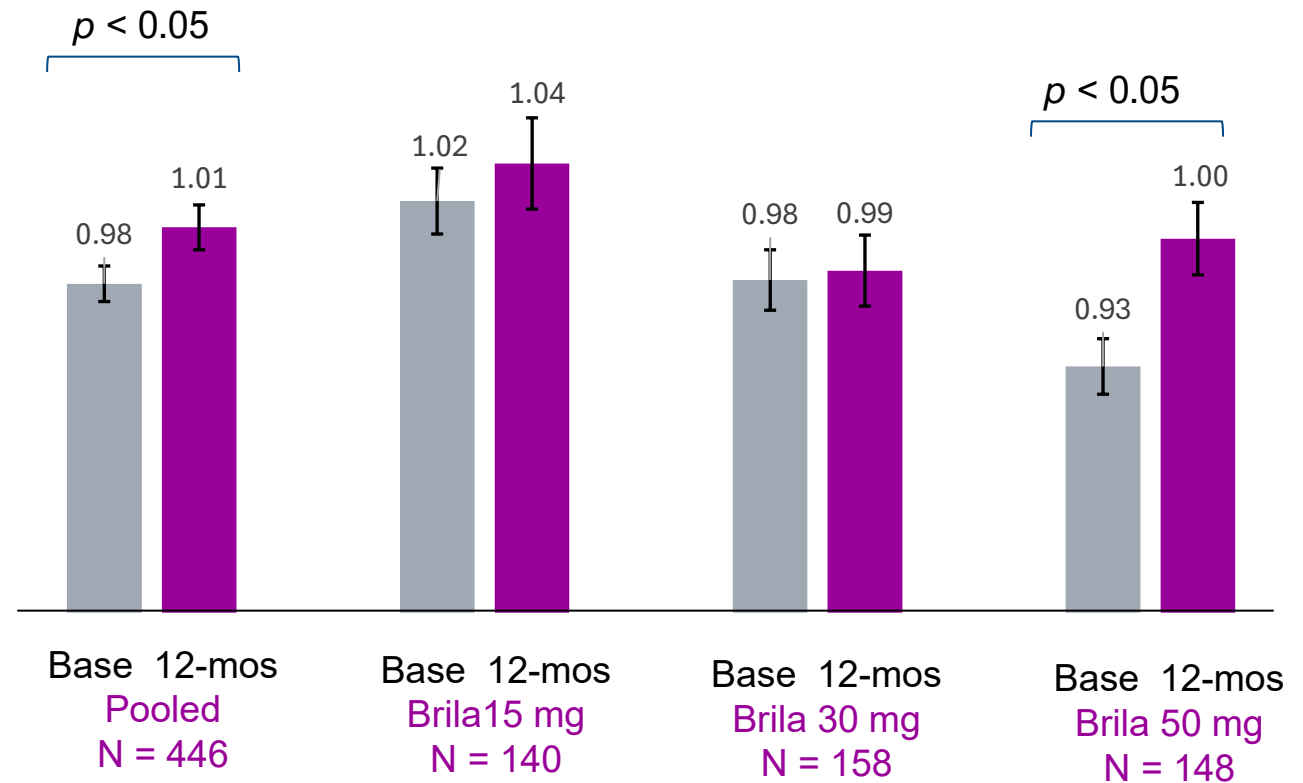
☞ Normal blood level of prolactin in men, $<15 \mu\text{g/L}$ and in female (not pregnant), $<20 \mu\text{g/L}$

Brilaroxazine Phase 3 OLE Trial: Change in Thyroid Hormone

Improvement in thyroid hormone levels across all doses of brilaroxazine over 12 months

IMPROVEMENT IN THYROID HORMONES

- Improvement in thyroid (T3) hormone levels across all doses of brilaroxazine from baseline to week-52/EOT
 - 0.033 ug/L in 15mg
 - 0.020 ug/L in 30mg
 - 0.076 ug/L in 50 mg, $P \leq 0.05$
 - 0.044 ug/L in overall, $P \leq 0.05$
 - Improvement in thyroid (T4) and decrease in TSH hormone levels across all doses of brilaroxazine
-
- Hypothyroidism reported in schizophrenia(negative symptom) and mood disorders (bipolar, depression)
 - Hypothyroidism implicated in antipsychotic induced metabolic (obesity) and immune disorders
 - Thyroid hormones are important for modulation of dopaminergic, serotonergic, glutamateric and GABAergic network.



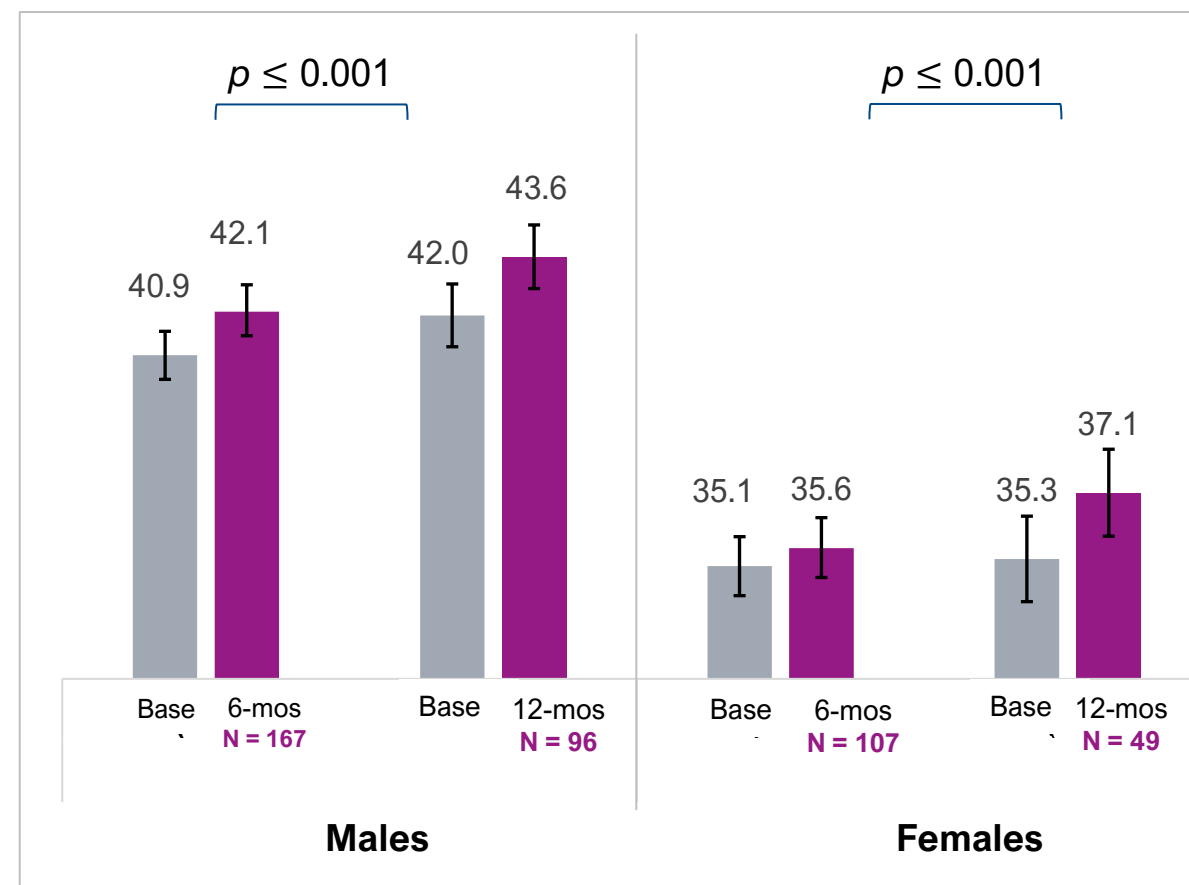
☞ Normal blood level of thyroid T3 hormone, 0.8- 2.2 µg/L

Sexual Function, CSFQ Score: Improvement in both Males and Females

Improvement in sexual function CSFQ Score over 12 months ($p \leq 0.001$)

SEXUAL FUNCTION, CSFQ SCORE

- Significant improvement in total sexual function score with brilaroxazine pooled (15, 30, & 50 mg) vs. baseline over 1-year ($p \leq 0.001$):
 - Males: 1.2 point in male (40.9 → 42.1) at 6M
1.6 point in male (42.0 → 43.6) at 12M
 - Females: 0.5 point in female (35.1 → 35.6) at 6M
1.8 point in female (35.3 → 37.1) at 12M
- 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



Brilaroxazine Phase 3 RECOVER Trial in Acute Schizophrenia

Safety, Tolerability and Compliance (double-blind trial for 4-week, N=411)

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, 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, Mean (SD)	2.20 (3.65)	2.50 (3.50)	0.94 (2.95)
≥7% Increase in Body Weight, n (%)	3 (2.1)	8 (5.9)	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)

Brilaroxazine Phase 3 RECOVER Trial in Stable Schizophrenia

Safety, Tolerability and Compliance (open-label trial for 52-week/1-year, N=446)

Variables	Brilaroxazine 15 mg (N=140)	Brilaroxazine 30 mg (N=158)	Brilaroxazine 50 mg (N=148)	Pooled (N=446)
Number of Treatment Emergent Adverse Event (TEAE)	85	91	104	280
Patients with any TEAE, n (%)	50 (35.7%)	49 (31.0%)	67 (45.3%)	106 (37.2%)
Patient with any related TEAE, n (%)	6 (4.3%)	13 (8.2%)	19 (12.8%)	38 (8.5%)
Discontinuation due to TEAE , n (%)	0	3(1.9%)	2 (1.4%)	5 (1.1%)
TEAE occurring in >2% participants				
Headache	1 (0.7%)	7 (4.4%)	4 (2.7%)	12 (2.7%)
Insomnia	3 (2.1%)	5 (3.2%)	10 (6.8%)	18 (4.0%)
Sleep Disturbance	2 (1.4%)	2 (1.3%)	9 (6.1%)	13 (2.9%)
Tremor (mild)	1 (0.7%)	3 (1.9%)	10 (6.8%)	14 (3.1%)
Metabolic Changes (weight and lipids), TEAE				
Body Weight Change in kg, Mean (SD)	1.58 (4.96)	1.85 (2.23)	1.28 (2.95)	1.52 (3.49)
≥7% Increase in Body Weight (AESI), n (%)	3 (2.1%)	2 (1.3%)	6 (4.1%)	11 (2.5%)
Cholesterol change in mg/dL, Mean (SD)	-8.6 (31.01)	-5.5 (23.50)	-10.9 (28.86)	-8.3 (27.82)
LDL change in mg/dL, Mean (SD)	-8.4 (25.52)	-4.5 (22.33)	-11.1 (24.57)	-8.0 (24.19)
HDL change in mg/dL, Mean (SD)	-0.6 (9.34)	-0.9 (8.72)	-0.1 (9.38)	-0.6 (9.12)
Extrapyramidal Symptoms, TEAE				
Barnes Akathisia Rating Scale Score, Mean (SD)	0.0	0.0	0.0	0.0
Abnormal Involuntary Movement Scale Score, Mean (SD)	-0.0 (0.29)	-0.2 (0.59)	-0.0 (0.36)	-0.0 (0.41)
Simpson-Angus Scale Score, Mean (SD)	0.0	0.1 (0.43)	0.0	0.0

Brilaroxazine Phase 3 Trial: Bodyweight Change in Acute vs Stable Patients

Bodyweight change profile in acute in-patient vs stable out-patient trials with brilaroxazine

	Acute Patients DB Inpatient Trial	Stable Patients OLE Outpatient Trial	
	4-Week N=411	24-Week N=303	52-Week N=159
Brila-15 mg, mean wt (SD), kg	2.20 (3.65)	0.32 (3.06)	1.56 (5.06)
Brila-30 mg, mean wt (SD), kg	---	0.67 (1.90)	1.88 (2.32)
Brila-50 mg, mean wt (SD), kg	2.50 (3.50)	0.62 (2.69)	1.28 (2.95)
Placebo, mean wt (SD), kg	0.94 (2.95)	---	---

	Bodyweight change in rollover patients, double-blind through OLE treatment over 13 months
Brila-50 mg, mean wt (N=21) Efficacious top dose	1.20 kg

Brilaroxazine Phase 3 Trial: Lipids Change in Acute vs Stable Patients

Lipids change in acute in-patient vs stable out-patient trials with brilaroxazine

	Change in total Cholesterol, mg/dL		Change in LDL Cholesterol, mg/dL	
	Acute Patients (N=411) DB, 1-month	Stable Patients (N=446) OLE, 12 Months	Acute Patients (N=411) DB, 1-month	Stable Patients (N=446), OLE, 12 Months
Brila-15 mg, mean (SD)	– 2.4 (27.99) [#]	– 8.6 (31.01)	– 4.38 (22.63) [#]	– 8.4 (25.52)
Brila-30 mg, mean (SD)	---	– 5.5 (23.50)	---	– 4.5 (22.33)
Brila-50 mg, mean (SD)	– 4.73 (26.13)[#]	– 10.9 (28.86)[*]	– 5.71 (22.06)[#]	– 11.1 (24.57)[*]
Placebo, mean (SD)	3.65 (28.47)	---	4.07 (24.07)	--

[#]*p*<0.05 vs placebo (DB)

^{*}*p*<0.05 vs baseline (OLE)

Brilaroxazine: Consistent Well-Tolerated Safety with Low Discontinuation Over 1-Year

Well-Tolerated in OLE Trial (N=446, 1-yr treatment)

Brilaroxazine (15, 30, and 50 mg) is safe and well-tolerated following 1-year of treatment. Most common TEAEs $\geq 2\%$ were headache (2.7%), insomnia (4.0%), sleep disturbance (2.9%) and mild tremor (3.1%). No drug related SAEs or major safety concerns reported. 35% total discontinuation rate

No Motor Side Effects

No clinically meaningful changes in movement disorder scales used for evaluating motor side effects such as akathisia and extrapyramidal symptoms

Low Metabolic Side Effects

Mild weight gain (1.52 kg) reported in the pooled brilaroxazine dose group. Weight gain was not dose dependent with least weight gain (1.28 kg) at 50 mg dose. Decrease in lipid levels (cholesterol, LDL cholesterol) and no significant change in blood sugar levels reported

No Endocrine / Sexual Effects

Brilaroxazine is not associated with hormonal imbalance and sexual side effects. Elevated prolactin levels reported at the beginning of the study were significantly reduced to normal or near normal in all three dose groups. Improvement in thyroid hormone levels and sexual function reported

No Cardiac, GI & Liver Side Effects

No incidence of clinically significant cardiac or gastrointestinal side effects
No incidence of drug induced liver injury (DILI)

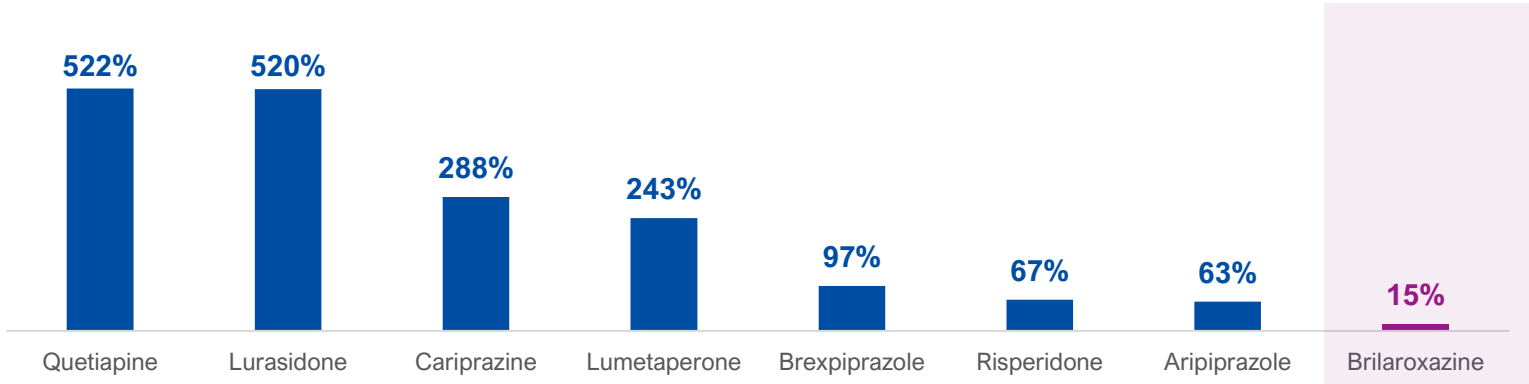
Lower Drug-Drug Interactions (DDIs) with Brilaroxazine vs. Standards of Care

DDIs and polypharmacy alter plasma drug concentrations, and can impact efficacy and side effect profiles of a drug¹¹ | ~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

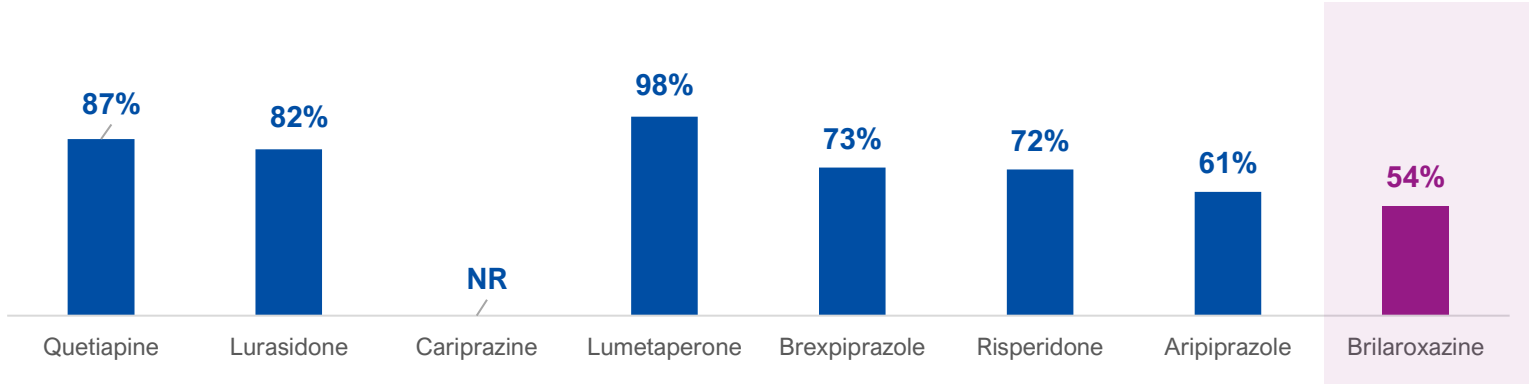
Change in drug concentration with a CYP3A4 Inhibitor¹

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

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



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



Lower is better

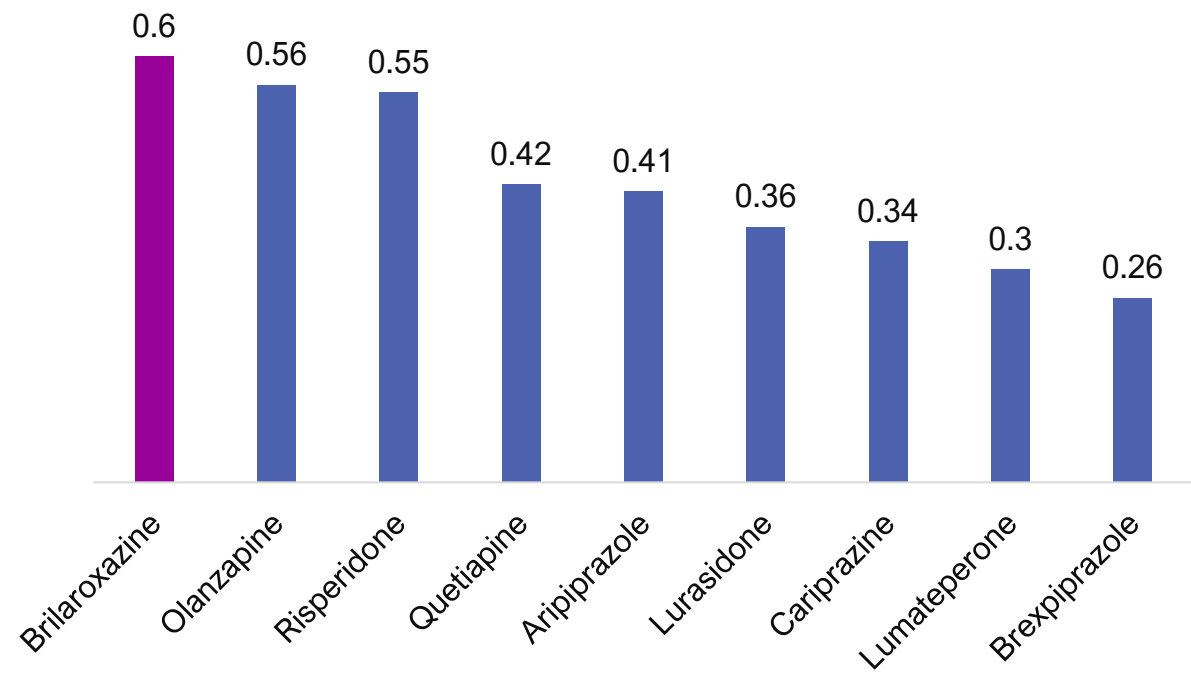
⁹Olanzapine not evaluated; metabolized by CYP1A2¹⁰

(1) Brilaroxazine data vs standard of care antipsychotic historical data. 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

Comparison of Treatment Effect Size: Brilaroxazine vs Standard of Care Antipsychotics

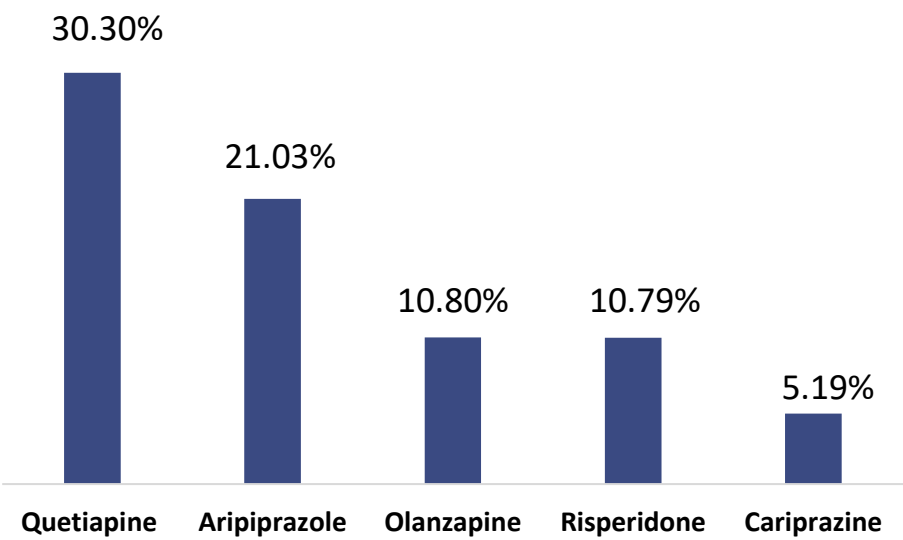
Phase 3 data of brilaroxazine (50 mg) vs. historical data of current standard of care antipsychotics

Brilaroxazine¹ vs Marketed Antipsychotics^{2,3}



Top 5 Antipsychotics Market Share in 2024⁴

(United States)



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; (4) Definitive Healthcare 2025

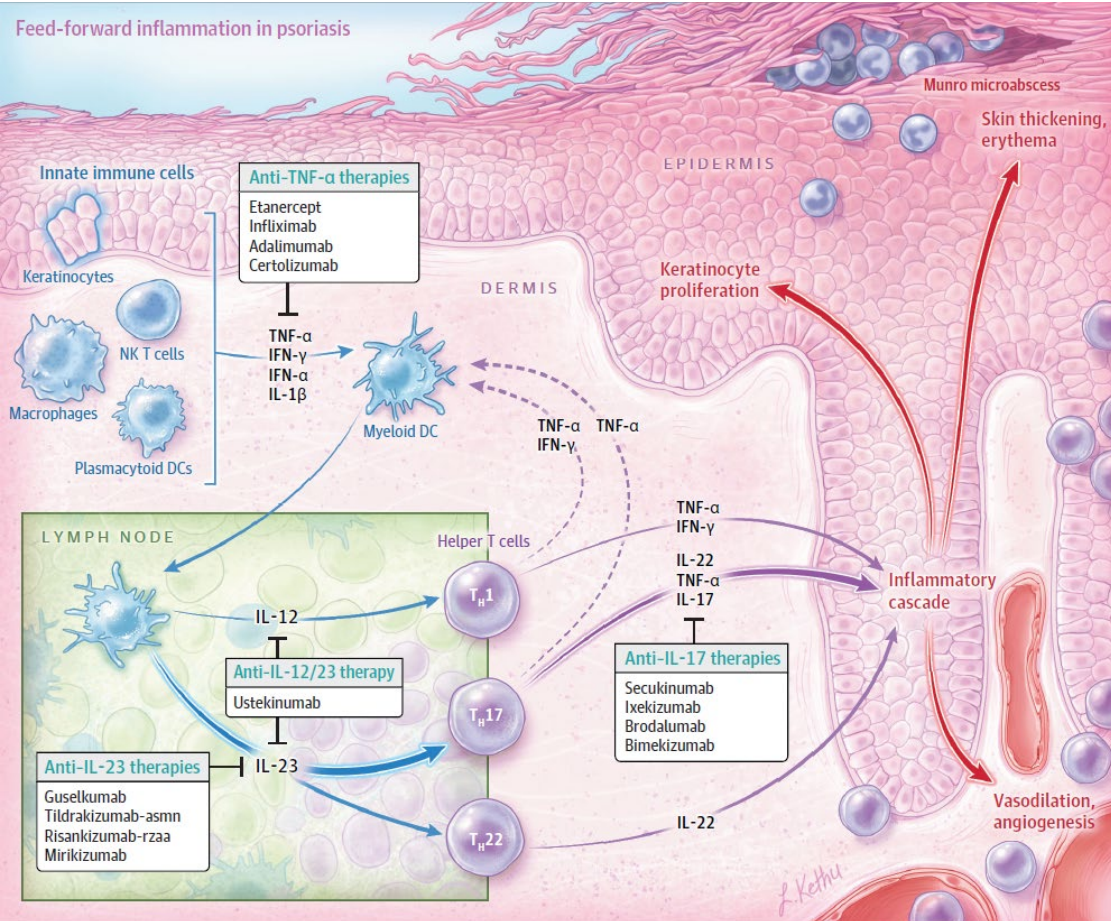
A doctor in a white lab coat with a stethoscope around their neck, holding a large X-ray of a human chest. The X-ray shows the ribcage and lung fields. The doctor is standing in front of a window with a blue frame.

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



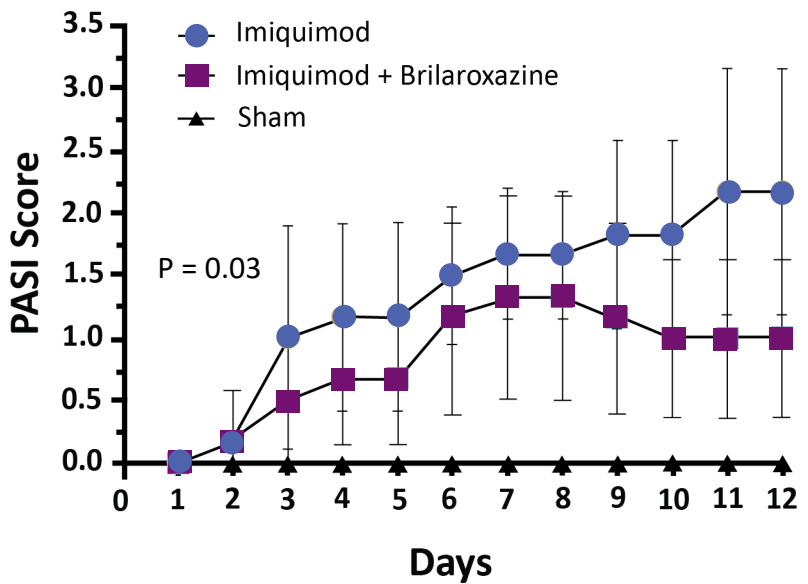
- Approx 3% of the US population and an estimated 125 million people worldwide suffer from psoriasis
- An estimated one-third of neuropsychiatric and neurodegenerative disease patients suffer from psoriasis
- Currently there is no known cure for psoriasis
- Approved treatments for management of psoriasis
 - 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

Bhat L et al. Skin Research & Technology 2024, 30:e13606; Sara Berg, AMA 2023; Armstrong AW. Pathobiology, clinical presentation, and Treatment of psoriasis, JAMA 2020, 323(19):1945-1960;

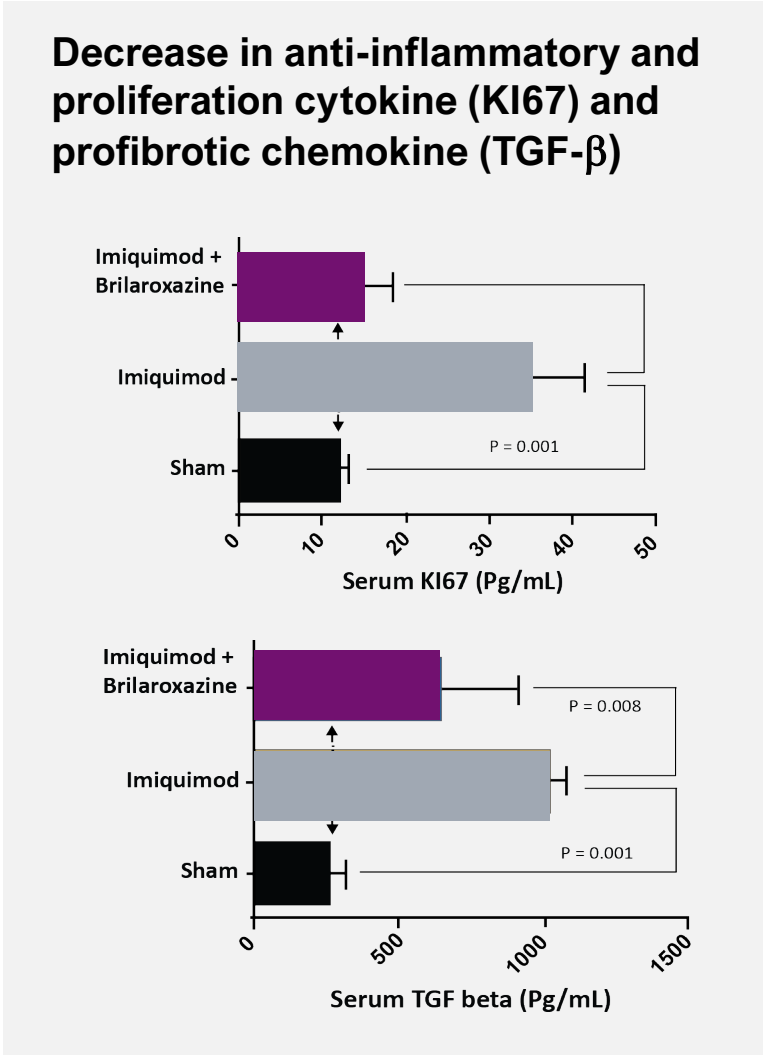
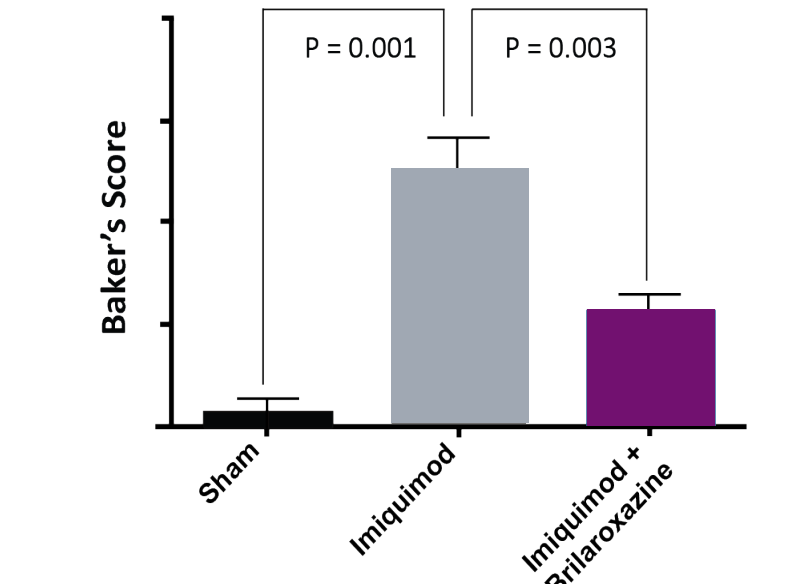
Brilaroxazine Demonstrated Encouraging Preclinical Efficacy

In an imiquimod induced mouse model of psoriasis

Psoriasis Area Severity Index (PASI)



Psoriasis Severity by Baker Score



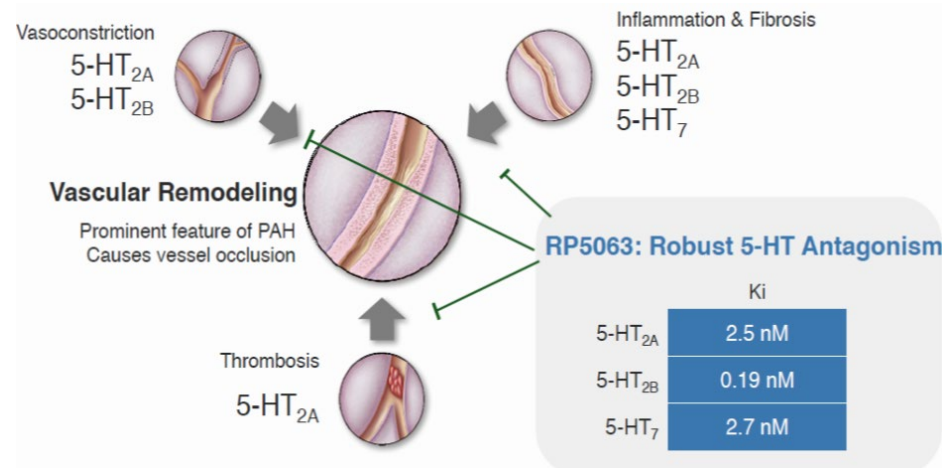
Brilaroxazine topical liposomal gel significantly decreased

- 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)

Brilaroxazine: Potential to Delay PAH and IPF Disease Progression

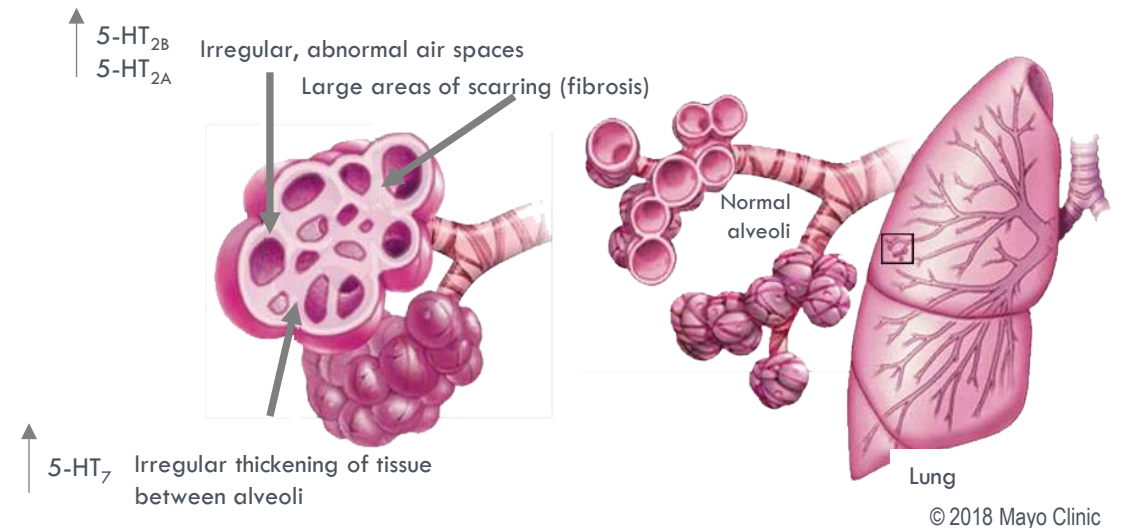
PAH and IPF are Orphan Diseases that involve dysfunctional serotonin signaling

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

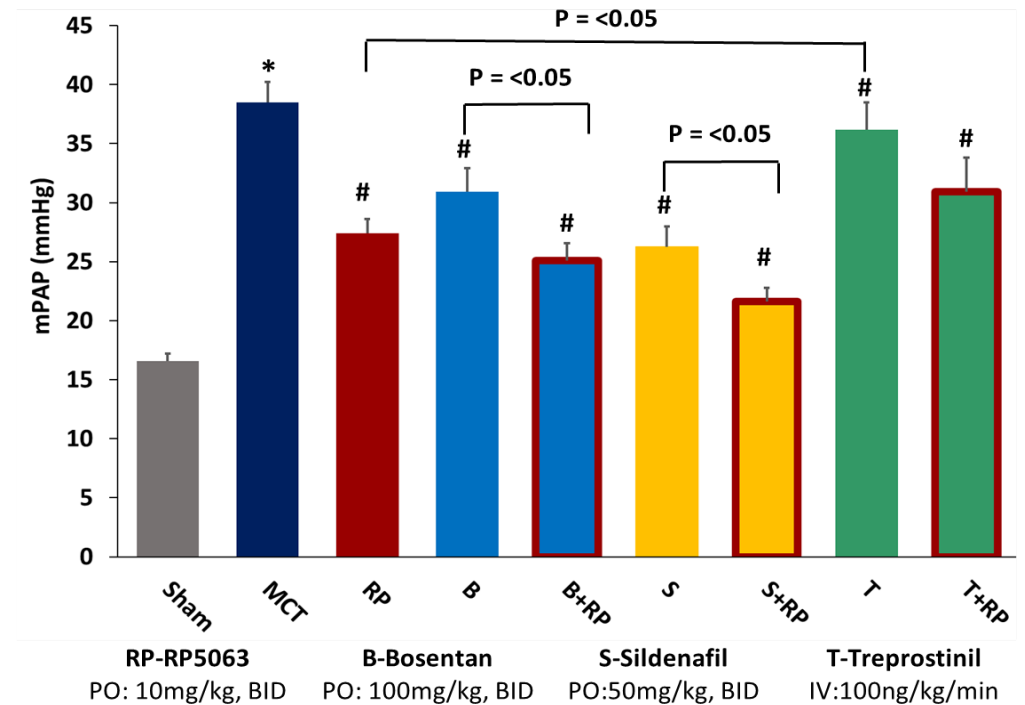
Brilaroxazine: Encouraging Results in PAH Translational Rodent Models

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 $\text{TNF}\alpha$, $\text{IL-}\beta$, IL-6 , and chemokine LTB4

Brilaroxazine mitigates pulmonary hypertension and lung fibrosis/collagen



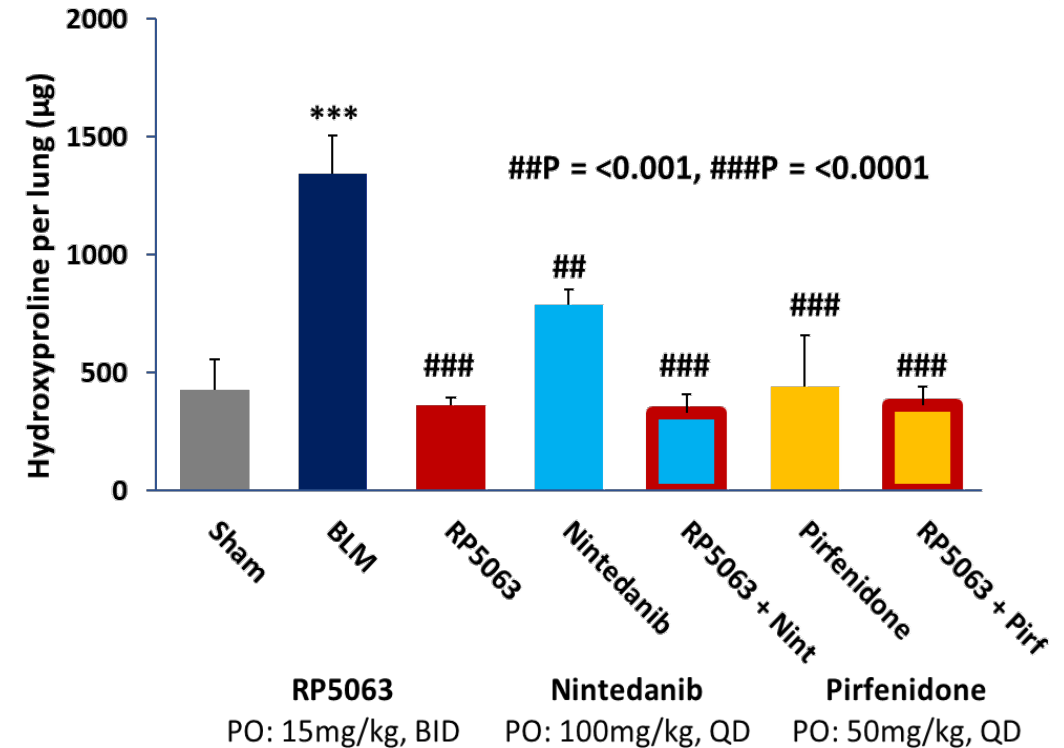
Brilaroxazine: Encouraging Results in Bleomycin-Induced IPF Rodent Model

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, IFN γ , MCP1, IL-6, and IL-17
- Improved survival rates

Brilaroxazine mitigates lung fibrosis / collagen (Decrease in Hydroxyproline)



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

Reviva Pharmaceuticals Holdings, Inc.

General Inquiries

info@Revivapharma.com

Business Inquiries

busdev.rp@Revivapharma.com

Investor Relations Contact

IR@Revivapharma.com



Global Operations

U.S. Headquarters

Cupertino, CA, USA

International Offices

Bangalore, India

