



# Reviva Pharmaceuticals

Corporate Presentation

May 2026

# 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 the Private Securities Litigation Reform Act, as amended, including those relating to the Company's plans for its brilaroxazine program including intended steps of advancing further clinical development and additional steps towards potential approval, the Company's statements regarding its planned registrational RECOVER-2 Phase 3 trial evaluating brilaroxazine for the treatment of schizophrenia, including the expected timing of initiation of patient enrollment, statements about the Company's planned use of a new form of brilaroxazine in its RECOVER-2 Phase 3 trial and in its future NDA submission, statements about anticipated FDA feedback, optimism about FDA alignment, and the timing thereof, statements about the Company's strategy to strengthen the long-term value of brilaroxazine and the potential to extend patent protection and commercial exclusivity, statements about potential NDA and other regulatory submissions, 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 and the timing thereof, including the anticipated timing of the availability of trial data, clinical and regulatory timelines and expenses, planned or intended additional trials or studies and the timing thereof, planned or intended regulatory submissions and the timing thereof, trial results, statements about the transition of the Company's common stock to quotation on the OTCQB Venture Market (which is subject to additional risks compared to being listed on a national securities exchange including the Company's ability to maintain compliance with the standards for continued quotation on the OTC Markets, together with limited liquidity, increased volatility, sporadic trading in the public market for the Company's common stock, and that our ability to raise additional capital while trading on the OTC Markets may be adversely impacted), market opportunity, ability to raise sufficient funding, the Company's cash position and its projected cash runway, statements about competitive position, possible or assumed future results of operations, business strategies, potential opportunities for development including partnerships, growth or expansion 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.

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# Schizophrenia: Common Psychiatric Condition With Multiple Symptom Domains

- Affects ~1.1% of the world's population
  - ~ 24 million globally; ~ 3.5 million people in USA
- Mix of heterogenous psychotic symptoms with varying degrees of severity
- Most patients requires lifelong treatment

## Key Unmet Needs:

~30% of patients are treatment refractory

High treatment discontinuation rate (30-74%)

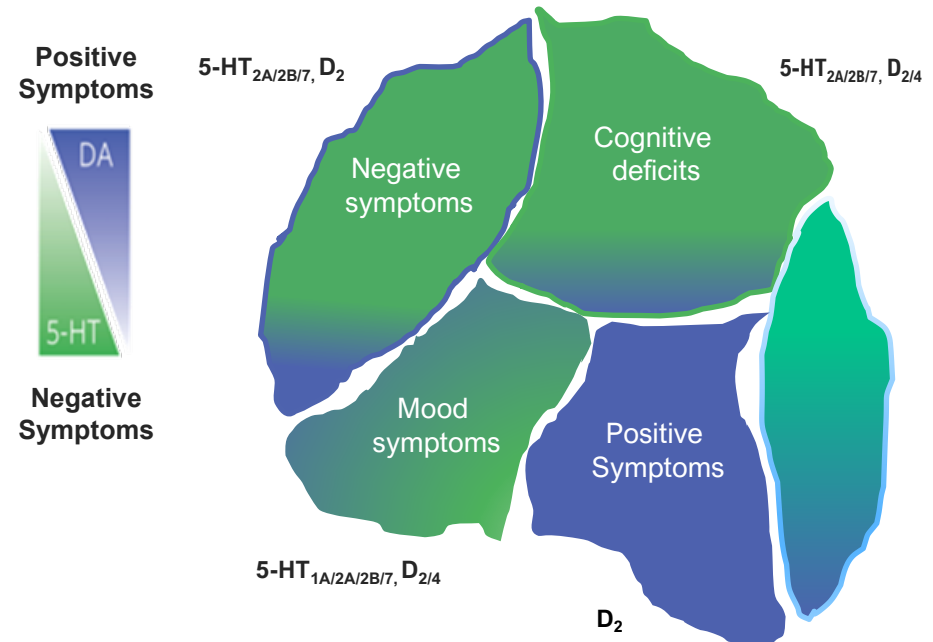
Relapse rate ~25% in 1 year and ~90% in 5 years

Treating neuroinflammation, a major contributing factor

Negative symptoms and nonadherence to treatment

## Major Symptom Domains of Schizophrenia

Primarily driven by dysfunctional serotonin and dopamine signaling



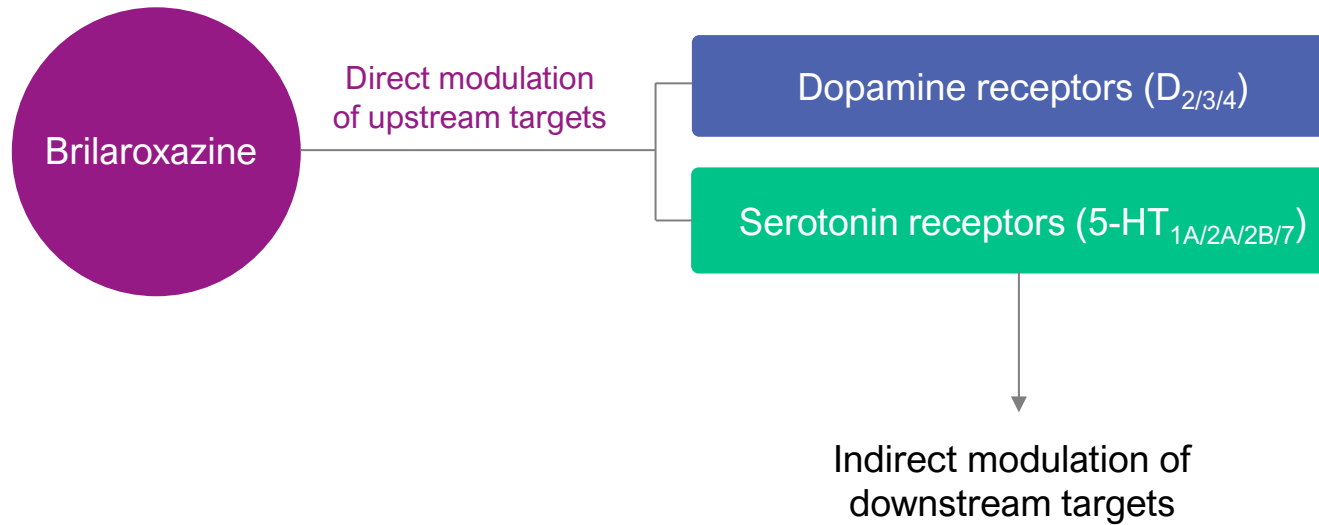
D = Dopamine signaling/ and 5-HT = Serotonin signaling

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://fherehab.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; Horvitz-Lennon et al. Am J Psych 2017, 17(5):421-426; 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 Receptor Activities

High ( $K_i$ , nM)*	Dopamine $D_2$	0.47
	Dopamine $D_3$	3.7
	Dopamine $D_4$	6
(5-HT <sub>2B</sub> > D <sub>2</sub> )	Serotonin 5-HT <sub>1A</sub>	1.5
	Serotonin 5-HT <sub>2A</sub>	2.5
	Serotonin 5-HT <sub>2B</sub>	0.19
Moderate ( $K_i$ , nM)	Serotonin 5-HT <sub>7</sub>	2.7
	Nicotine $\alpha_4\beta_2$	36.3
Weak or no significant activity	Serotonin 5-HT <sub>6</sub>	51
	No significant activities at therapeutic dose for off-targets 5-HT <sub>2C</sub> , $\alpha_{1,2}$ , and $M_{1-4}$ implicated in cardiometabolic, metabolic, or GI side effects	

\*partial agonists for  $D_{2,3,4}$  and 5-HT<sub>1A/2A</sub> receptors

Inflammatory cytokines

Implicated in inflammation and immune dysfunction

Nicotinic receptors

Implicated in positive symptoms and cognition

NMDA/Glycine receptors

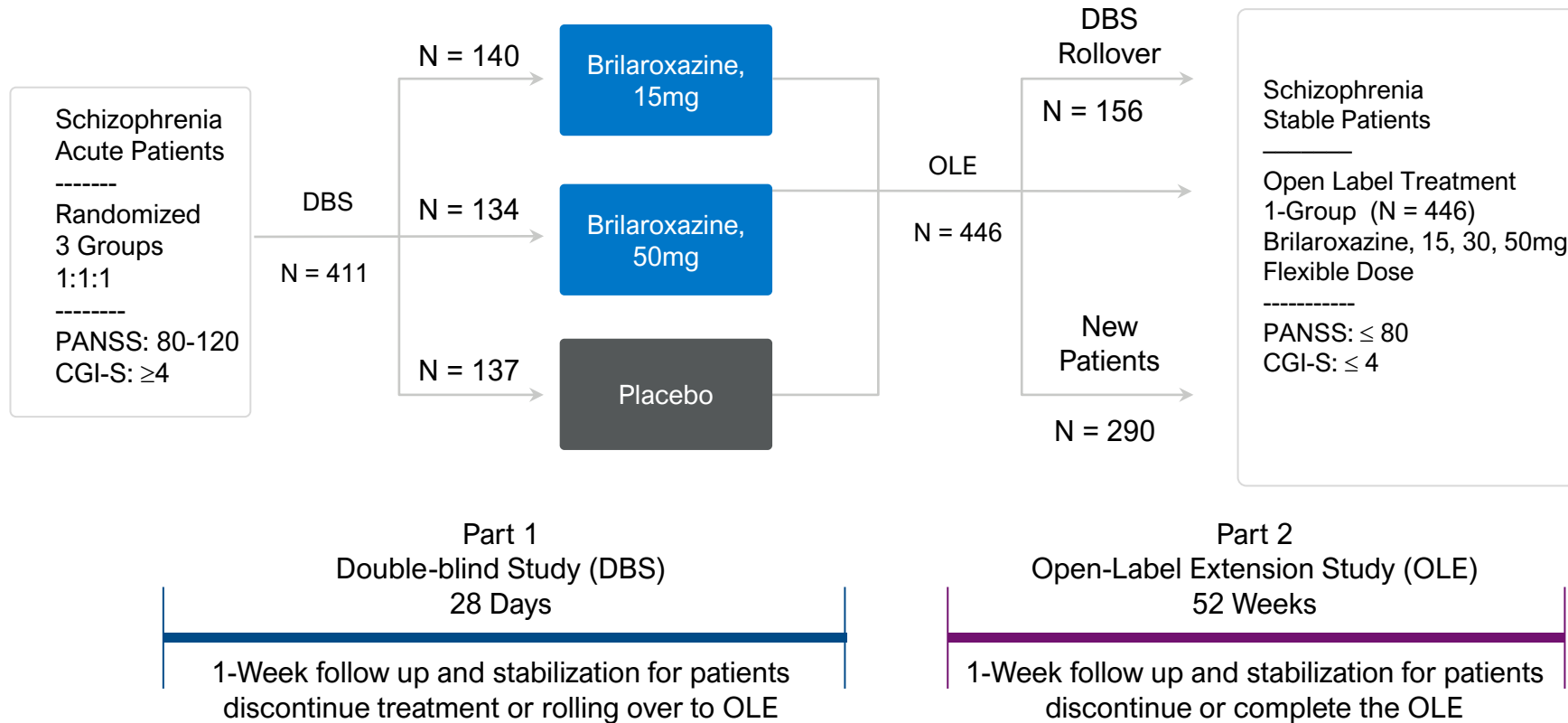
Implicated in negative symptoms and cognition

GABA receptors

Implicated in mood

# 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

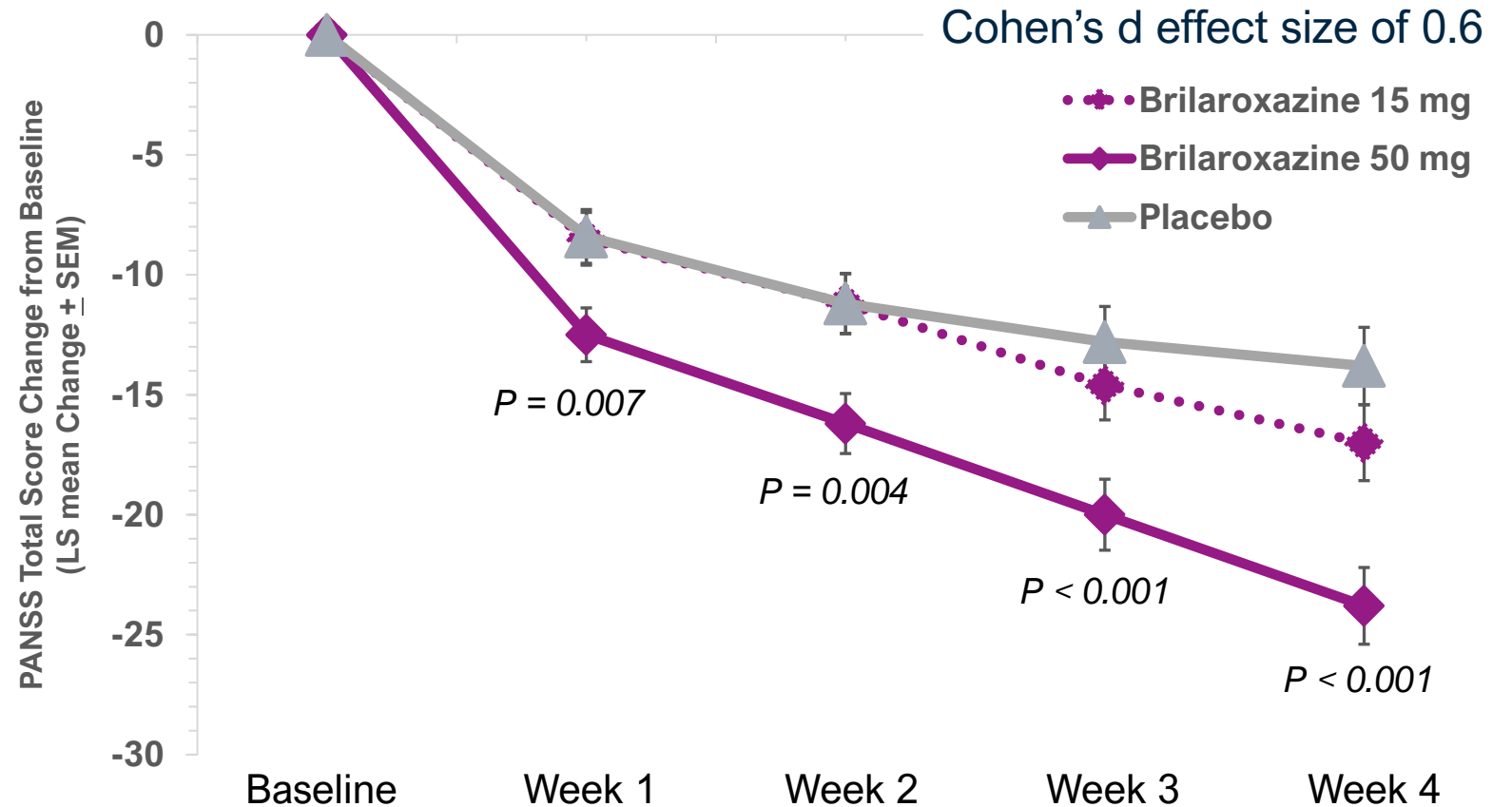
**Pharmacokinetics:**  
Population pharmacokinetics

# 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)

## Decrease in PANSS Total Score

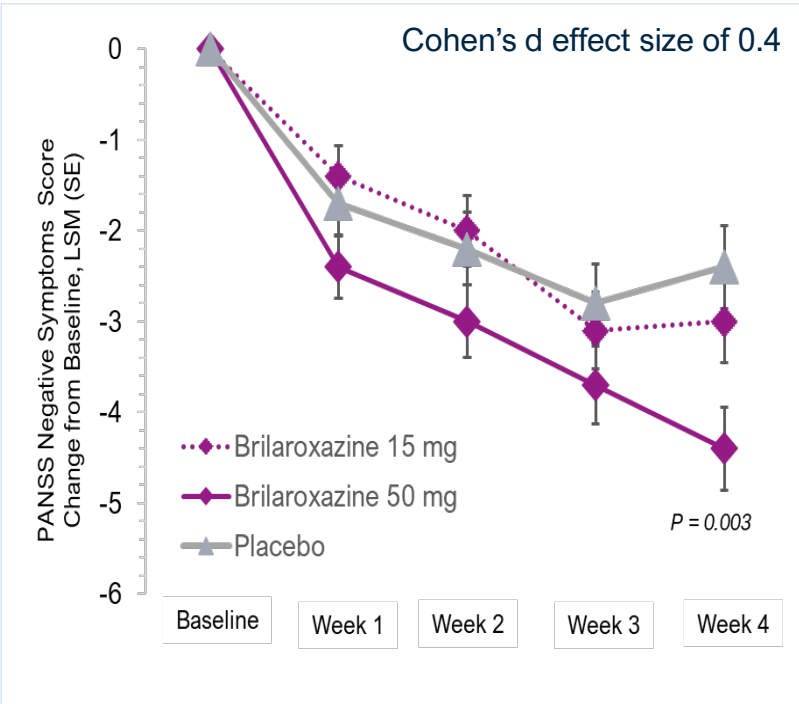
- Successfully met PANSS Total Score primary endpoint for brilaroxazine 50 mg
- Separation for brilaroxazine 50 mg from placebo within a week
- Brilaroxazine 15 mg numerically separated from placebo
- Results further supported by vocal and blood biomarkers data



# Phase 3 RECOVER Trial Efficacy for Negative Symptoms

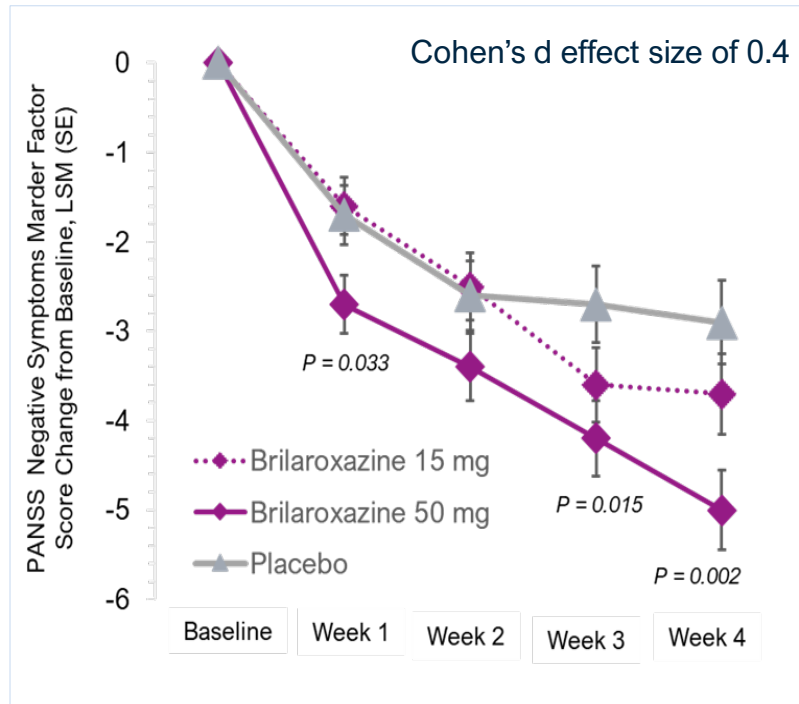
Significant efficacy for negative symptoms further supported by voice biomarker (VB)

## PANSS Negative Symptom Scores



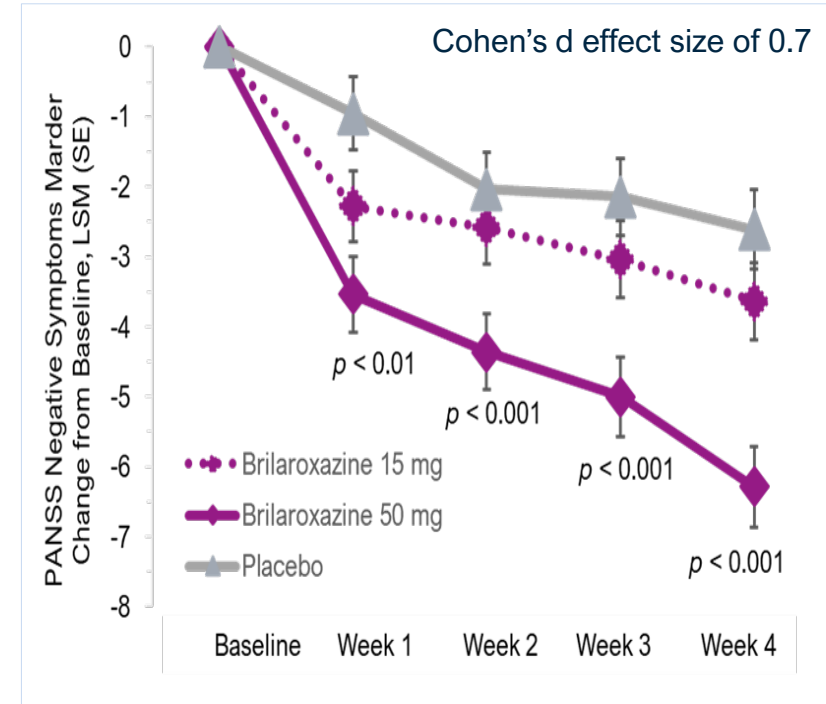
- 2.0 points decrease in Brila-50mg vs placebo (P=0.003) over 4 weeks
- Early onset strong and progressive efficacy

## PANSS Negative Marder Scores



- 2.1 points decrease in Brila-50mg vs placebo (P=0.002) over 4 weeks
- Early onset strong and progressive efficacy
- Significant improvement in Marder scores for depression, hostility & disorganized thoughts

## PANSS Negative Marder Scores in VBP



- 3.7 points decrease in Brila-50mg vs placebo (P=<0.001) over 4 weeks in VB positive patients
- Early onset strong and progressive efficacy
- Significant improvement in Marder scores for depression, hostility & disorganized thoughts

# Brilaroxazine Phase 3 Trial: Favorable Efficacy, Safety & Adherence

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

## Acute Schizophrenia Patients

Brilaroxazine 50mg vs Placebo

Symptom Domains	Point Improvement*	Cohen's d Effect Size
PANSS Total Score	-10.1	0.6
PANSS Positive Symptoms	-2.8	0.5
PANSS Negative Symptoms	-2.0	0.4
PANSS Negative Marder Factor	-2.1♦♦	0.4
PANSS Social Cognition	-1.6	0.5
PANSS Excitement/Agitation	-2.1	0.5
PANSS Gen Psychopathology	-5.3	0.6
Personal & Social Performance	6.3	0.5
CGI-S Score	-0.5 (≥1-point in 78%)	0.5
<b>Treatment Discontinuation</b>	16% (vs. placebo, 22%)	

## Primary Negative Symptom Patients

### Vocal Biomarker Positive

Brilaroxazine 50mg vs Placebo

Point Improvement*	Cohen's d Effect Size
-15	0.9
-3.5	0.8
---	---
-3.7	0.6
-3.8	0.8
---	---
---	---
6.3	0.6
-0.7	0.7

## Acute Patients

### Blood Biomarkers

<b>Neurotrophins*</b> BDNF
<b>Hormones*</b> Prolactin Thyroid T3
<b>Cytokines*</b> IL-6 IL-8 IL-10 IFN-γ/IP-10 TNF-α MIP-1

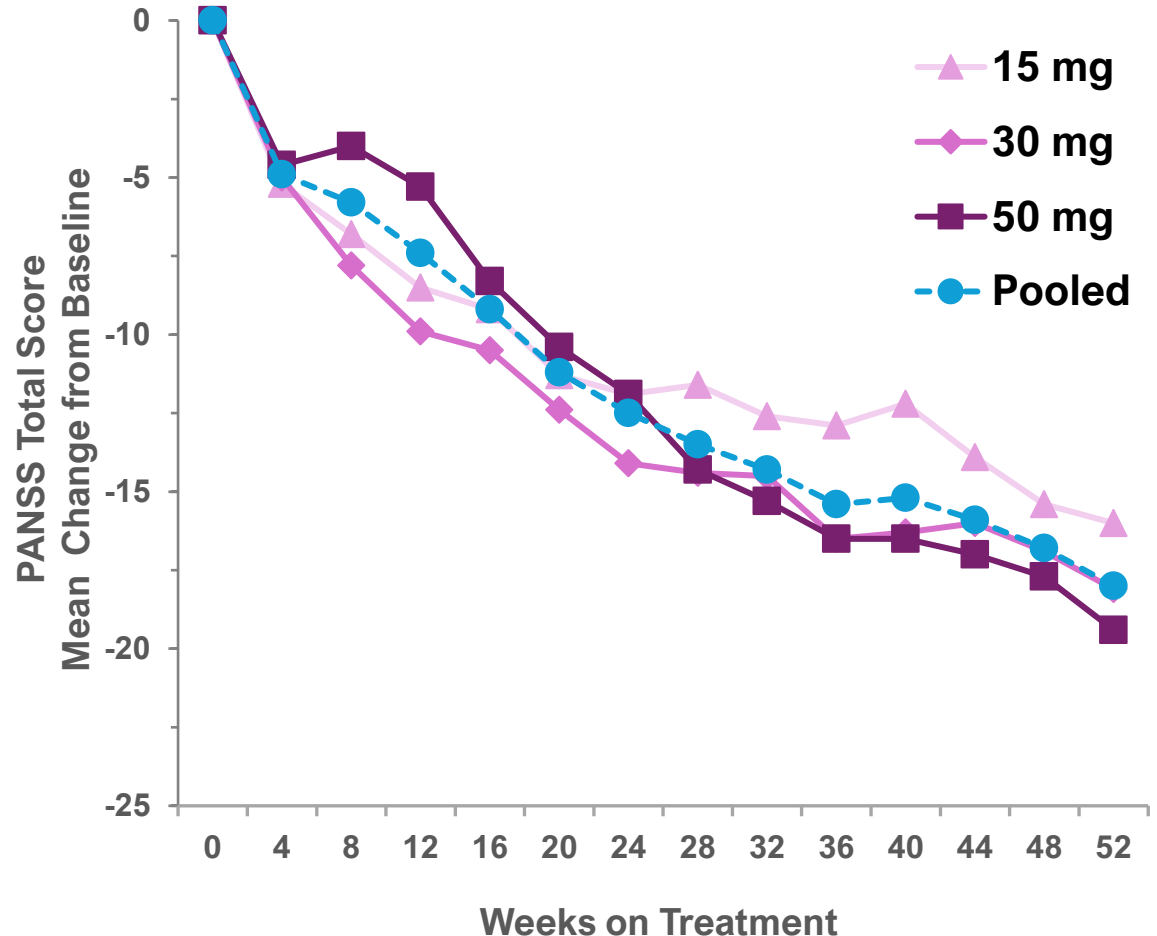
\*Improved vs placebo

# PANSS Total Score: Progressive & Durable Effect Sustained Over 1-year

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

## CHANGE IN PANSS TOTAL SCORE

- Strong, progressive and durable effect on PANSS score from acute through maintenance treatment with <1% report of exacerbation or relapse of symptoms over 1-year treatment
- Dose dependent decrease from baseline to Week-52 (1-year)
  - 16.0-point decrease in 15 mg (61.2 → 45.2)
  - 18.1-point decrease in 30 mg (69.7 → 51.7)
  - 19.4-point decrease in 50 mg (75.6 → 56.2)
  - 18.0-point decrease in pooled (69.9 → 51.8)
- Decrease in PANSS total score in rollover patients (N=50) from the double-blind trial to OLE over 1-year treatment (Baseline to Week-56):
  - 46.1-point decrease in 15 mg (97.4 → 51.3)
  - 49.7-point decrease in 50 mg (102.7 → 53.1)



# Brilaroxazine Phase 3 Trial OLE: Favorable Efficacy and Adherence Results

Progressive and durable broad-spectrum efficacy results across all three doses of brilaroxazine (15, 30 and 50 mg)

Clinically Stable Schizophrenia Patients (N=446, 52 Weeks / 12 Months)

Mean Change from Baseline in Brilaroxazine overall (15+30+50mg)

Symptom Domains	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
PANSS Positive Symptoms	-3.3	-5.0	-14.0
PANSS Negative Symptoms	-2.8	-4.4	-10.5
PANSS Negative Marder Factor	-3.0♦	-4.4♦	-10.5♦
PANSS Social Cognition	-1.5	-2.9	-7.9
PANSS Excitement/Agitation	-1.4	-3.1	-8.3
PANSS Gen Psychopathology	-4.7	-8.7	-23.2
Personal & Social Performance (PSP)	4.5	11.3	32.7
CGI-S Score	-0.4 (≥1 point in 37%)	-0.8 (≥1 point in 59%)	-2.5 (≥1 point in 100%)
<b>Treatment Adherence</b>	Discontinuation rate, 36% (Historical, up to 80%) <sup>1</sup>		

## Blood Biomarkers

### Neurotrophins\*

BDNF

### Hormones\*

Prolactin

Thyroid T3

### Cytokines\*

IL-6

IL-8

IL-10

IFN-γ/IP-10

TNF-α

MIP-1

\*Improved vs Baseline

♦Significant improvement in Marder scores for depression, hostility and disorganized thoughts

\*Baseline to EOT, P = ≤0.001; OLE: Open Label Extension; \*\*Brila-15 & 50mg patients rolled over from DB to OLE;

<sup>1</sup>Khandkar R et al. Schizophrenia Res. 2025, 283:152-162; Desai R et al. JMCP 2019, 25(1):37-44

# Brilaroxazine Phase 3 RECOVER Trial Safety Data Over 52 Weeks / 1-year

Acute Schizophrenia (Double-blind, 4-week) and Stable Schizophrenia (Open-label, 52-week)

Adverse Events	Acute Schizophrenia (N=411, 4-Week)		Stable Schizophrenia (N=446, 52-Week)	
	Placebo (N=137)	Brila-50 mg (N=134)	Brila-50 mg (N=148)	Brila-(Pool:15+30+50mg) (N=446)
<b>Number of subjects with any TEAE</b>	58 (42.3%)	62 (46.3%)	67 (45.3%)	166 (37.2%)
<b>TEAE occurring in &gt;2% participants</b>				
Headache	3 (2.2%)	7 (5.2%)	4 (2.7%)	12 (2.7%)
Insomnia	3 (2.2%)	2 (1.5%)	10 (6.8%)	18 (4.0%)
Somnolence	3 (2.2%)	10 (7.5%)	0	0
<b>Metabolic Changes (weight and lipids), TEAE</b>				
Body Weight Change in kg, Mean (SD)	0.90 (2.9)	2.5 (3.5)	1.0 (3.7)	0.89 (3.4)
≥7% Increase in Body Weight, n (%)	4 (2.9)	8 (5.9)	6 (4.1%)	11 (2.5%)
Cholesterol change in mg/dl, Mean (SE)	2.3 (2.61)	-5.1 (2.4)*	-9.0 (2.36)	-7.0 (1.36)
LDL change in mg/dL, Mean (SE)	3.0 (2.17)	-6.1(1.97)*	-9.8 (2.04)	-6.9 (1.19)
HDL change in mg/dL, Mean (SE)	-2.4 (0.89)	0.2 (1.19)	0.4 (0.79)	-0.3 (0.44)
<b>Extrapyramidal Symptoms, TEAE</b>				
Barnes Akathisia Rating Score, Mean (SD)	0.1 (0.35)	0.0 (0.19)	0.0	0.0
Abnormal Involuntary Movement Score, Mean (SD)	0.0 (0.48)	-0.0 (0.28)	-0.0 (0.31)	-0.0 (0.36)
Simpson-Angus Score, Mean (SD)	0.3 (0.71)	0.2 (0.48)	0.0	0.0

TEAE = Treatment Emergent Adverse Event; Brila = Brilaroxazine

\*P ≤0.05 vs Placebo

# RECOVER DB Trial Efficacy & Safety Biomarker: Reduction in Elevated Prolactin

Clinically significant decrease in elevated prolactin in brilaroxazine (15 and 50mg) vs placebo over 4-week

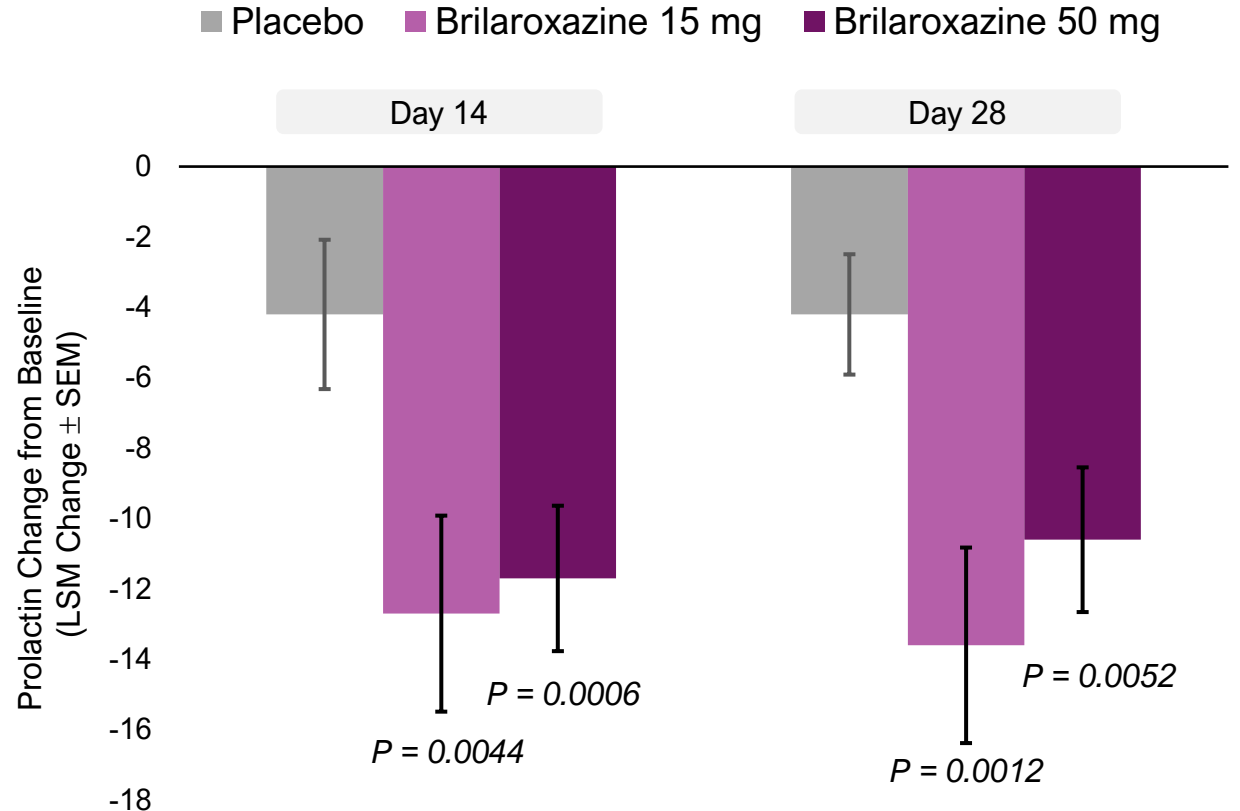
## Decrease in Elevated Serum Prolactin Levels

- Clinically significant decrease on Day 14 and Day 28 in brilaroxazine (15 and 50 mg) vs placebo
- Elevated prolactin reduced to normal level\* in 4 weeks and maintained the normal level over 1 year

### Hyperprolactinemia is:

- a common condition in schizophrenia/psychiatric disorders
- associated with immune disorders / diseases and believed to play crucial role in their pathogenesis
- associated with weight gain, breast tenderness and enlargement, sexual dysfunction (lack of libido) in both men and women, and erectile dysfunction in men

## Change in Serum Prolactin ( $\mu\text{g/mL}$ )



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

# Brilaroxazine: Strong Efficacy Results & Generally Well-Tolerated with Favorable Discontinuation Over 1-Year RECOVER Phase 3 trials in acute and stable schizophrenia patients (total patients enrolled, N=857)

## Strong, Durable Efficacy Results

Demonstrated a significant, sustained, and durable broad-spectrum efficacy results in both acute and stable schizophrenia patients with <1% patients reported symptom relapse on treatment over 1-year. Favorable treatment adherence observed both in acute and stable patients

## Well-Tolerated over 1 year

Generally safe and well-tolerated after 1-year of treatment. Most common TEAEs (>2%) were headache, insomnia, sleep disturbance and tremor. No drug related SAEs or major safety concerns.

## 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

Benign weight gain (1.52 kg) in pooled dose group over 1 year; 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

## No Endocrine / Sexual Effects

No hormonal imbalance and sexual side effects. Elevated prolactin levels initially during study were significantly reduced to normal or near normal in all three dose groups. Improvement in thyroid hormone levels and sexual function

## No Cardiac, GI & Liver Side Effects

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

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

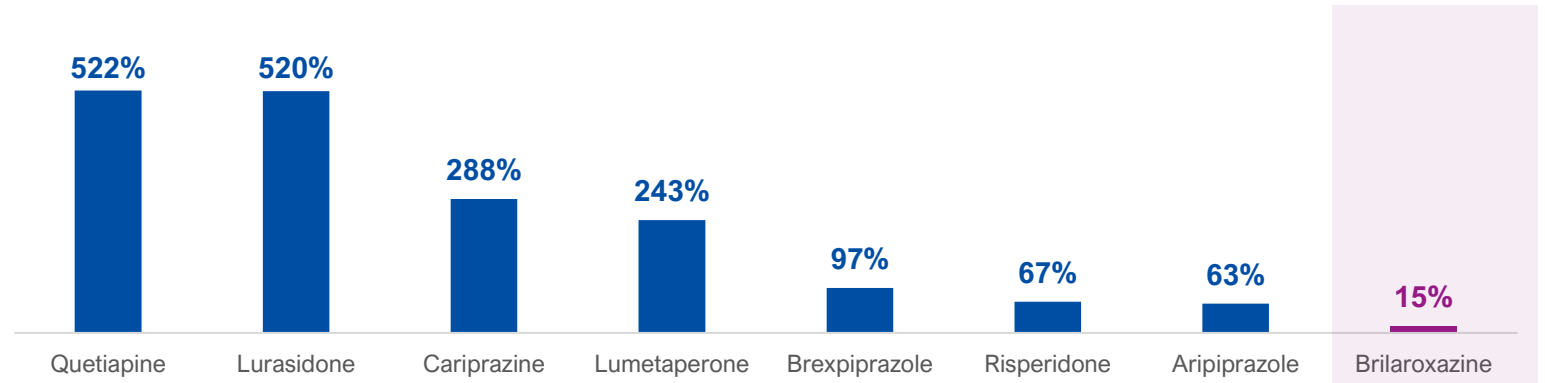
DDIs and polypharmacy alter plasma drug concentrations, and can impact efficacy and side effect profiles of a drug<sup>11</sup>

~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

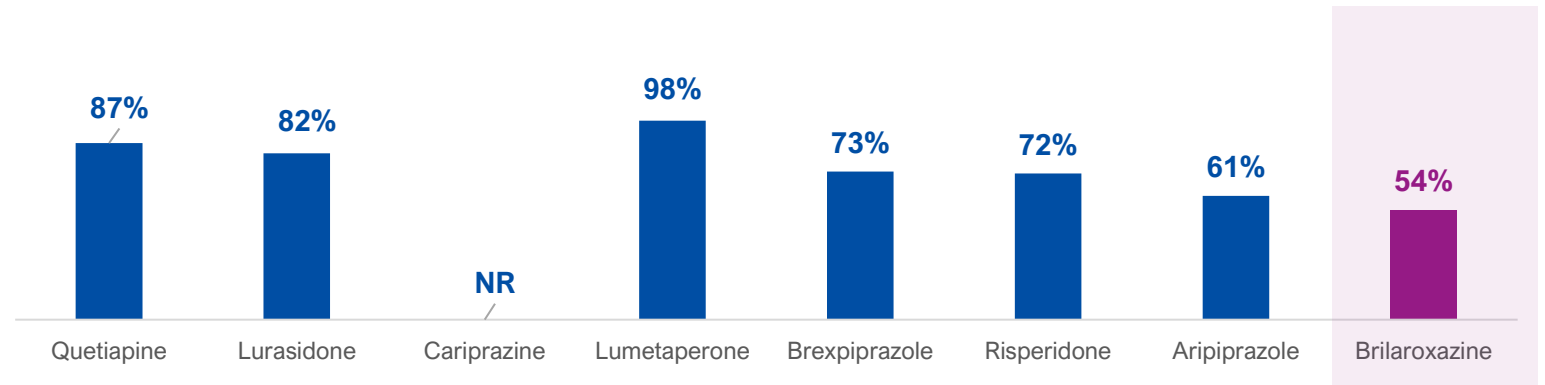
## Change in drug concentration with a CYP3A4 Inhibitor<sup>1</sup>

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  
↓

\*Olanzapine<sup>9</sup> not evaluated; metabolized by CYP1A2<sup>10</sup>

# Positive Registrational Trials To Date for Brilaroxazine in Schizophrenia

NDA-enabling safety pharmacology, toxicology & carcinogenicity studies, & CMC development largely complete

PHASE 1A and 1B, Clin Pharm Studies ☑ Completed	PHASE 2 REFRESH, DB NCT01490086 ☑ Completed	PHASE 3 RECOVER, DB NCT05184335 ☑ Completed	PHASE 3 RECOVER, OLE NCT05184335 ☑ Completed	PHASE 3 RECOVER-2, DB TBD Planned: Q3 2026 – Q4 2027
<b>Phase 1A</b> Healthy subjects, double-blind, safety and tolerability, pharmacokinetics (PK)	<b>N = 234 (4-Week)</b> <b>Acute schizophrenia or schizoaffective disorder</b>	<b>N = 411 (4-Week)</b> <b>Acute schizophrenia</b>	<b>N = 446 (52-Week/1-Year)</b> <b>Stable schizophrenia</b>	<b>N = 450 (4-Week)</b> <b>Acute schizophrenia</b>
<b>Phase 1B</b> 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	Efficacy and safety of brilaroxazine vs placebo
<b>ADME &amp; Bioavailability</b> 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	1:1:1 Randomized, 4-week, double-blind, placebo-controlled, multicenter
<b>Drug-Drug Interactions</b> 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	Once daily brilaroxazine 30, 50 mg
	Completed and met primary and multiple secondary endpoints	Completed and met primary and multiple secondary endpoints	Completed and met primary and multiple secondary endpoints	Expected to start in H1-2026 and topline data in Q4-2027

# Brilaroxazine Phase 2 and Phase 3 Trials Data Comparison

Early onset of action with progressive and durable broad-spectrum efficacy results sustained over 52 weeks (1 year)

Symptom Domains	Phase 2 REFRESH (DB, 4-Week) Acute Schizophrenia		Phase 3 RECOVER (DB, 4-Week) Acute Schizophrenia		Phase 3 RECOVER (OLE, 1 Year) Stable Schizophrenia
	Brilaroxazine 50mg vs Placebo		Brilaroxazine 50mg vs Placebo		Brilaroxazine (15/30/50mg) <sup>P</sup>
	Point Decrease / Improvement*	P-Value (Effect Size)	Point Decrease / Improvement*	P-Value (Effect Size)	Point Decrease / Improvement*
<b>Primary Endpoint: PANSS Total Score</b>	-9.1	< 0.001 (1.15)	-10.1	< 0.001 (0.6)	-18.1
PANSS Positive Symptoms	-2.6	<0.01 (1.31)	-2.8	< 0.001 (0.5)	-5.0
PANSS Negative Symptoms	-2.3	<0.01 (0.78)	-2.0	<0.01 (0.4)	-4.4
PANSS Negative Marder Factor	-1.6 <sup>♦♦</sup>	0.04 (0.70)	-2.1 <sup>♦♦</sup>	< 0.001 (0.4)	-4.4 <sup>♦♦</sup>
PANSS Social Cognition	-1.7	<0.01 (0.90)	-1.6	< 0.001 (0.5)	-2.9
PANSS Excitement/Agitation	-1.9	0.01 (0.70)	-2.1	< 0.001 (0.5)	-3.1
PANSS Gen Psychopathology	-4.3	<0.01 (0.96)	-5.3	< 0.001 (0.6)	-8.7
Personal & Social Performance	---	---	6.3	< 0.001 (0.5)	11.3
CGI-S score	-0.5 (≥1-point in 72%)	< 0.001 (1.25)	-0.5 (≥1-point in 78%)	< 0.001 (0.5)	-0.8 (≥1-point in 59%)
<b>Treatment Discontinuation</b>	12% (Placebo 28%)		16% (Placebo, 22%)		36% (Historical, up to 80%) <sup>1</sup>

♦Mean Change; ♦♦Significant improvement in Marder scores for depression, hostility and disorganized thoughts

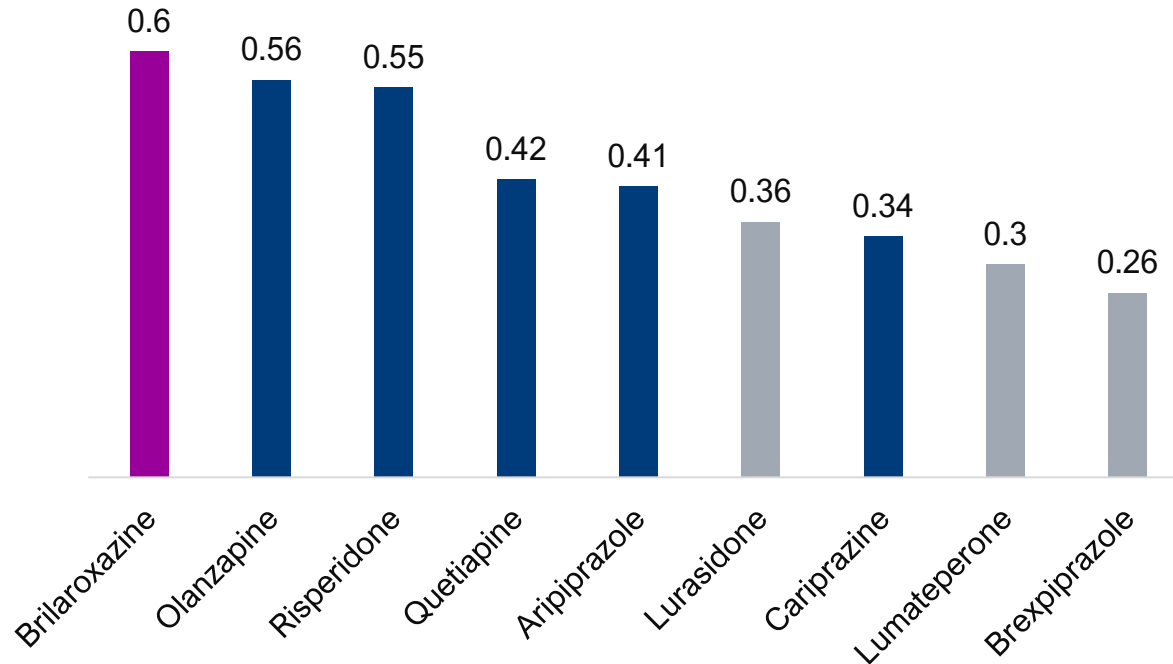
DB=Double-blind (4-week/1 month); OLE=Open-Label Extension (52-week/1 year); P=pooled data of 15, 30 and 50mg doses

<sup>1</sup>Khandkar R et al. Schizophrenia Res. 2025, 283:152-162; Desai R et al. JMCP 2019, 25(1):37-44

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

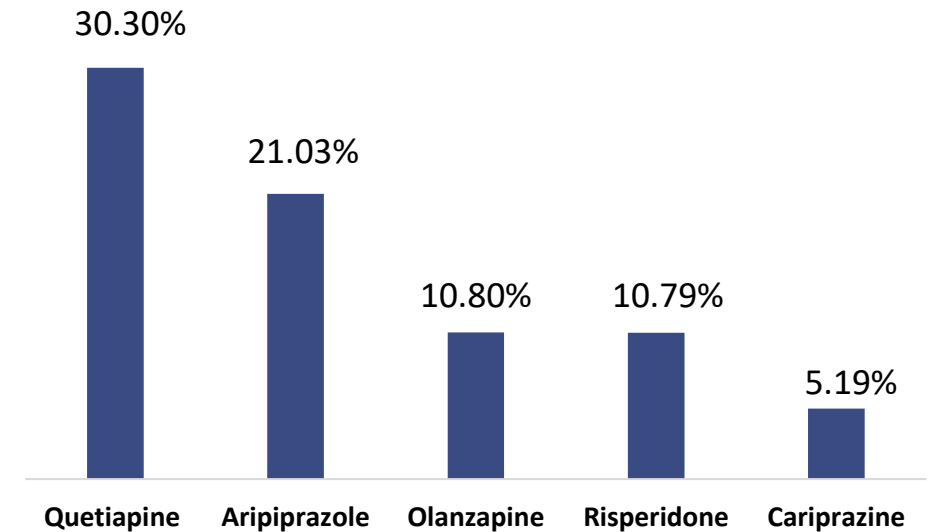
Phase 3 data of brilaroxazine (50 mg) vs. historical data of current standard of care antipsychotics

## Brilaroxazine<sup>1</sup> vs Marketed Antipsychotics<sup>2,3</sup>



## Top 5 Antipsychotics Market Share in 2024<sup>4</sup>

(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

# Clinical Profile Comparison of Brilaroxazine and Lumetaperone (Caplyta)\*

Johnson & Johnson acquired ITCI/Caplyta<sup>3</sup> in January 2025 for ~\$14.6 billion

Efficacy Scale	Brilaroxazine <sup>1</sup> Phase 3 (4-week) <sup>a</sup>	Caplyta <sup>2</sup> Phase 3 (4-week) <sup>b</sup>
<b>Primary Endpoint</b>		
PANSS Total Score	-10.1 P=<0.001 (ES, 0.6)	-4.2 P=0.04 (ES, 0.3)
<b>Secondary Endpoints</b>		
CGI-S score	-0.2 P=<0.001 (ES, 0.5)	-0.3 P=0.04 (ES, 0.3)
PANSS Positive Symptoms	-2.8 P=<0.001 (ES, 0.5)	-1.7 P=0.006 (ES, 0.3)
PANSS Negative Symptoms	-2.0 P=0.003 (ES, 0.4)	-0.9 P=Not Significant
PANSS Negative, Marder Factor	-2.1 P=0.002 (ES, 0.4)	Not reported
PANSS General Psychopathology	-5.3 P=<0.001 (ES, 0.6)	-2.4 P=0.01 (ES, 0.2)
Personal & Social Performance	+6.3 P=<0.001 (ES, 0.5)	+3.3 P=0.05 (ES, 0.2)
PANSS Social Cognition	-2.1 P=<0.001 (ES, 0.5)	Not Reported

Adverse Events	Brilaroxazine <sup>1</sup> Phase 3 (4-week) <sup>a</sup>	Caplyta <sup>2</sup> Phase 3 (4-week) <sup>b</sup>
<b>TEAEs &gt;5%</b>		
Headache	7 (5.2%)	29 (19.3%)
Somnolence	10 (7.5%)	26 (17.3%)
Sedation	--	19 (12.7%)
Constipation	--	10 (6.7%)
Fatigue	--	8 (5.3%)
<b>TEAEs of Special Interest (AESIs)</b>		
Body weight change, mean, kg	2.41	1.4
Extrapyramidal Symptoms (EPS)	1 (0.7%)	6 (4%)

- FDA approved Caplyta NDA based on the efficacy outcome of a Phase 2 and a Phase 3 trials in acute schizophrenia. Caplyta did not separate from placebo in the 2<sup>nd</sup> Phase 3 trial on primary endpoint, PANSS Total.
- Caplyta 42 mg showed -4.2 points separation from placebo in the 1<sup>st</sup> Phase 3, and -5.8 points in the Phase 2 trials on PANSS Total.

\*No head-to-head studies of brilaroxazine and Caplyta have been conducted. Because of differences in patient populations, study designs and numerous other factors, cross trial comparisons must be interpreted with caution, and no conclusions can be drawn.

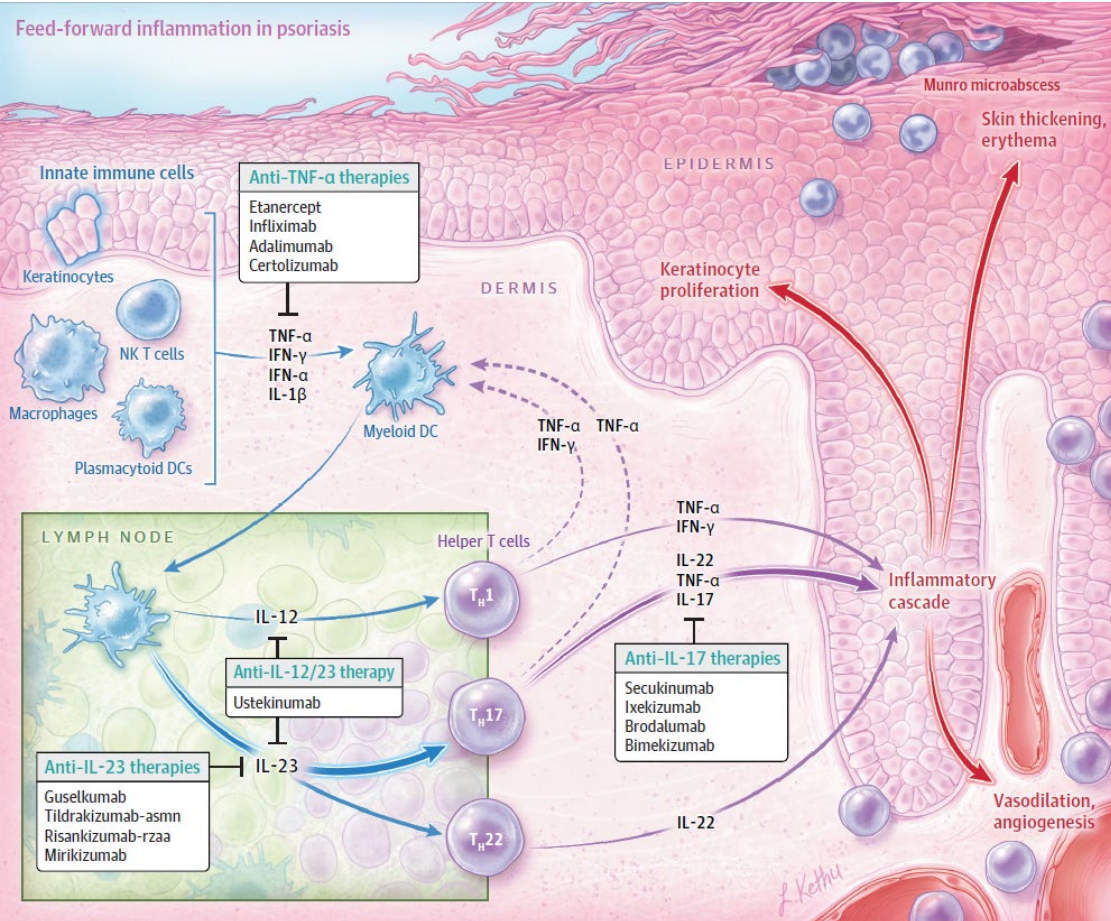


## Inflammatory / Immune Disease Programs

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

# Brilaroxazine has Potential to Treat Psoriasis

Inflammatory skin disease driven by dysfunctional serotonin-dopamine signaling



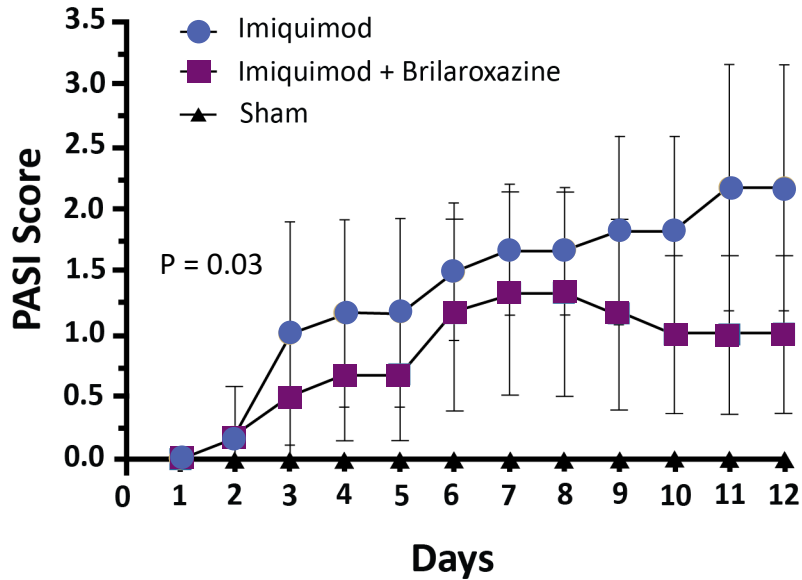
- ~3% of the US population and ~125 million people worldwide suffer from psoriasis
- ~One-third of neuropsychiatric and neurodegenerative disease patients suffer from psoriasis
- Currently there is no known cure for psoriasis
- Approved treatments for management of psoriasis
  - Topical corticosteroids therapies are cornerstone for mild psoriasis
  - Biologics that inhibit cytokines TNF- $\alpha$ , 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;

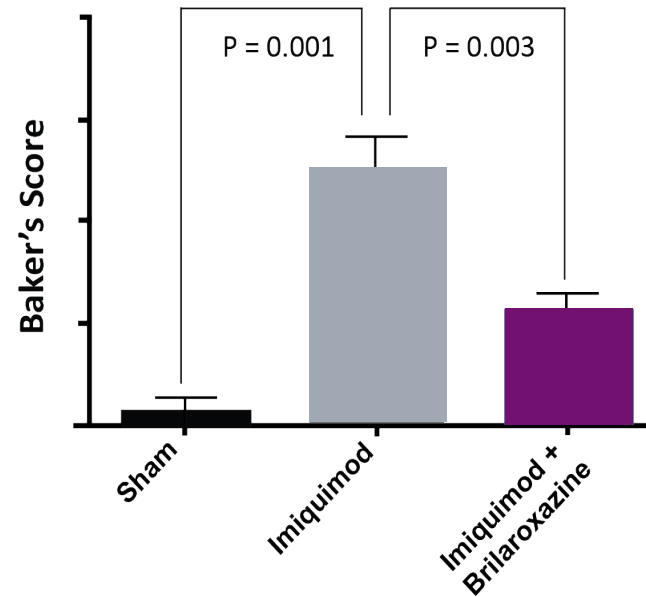
# Brilaroxazine Demonstrated Encouraging Preclinical Efficacy

In an imiquimod induced mouse model of psoriasis

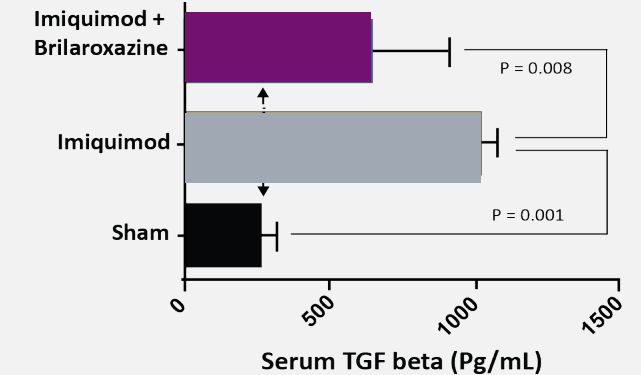
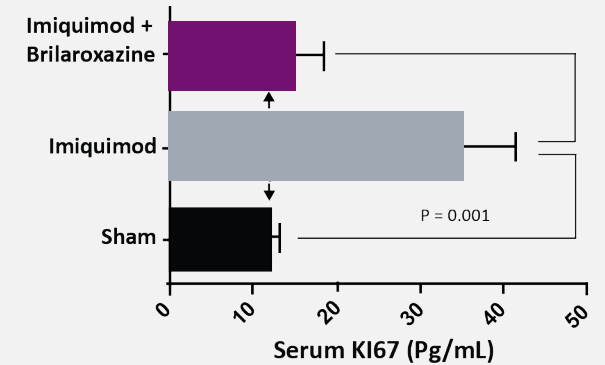
## Psoriasis Area Severity Index (PASI)



## Psoriasis Severity by Baker Score



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



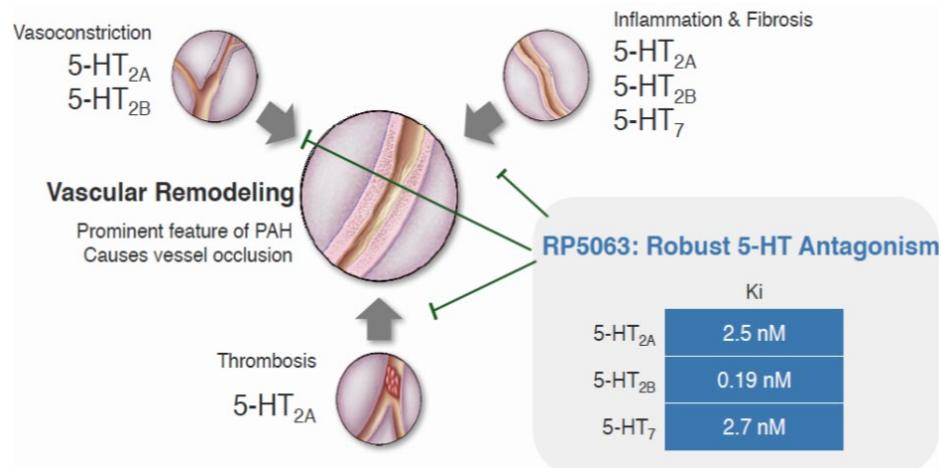
**Brilaroxazine topical liposomal gel significantly decreased**

- 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

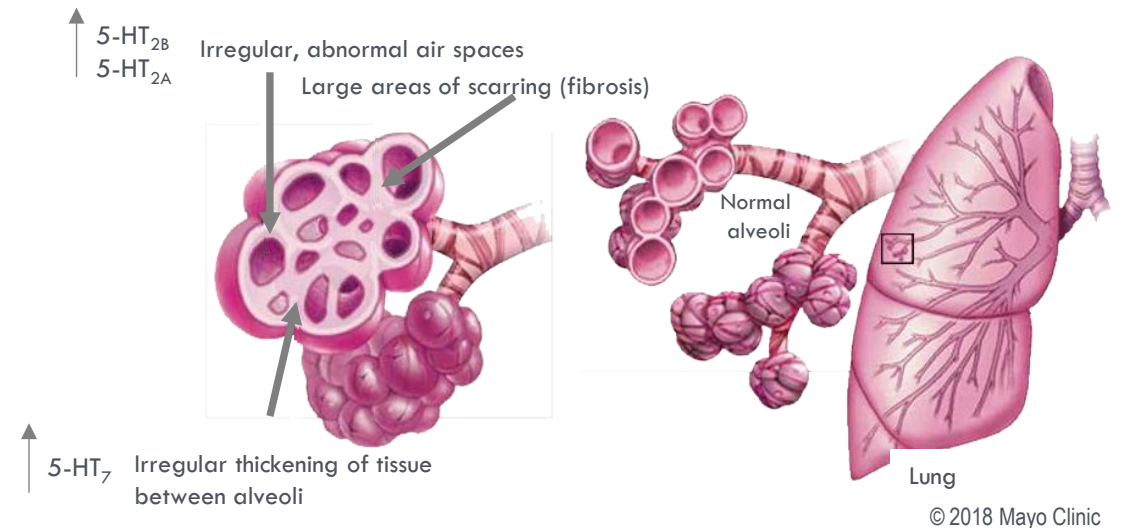
PAH and IPF are Orphan Diseases that involve dysfunctional serotonin signaling

## 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<sub>2A/2B/7</sub> 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

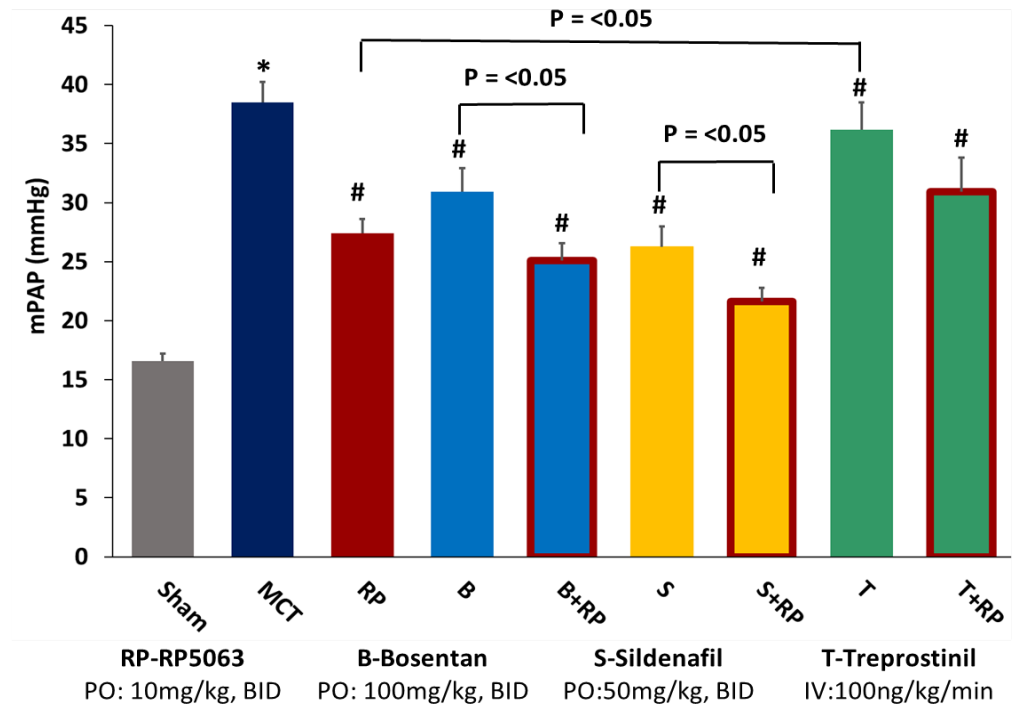
# Brilaroxazine: Encouraging Results in PAH Translational Rodent Models

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  $\text{TNF}\alpha$ ,  $\text{IL-}\beta$ ,  $\text{IL-6}$ , and chemokine  $\text{LTB}_4$

## Brilaroxazine mitigates pulmonary hypertension and lung fibrosis/collagen



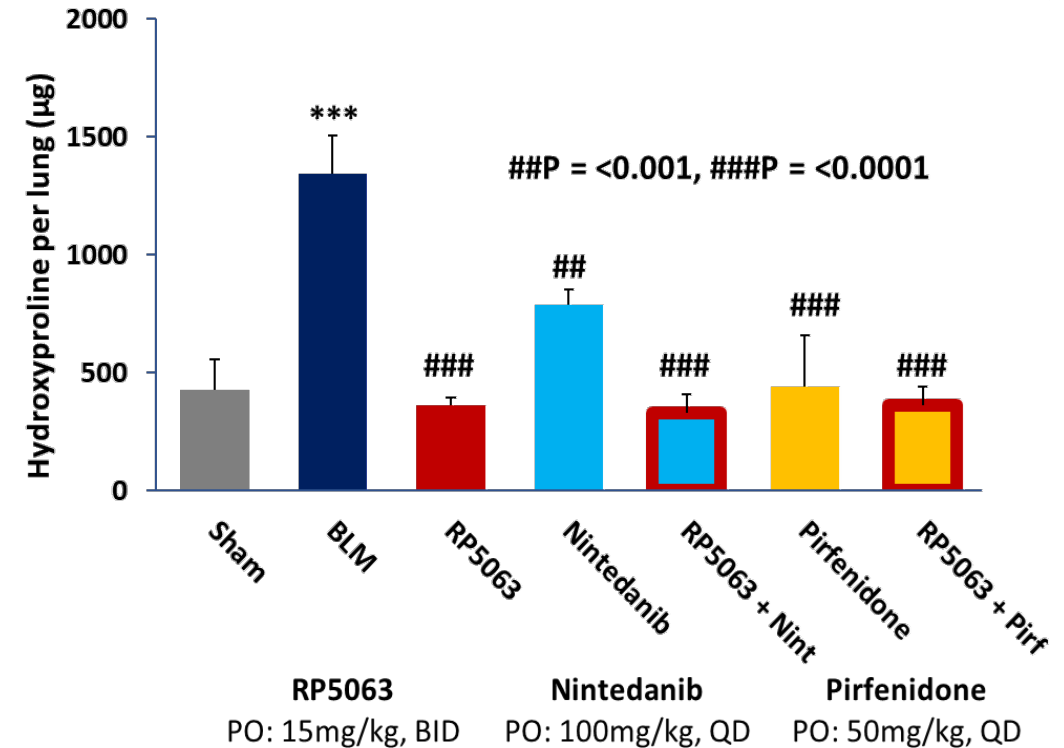
# Brilaroxazine: Encouraging Results in Bleomycin-Induced IPF Rodent Model

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,  $IFN\gamma$ , 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
- A generally well-tolerated safety profile, observed in the over 900 subjects treated to date
- 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 & 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](mailto:info@Revivapharma.com)

Business Inquiries

[busdev.rp@Revivapharma.com](mailto:busdev.rp@Revivapharma.com)

Investor Relations Contact

[IR@Revivapharma.com](mailto:IR@Revivapharma.com)



## Global Operations

### U.S. Headquarters

Cupertino, CA, USA

### International Offices

Bangalore, India

