REVIVA PHARMACEUTICALS HOLDINGS, INC.

KOL Webinar, May 2, 2023

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 RECOVER Phase 3 trial, product development and clinical trial plans, clinical and regulatory timelines, trial results, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth and financing opportunities and other statements that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions. These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or the Company's financial performance and involve known and unknown risks, uncertainties, and other factors, including the potential impact of the COVID19 pandemic and the potential impact of sustained social distancing efforts, on the Company's operations, clinical development and clinical trial plans and timelines, which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the Securities and Exchange Commission. 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.

Agenda

Welcome and Introduction	Welcome and Introduction Laxminarayan Bhat, Founder, President and CEO, Reviva Pharmaceuticals
Antipsychotic Overview Unmet Needs, and Translational Aspects	Current Treatment Options, Unmet Needs, and Translational Aspects in the Development of New Treatments for Schizophrenia and Related Psychiatric Disorders Larry Ereshefsky PharmD, BCPP, FCCP, Retired professor of Psychiatry, Pharmacology and Psychiatry, The University of Texas; Chief Scientific Officer, Owner, Follow the Molecule LLC
Development of Brilaroxazine	Development of Brilaroxazine (RP5063) for Schizophrenia and other Psychiatric Disorders Laxminarayan Bhat, Founder, President and CEO, Reviva Pharmaceuticals
Q&A Session	Q&A Session

KOL Biography

Larry Ereshefsky, PharmD, BCPP, FCCP

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

Chief Scientific Officer, Owner
Follow the Molecule LLC

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

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

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

Treatment considerations for Schizophrenia and Related Psychiatric Disorders

Dr. Larry Ereshefsky, PharmD, BCPP, FCCP

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

Chief Scientific Officer, Owner

Follow the Molecule LLC

Disclosure

Consultant:

AbbVie/Allergan, Acadia, Alkermes, Axsome, BioXcel, Boehringer Ingelheim, Cadent Therapeutics, Cerevel, Digestome, Esai, Intra-Cellular Therapies, Janssen, Karuna, Lundbeck, Lyndra, Praxis, Reviva, Sunovian, Supernus, and Tranquis.

Investments:

Options in Athira, Digestome, Reviva, and Tranquis

Stocks (common stock):

Amgen, Atai, Biogen, BioXecel, Bristol-Myers Squibb, Eli Lilly, Ionis, Intra-Cellular Therapies, Johnson & Johnson, Karuna, Merck, Praxis, and Sage.

Clinical Features of Schizophrenia: Treatment SHOULD be Individualized

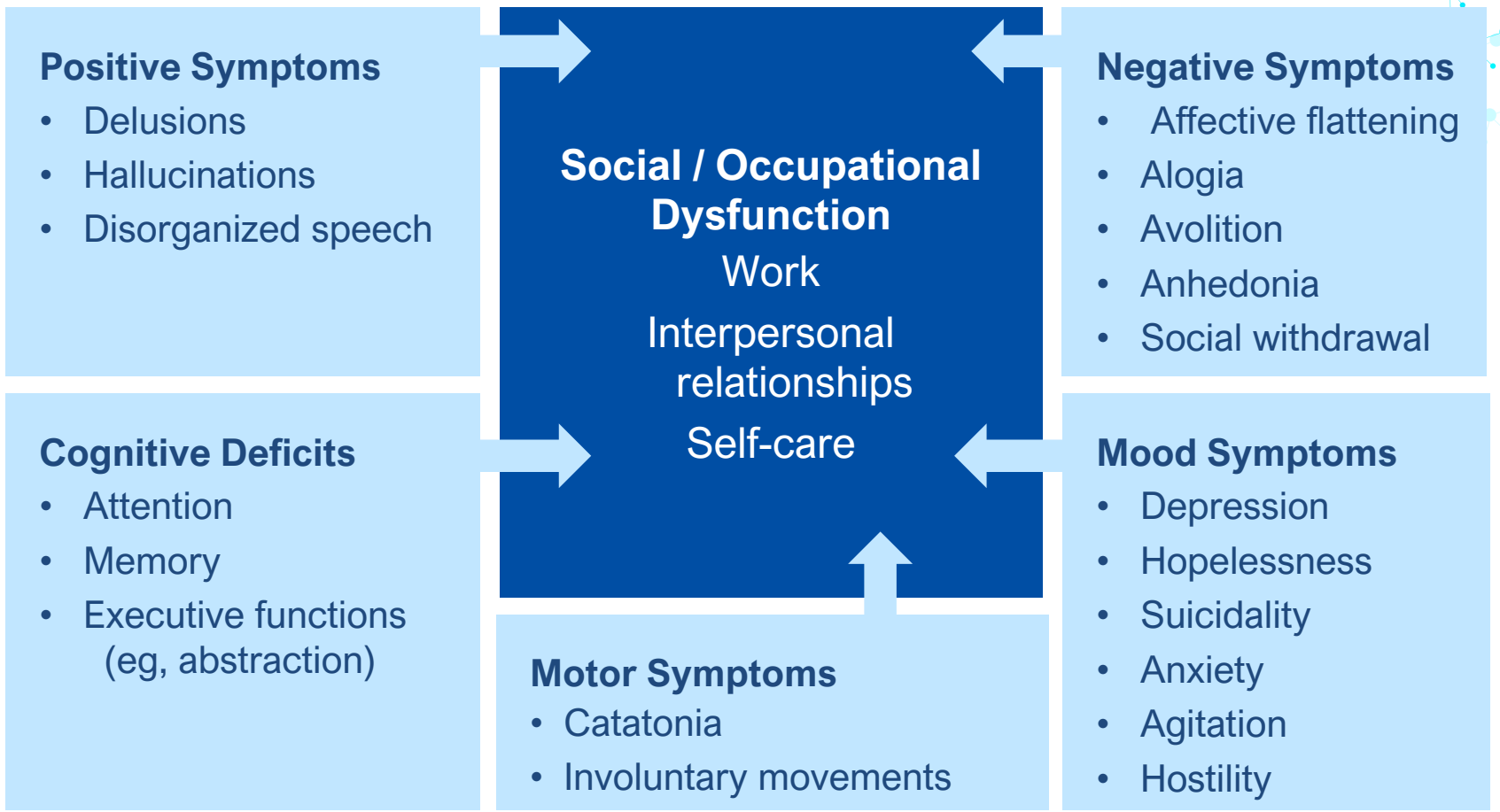
Schizophrenia affects ~1.1% of the world's population and ~3.5 million people in the US and ~24 million globally

Drugs are the mainstay; yet recovery/remission is not possible for a large majority of patients, therefore requiring a multidisciplinary approach

Cognitive remediation and vocational rehabilitation for functionality

Supportive/supported employment and housing may be needed to ensure above is successful

Intensive Care Management or Assertive Community Treatment for some

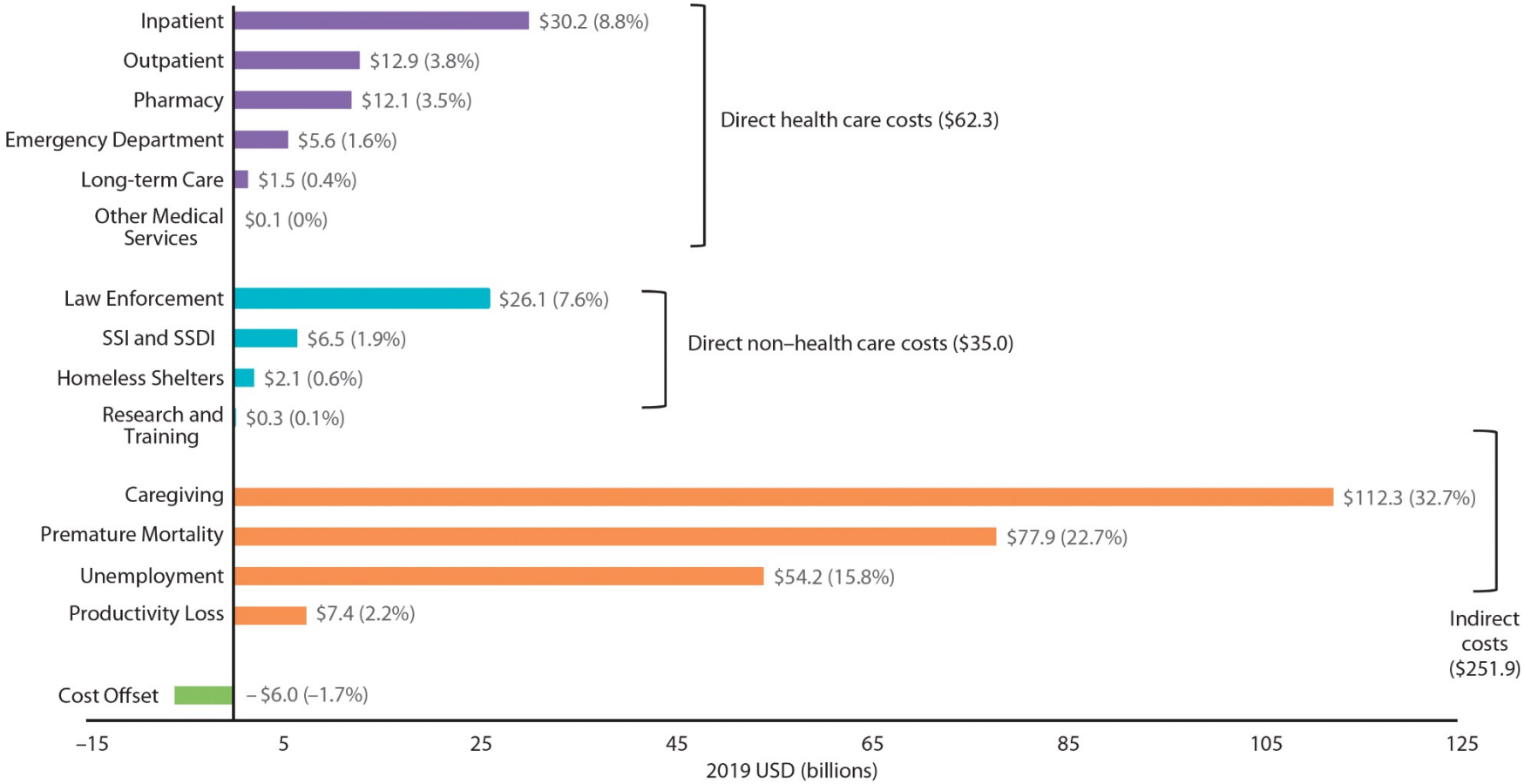


Mentalhealth.net American Addiction Centers Resource, https://www.mentalhelp.net (March 18, 2022); https://www.who.int/news-room/fact-sheets/detail/schizophrenia (March 18, 2022); Maguire GA. Am J Health Syst Pharm. 2002;59(17 Suppl 5):S4-S11.

Impact of Schizophrenia Beyond the Patient and Direct Healthcare Costs

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

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

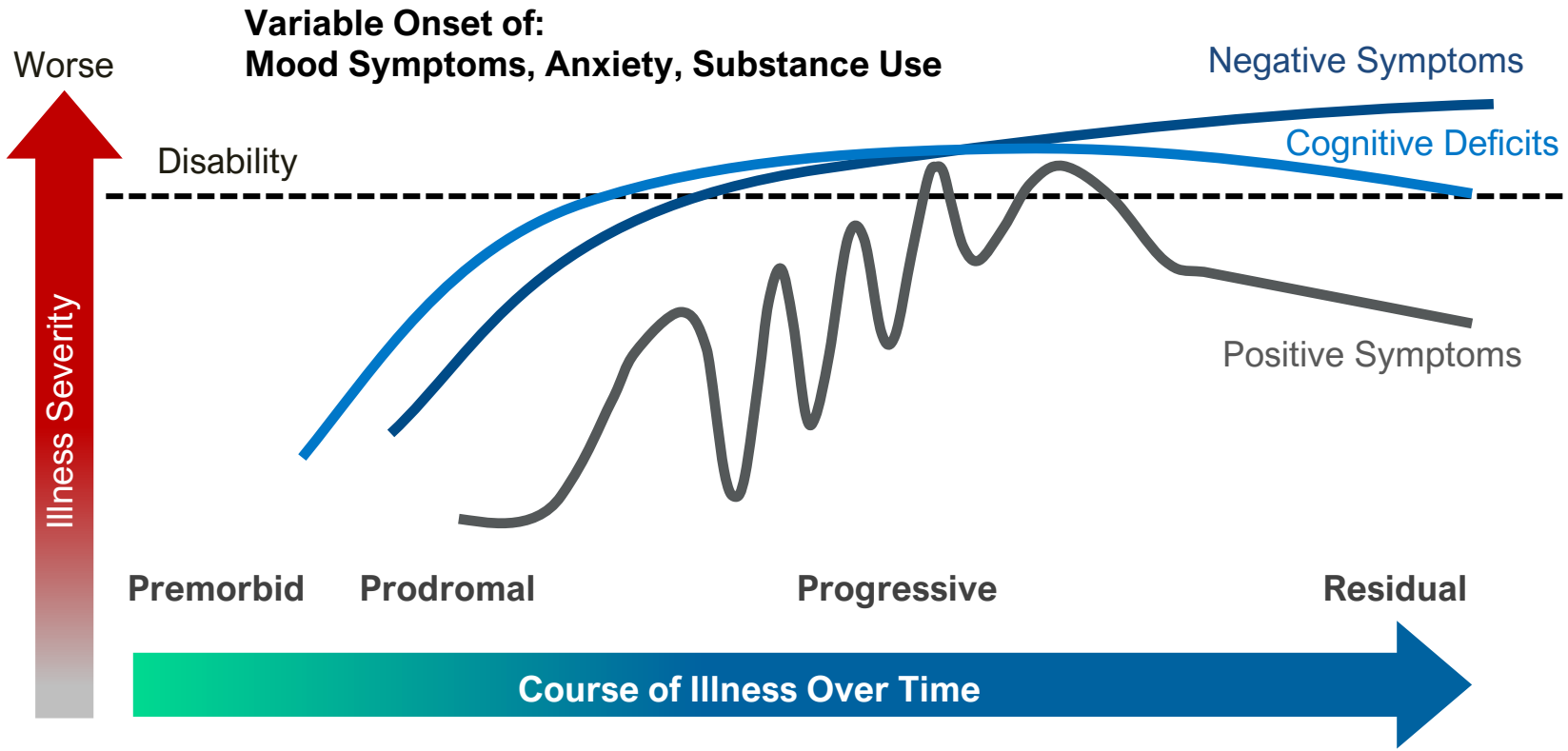


Kadakia A, et. Al. J Clin Psychiatry. 2022;83:e1-e9; Millier A, et al. J Psychiatr Res. 2014;54:85-93; Wu EQ, et al. J Clin Psychiatry. 2005;66:1122-1129.

Clinical Features Of Schizophrenia Demonstrate Illness Complexity And Multiple Symptom Domains

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

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



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

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

Symptoms of Disease and Side Effects of Treatments Impose a Burden

Suboptimal Efficacy[1]

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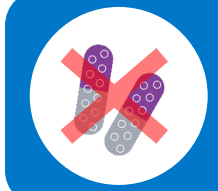


Poor Tolerability/ Side Effects[1]

High Discontinuation/ Non-Compliance[1]

Estimated treatment discontinuation rates[1]:

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

77% Reported medication side effects[2]

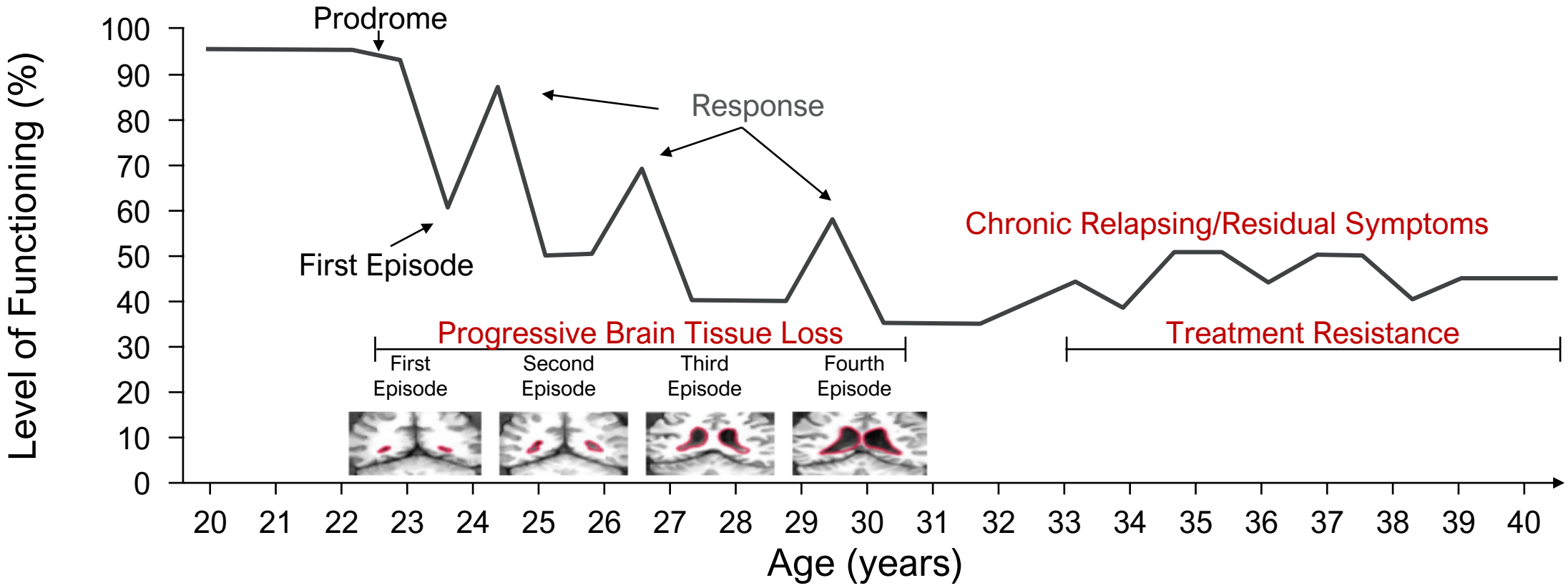
61% Reported impairment in their daily life as a result of medication side effects[2]

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

Study of 1825 participants with psychosis[2]

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

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



Gardner KN, et al. Current Psychiatry. 2015;14(7):33-45. Lieberman JA. J Clin Psychiatry. 1996;57 Suppl 11:68-71. Birchwood M, et al. Br J Psychiatry Suppl. 1998;172(33):53-59.

Reflecting on the Past to Guide the future

The need: better efficacy with fewer side effects

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

Major Symptoms

Positive symptoms	Negative symptoms	Mood Symptoms
Cognition Impairment	Impaired function	

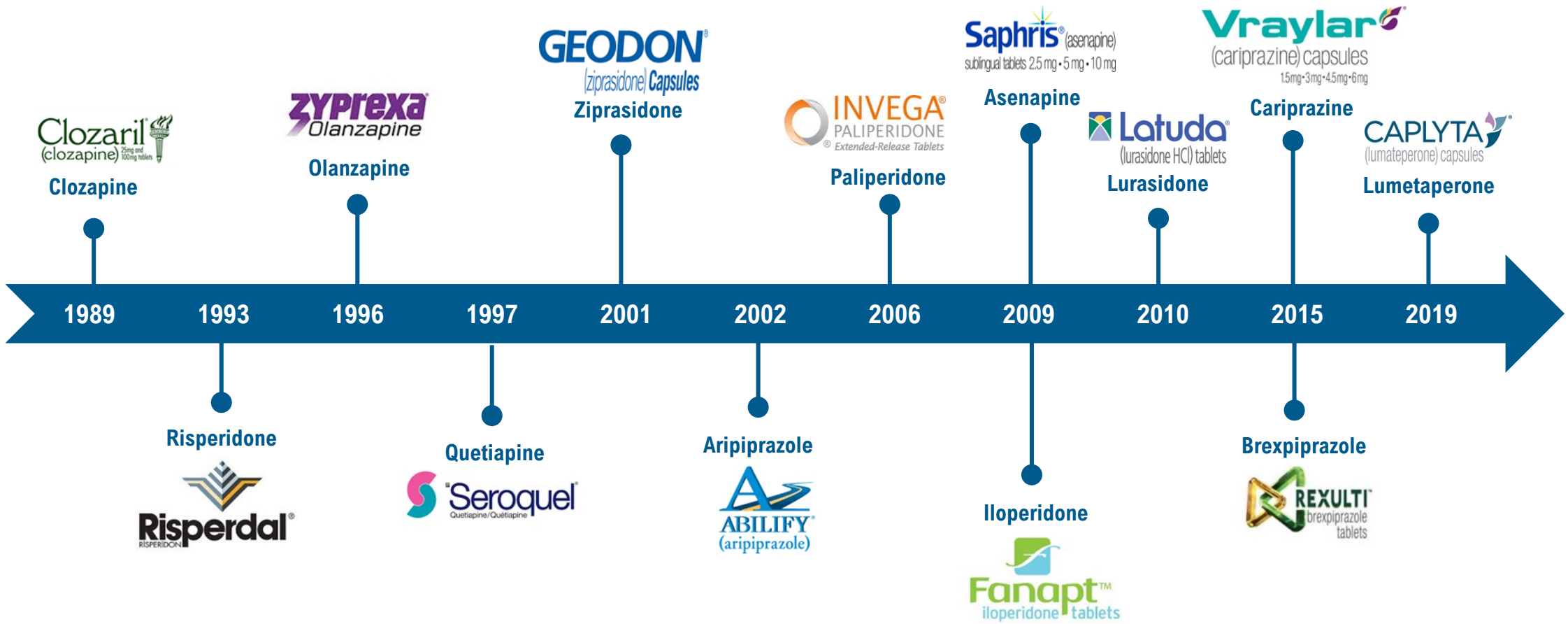
Major Side Effects of Standard of Care

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

Emerging role for neuroinflammation: Associated with negative sx (Anhedonia, Apathy) and cognitive impairment

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

New Antipsychotics Approved Over Last 40 Years



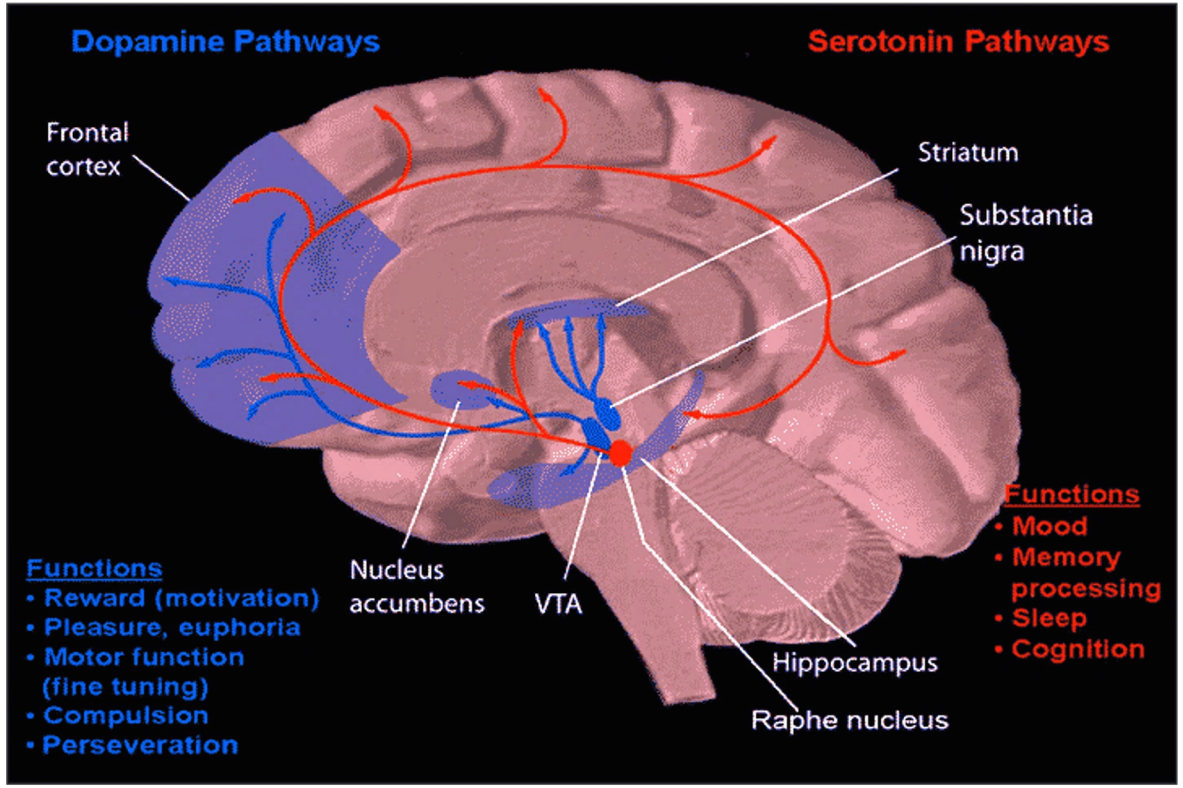
Source: H.C. Wainwright, Equity Research (RVPH), January 24, 2022

Brilaroxazine Schizophrenia Program

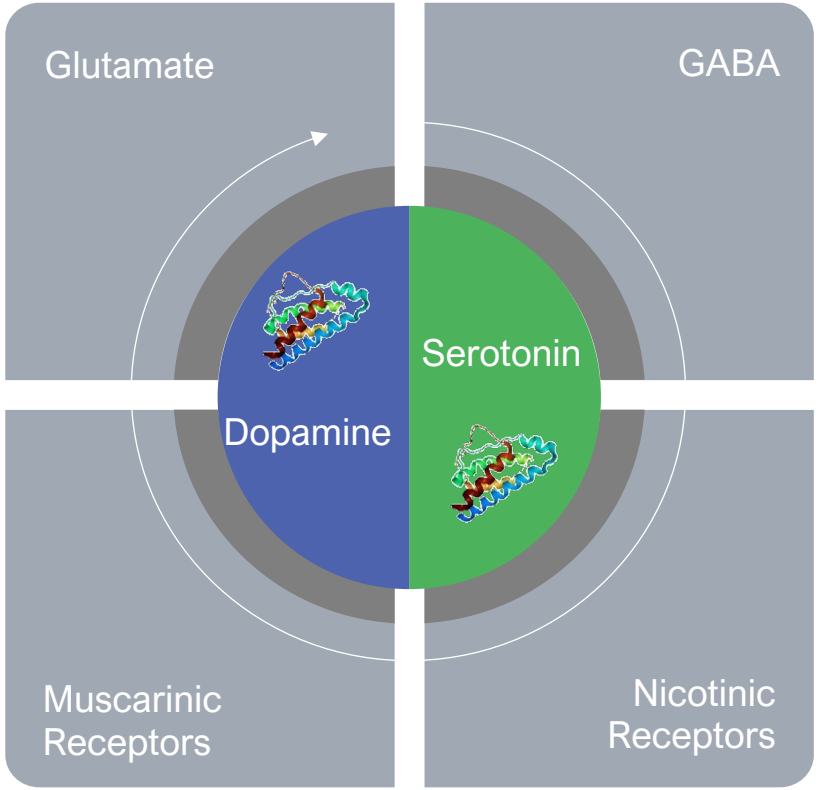
Pharmacology and Non-clinical Translational Studies

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

Targeting serotonin and dopamine receptors can treat schizophrenia and comorbid symptoms



Source: American Society for Pharmacology and Experimental Therapeutics

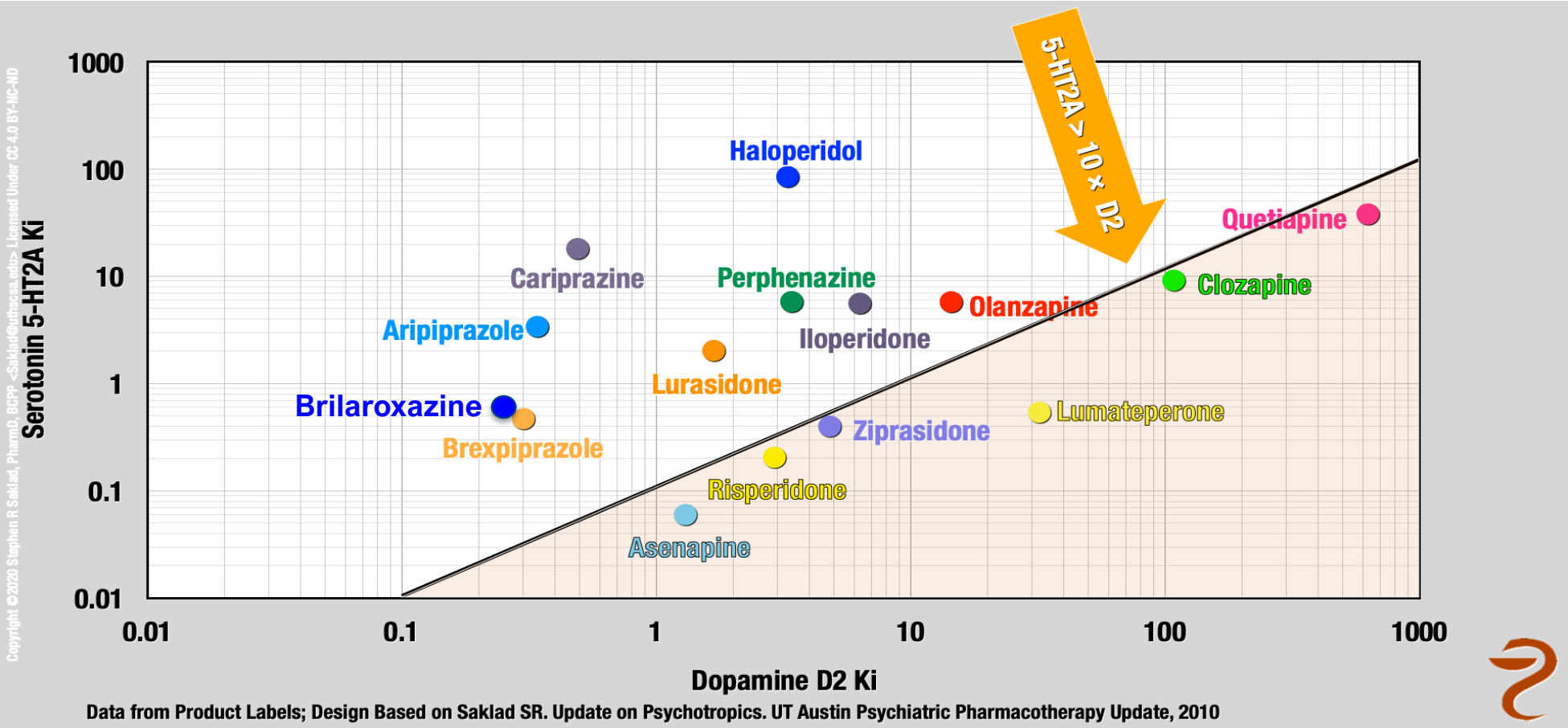


Stepnicki P et al. Molecules 2018, 23:2087.

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

Relative D2 Receptor to 5-HT2A Receptor Binding D2 vs 5-HT2A

Brilaroxazine is highly potent in all animal apomorphine, MK801 and PCP reversal models for antipsychotic effects

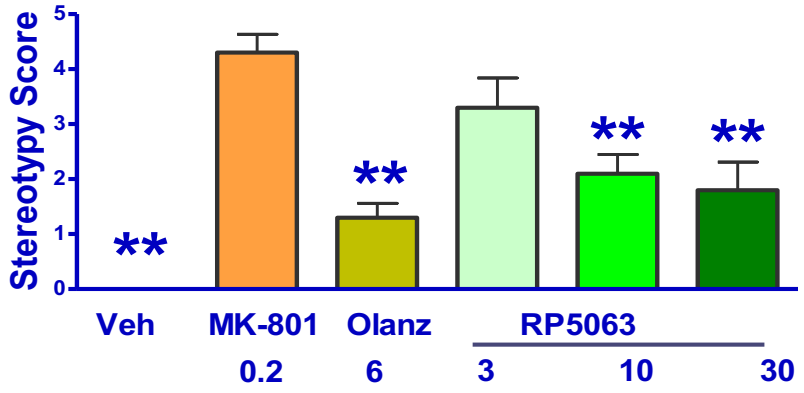


(1) Bhat et al. Med Res Arch 2023 (in print). (2) Meltzer et al, Behavioral Brain Research 2017, 332;180-199.

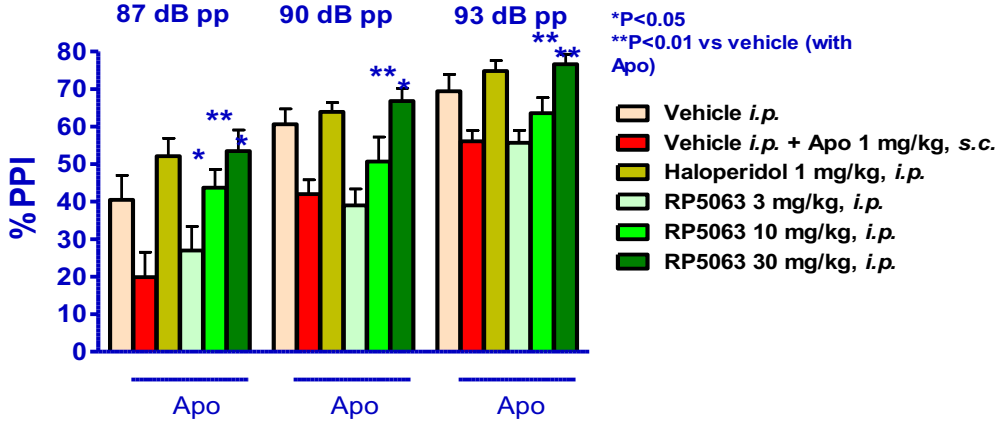
Brilaroxazine (RP5063) Preclinical Efficacy for Schizophrenia

Gold Standard Translational Rodent Models

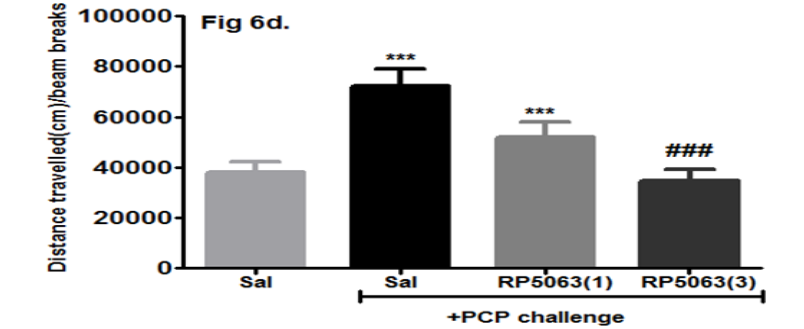
RP5063 reduces MK-801 (NMDA) induced stereotypy[1]



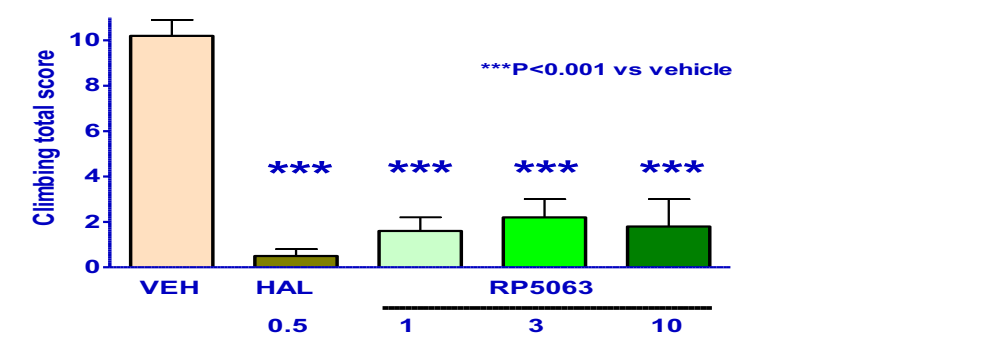
RP5063 reverses apomorphine (dopamine) induced PPI[1]



RP5063 reduces PCP (NMDA) induced locomotor activity[2]



RP5063 attenuates apomorphine (dopamine) induced climbing[1]



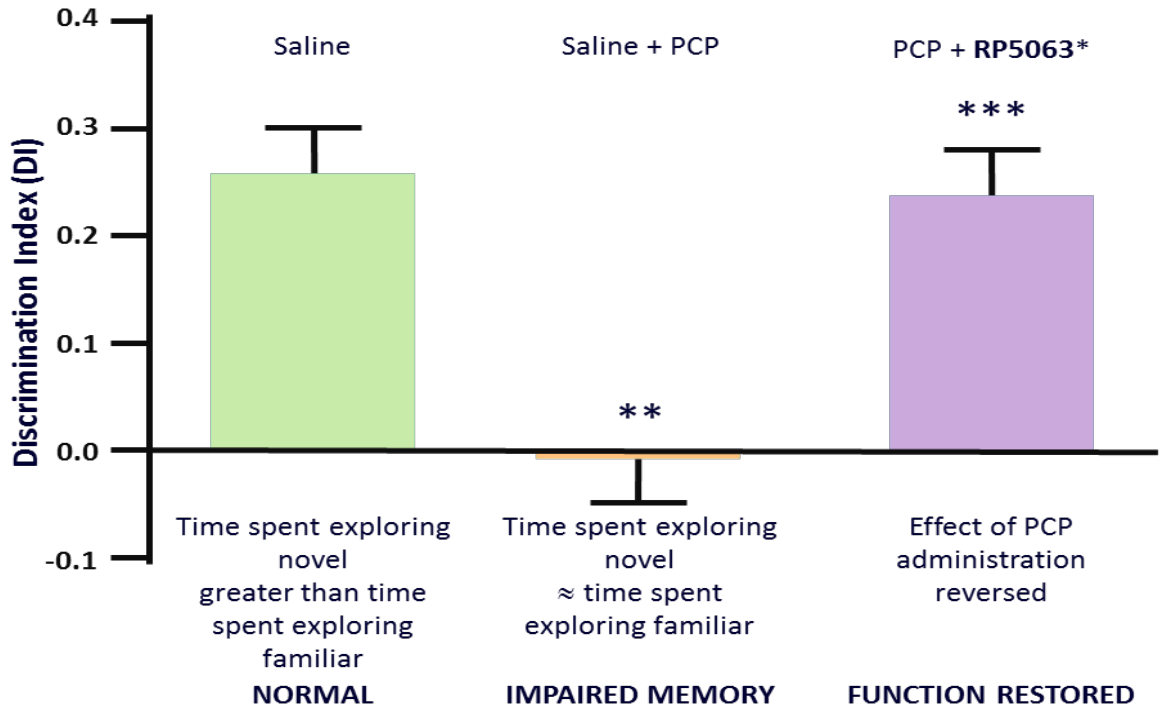
(1) Bhat et al. Med Res Arch 2023 (in print). (2) Meltzer et al, Behavioral Brain Research 2017, 332;180-199.

Brilaroxazine (RP5063) Preclinical Efficacy for Cognition

Contributing Factor for Clinical Differentiation

Cognitive Enhancement in Rodent Novel Object Recognition (NOR) Model

Brilaroxazine improves cognition via multimodal neuromodulation of key dopamine D_2, D_4 and serotonin 5-HT_{1A}, 5-HT_{2A}, 5-HT_{2B}, 5-HT_6 and 5-HT_7 receptors



* 1 mg/kg; i.p. ** p<0.01 compared to saline

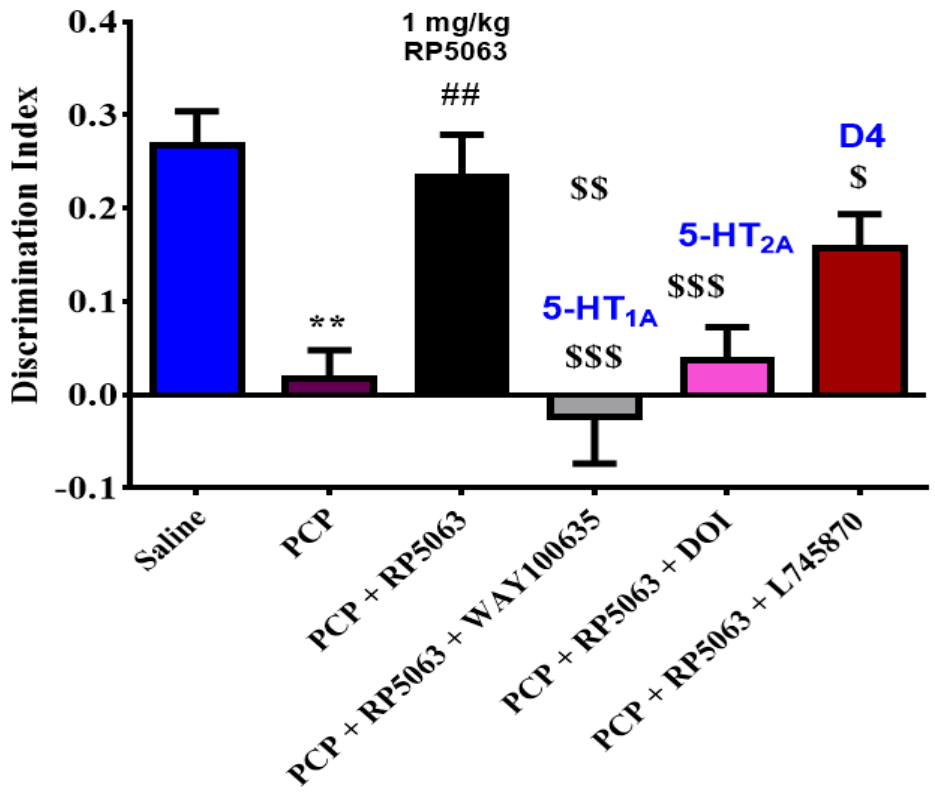
*** p<0.001 compared to PCP-treated mice

Rajagopal et al, RP5063, an atypical antipsychotic drug with a unique pharmacologic profile, improves declarative memory and psychosis in mouse models of schizophrenia, Behavioral Brain Research 2017, 332;180-199.

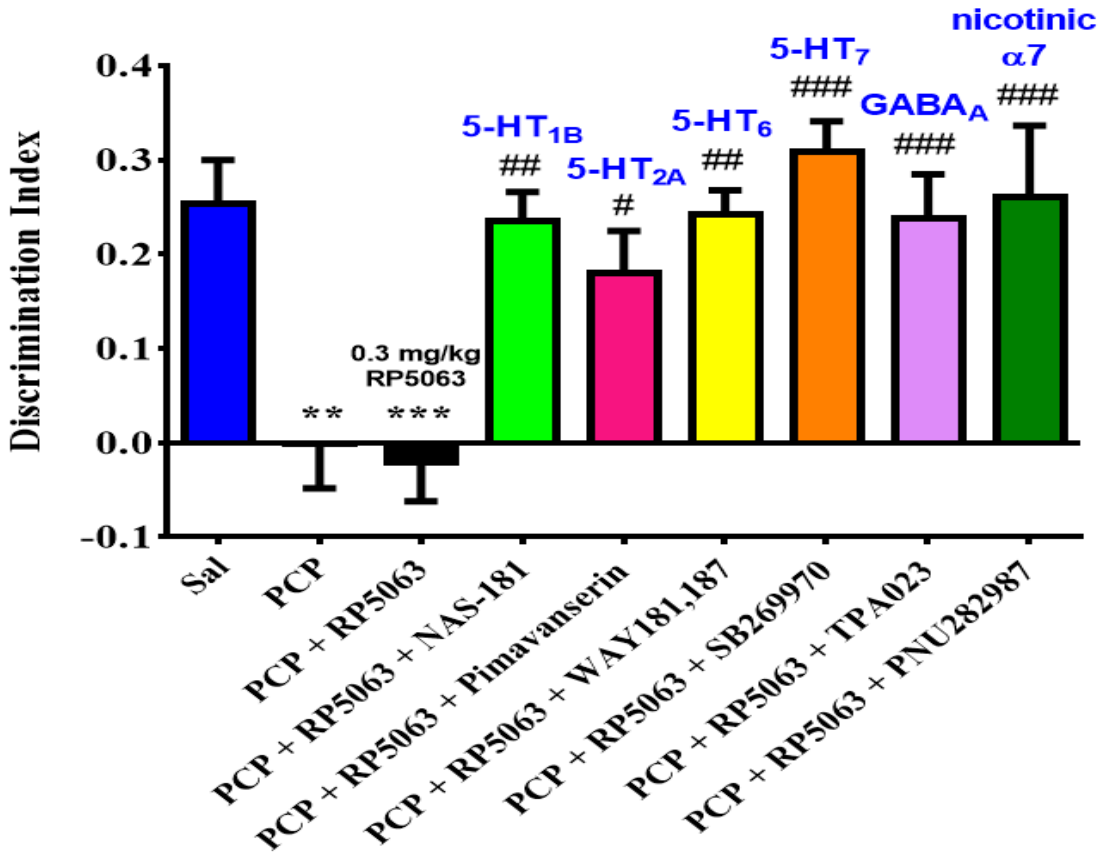
Brilaroxazine (RP5063) Efficacy for Cognition in Rodent NOR Model

Cognitive enhancement via multimodal neuromodulation: contributing factor for clinical differentiation

Cognitive Enhancement via 5-HT_{1A} , 5-HT_{2A} , D_4



Potentiation of Key Pro-cognitive Receptors



Rajagopal et al, RP5063, an atypical antipsychotic drug with a unique pharmacologic profile, improves declarative memory and psychosis in mouse models of schizophrenia, Behavioral Brain Research 2017, 332;180-199.

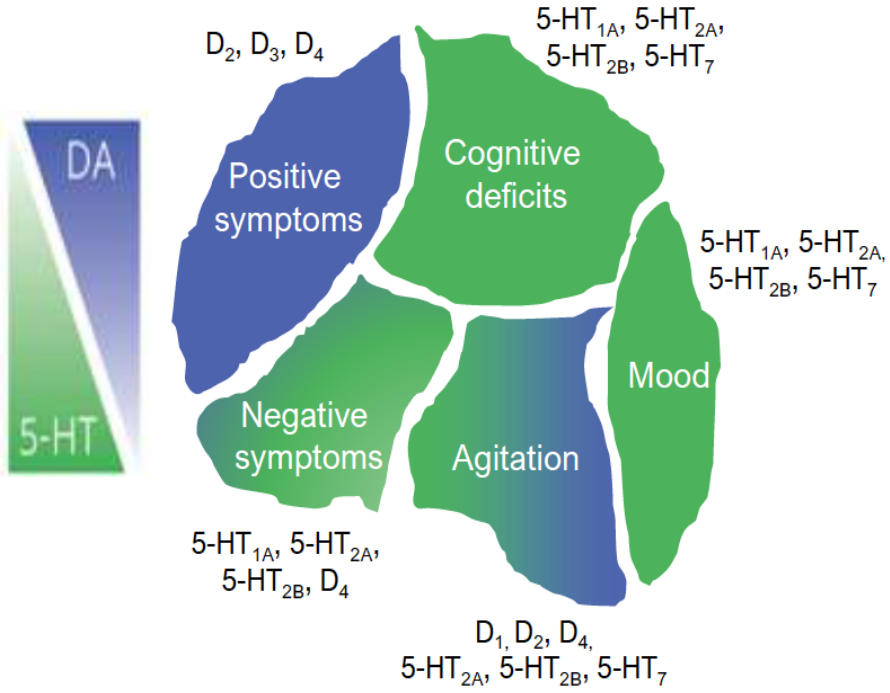
Brilaroxazine Target Receptor Activity Profile

Modulator of Dopamine – Serotonin Receptors / Signaling Pathways

Target Receptors	Functional Activity	Binding Affinity, Ki (nM)
Dopamine, D_{2L}	Partial agonist	0.45
Dopamine, D_{2S}	Partial agonist	0.28
Dopamine, D_3	Partial agonist	3.7
Dopamine, $D_{4.4}$	Partial agonist	6.0
Serotonin, 5-HT_{2B}	Antagonist	0.19
Serotonin, 5-HT_{1A}	Partial agonist	1.5
Serotonin, 5-HT_{2A}	Partial agonist/Neutral antagonist	2.5
Serotonin, 5-HT_7	Antagonist	2.7
Serotonin, 5-HT_{2C}	Antagonist	39
Serotonin, 5-HT_6	Antagonist	51
Nicotine-nAChR, $\alpha_4\beta_2$	Agonist	36.3
SERT	----	100

Cantillon M et al. Eur J Drug Metab Pharmacokinet (2018) 43:573–585

Implications for Receptor and Neurotransmitter Effects: Putative treatment targets; which is better for the illness shot gun or bullet?



Target	Potential Treatment and Physiological Effects
D_2 partial/full antagonist	Positive symptoms/acute mania, anti-agitation / aggression (full antagonist increases EPS)
D_3 partial antagonists	Negative symptoms, cognitive deficits
D_4 partial/full antagonist	Cognition, memory, addiction, depression
5-HT_{1A} partial/full antagonist	Depression and anxiety, possibly cognitive deficits
5-HT_{2A} antagonist	Negative symptoms; cognitive deficits, mood, reduce EPS; weak antipsychotic effects
5-HT_{2B} antagonist	Neurodegenerative disorders including schizophrenia, addiction, and neuroinflammation
5-$HT_{6/7}$ partial/full antagonist	Depression, anxiety, cognitive deficits
5-HT_{2C} antagonist	Cause metabolic side effects
DA / NE increases in frontal cortex	Negative symptoms, depression, cognition/functional deficits
Net effect on DA/5-HT indirectly modulates GLU, GABA, and Cholinergic systems	Supporting 'downstream' effects on cognitive deficits, mood symptoms
Direct pharmacologic engagement of M_4, Glyt-1, or TAAR1 indirectly modulate DA/5HT	Case by case effect size for treatment of positive, negative symptoms, mood disorders, and cognitive deficits; one drug might not address all domains
5-HT_2 antag, presyn D_2 pag, postsyn D_2 antag, D_1 modulates GLU, SERT	Moderate antipsychotic effect, improve mood disorders

Luisa-Sophie Koster, Maren Carbon, & Christoph U Correll. Expert Opin. Emerging Drugs (2014) 19(4). Based on Measurement and Treatment Research to Improve Cognition in Schizophrenia. Marder S, et al. 2007; Stahl SM, Stahl's Essential Psychopharmacology, 4th Edition, Cambridge University Press, 2013; Shayegan DK et al. CNS Spectr 2004;9(10 Suppl 11):6-14. Giorgioni G et al. Eur J Med Chem 2021, 212:113141 ; Furth KE et al. Front Cell Neurosci 2013, 7:102. Devroye C et al. Neuropsychopharmacology 2016, 109:59-68. D'Andrea I et al. Handbook of the Behavioral Neurobiology of Serotonin 2020, pp589-599

Imbalance of Cytokines in Schizophrenia: Putative Treatment Targets

Cytokines are critical components of the inflammatory response and are crucial mediators of cross-talk between the nervous and immune systems

Key Cytokines	Relationship with Schizophrenia Symptoms
IL-6 and IL-4	Longer disease duration
IL-6 and IL-1β	More severe positive symptoms
IL-6, TNF-α, INF-γ, TGF-β, IL-1β and IL-4	Exacerbated negative symptoms
IL-6	Worse cognitive abilities
IL-6, IL-17, and TGF-β	Increased PANSS score

A meta-analysis of 40 clinical studies in schizophrenia showed that patients with first-episode psychosis and those with acute relapse of psychosis had significantly elevated levels of TNF-α, TGF-β, IFN-γ, IL-6, IL-1β, and IL-12

Reale M et al. Frontiers in Psychiatry 2021, 12:536257; Monji A et al. Japanese Society of Psychiatry and Neurology 2009, 63:257-265.

Brilaroxazine Significantly Reduced Inflammatory Cytokines and Chemokines in Different Translational Animal Models

Elevated levels of the following cytokines and chemokines are reported in schizophrenia patients: TNF-α, TGF-β, IFN-γ, IL-6, IL-1β, and MCP1

Key Cytokines and Chemokines	Animal Models
TNF-α, IL-6, and IL-1β	Brilaroxazine significantly reduced these cytokines in the MCT-induced rat model for PAH Bhat L, et al. European Journal of Pharmacology 2017, 810:92-99
IL-6, INF-γ (IP10), MCP1, and RANTES	Brilaroxazine significantly reduced these cytokines and chemokines in the bleomycin-induced rat model for IPF Bhat L, et al. Medical Research Archives 2023 (accepted)
TNF-α, TGF-β, and KI-67	Brilaroxazine significantly reduced these cytokines and chemokines in the imiquimod-induced mouse model for psoriasis Bhat L, et al. International Society for Investigative dermatology (ISID) meeting, May 10-13, 2023 (poster presentation accepted)

IL: Interleukin; TNF: Tumor necrosis factor ; TGF: Transforming Growth Factor; INF: Interferon (IP: Inducible Protein); MCP: Monocyte Chemoattractant Protein; RANTES: Regulated upon Activation, Normal T Cell Expressed and Presumably Secreted; KI: Gene Marker of Proliferation

Reale M et al. Frontiers in Psychiatry 2021, 12:536257; Monji A et al. Japanese Society of Psychiatry and Neurology 2009, 63:257-265.

Treatment Strategies: Target Engagement and Mechanism of Action

Targeting serotonin and dopamine receptors can treat schizophrenia and comorbid symptoms

Antipsychotic

Brilaroxazine
(RP5063)

Orthosteric / Direct modulation

Dopamine receptors ($D_{2/3/4}$)
Serotonin receptors ($5\text{-}HT_{1A/2A/2B/7}$)

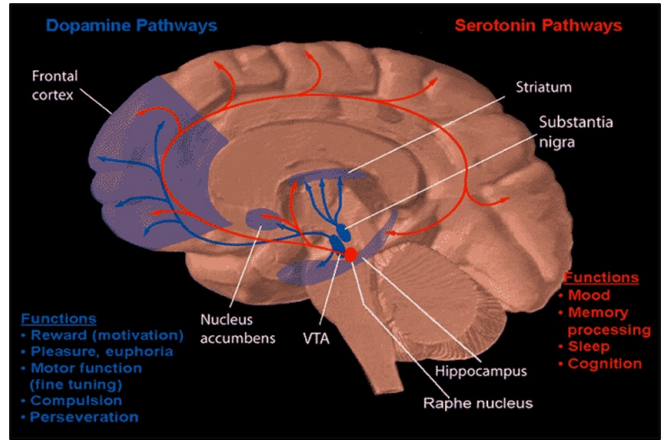
Allosteric / Indirect modulation

Downstream Targets

- NMDA/Glycine receptors
- GABA receptors
- Cholinergic receptors (nicotinic & muscarinic)
- Inflammatory cytokines

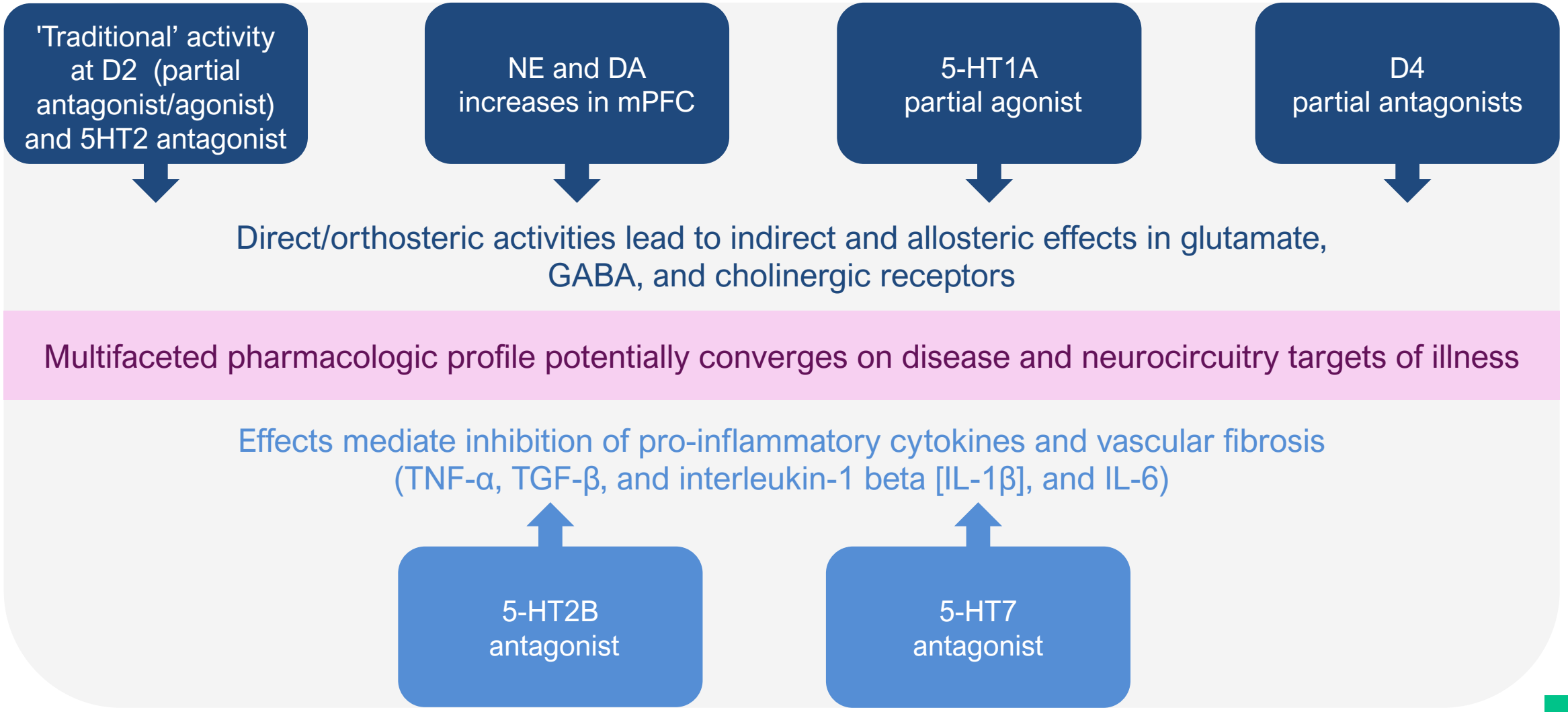
Treatment Effect

Schizophrenia



Bhat et al. Med res Arch 2023 (in print); Stepnicki P et al. Molecules 2018, 23:2087.

Unique And Convergent Mechanisms Of Action Potentially Differentiate Brilaroxazine



Serotonin and Dopamine Receptors are Primary Targets for Approved Antipsychotics

1st-Generation
Dopamine D2 Receptor Antagonists

Positive Symptoms

2nd-Generation
Dopamine & Serotonin Receptor Antagonists

Positive >>> Negative Symptoms

3rd-Generation
Dopamine & Serotonin Partial Agonist/Antagonist

Positive >> Negative Symptoms

Next-Generation
Dopamine & Serotonin Partial Agonist/Antagonist

Anticipated profile: Positive ≈ Negative > Cognition, Depression

Haldol	Risperdal, Zyprexa, Seroquel	Abilify	Brilaroxazine – Phase 3 underway
● D_2	● D_2 / 5-HT_{2A}	◐ D_2 / ● 5-HT_{2A}	◐ $D_{2/4}$ / ● 5-$HT_{2A/2B/7}$

FDA APPROVED

Antipsychotics with other novel mechanisms are in development. Previous attempts include several that appeared to fail.

Glutamate Receptor
Bitopertin (Roche)
Ph 3 Discontinued
Boehringer Ingelheim's Iclepertin add-on for cognitive symptoms in Ph 3

Trace Amine Receptor1
Ulotaront (Sunovion) Late Ph 3 potential efficacy for positive (acute) and negative symptoms; Ph 3 for MDD

Nicotinic Receptor
Encenicline (Forum)
Ph 3, Discontinued
Bradanicline (Targacept)
Ph 2, Discontinued

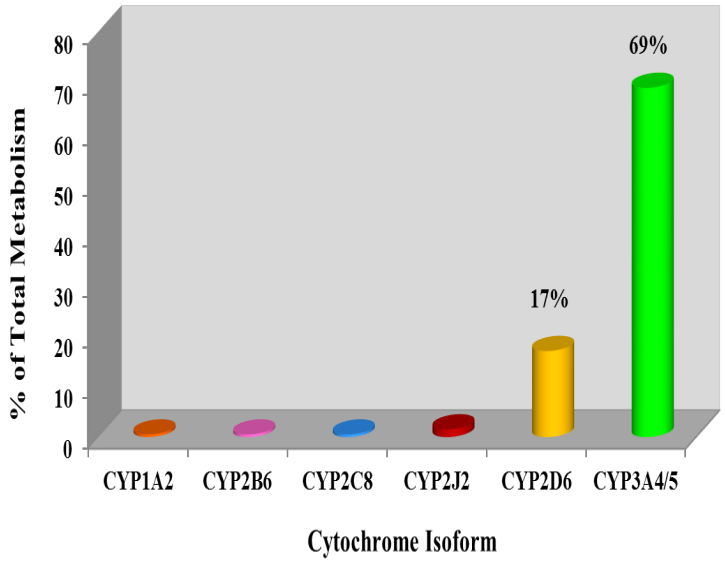
Muscarinic Receptor
Xanomeline (Eli Lilly)
Ph 2; efficacy DC'd side effects.
Kar-XT in combination with trospium in late Ph 3 (acute); other M4s in development

Bitopertin: https://en.wikipedia.org/w/index.php?title=Bitopertin&oldid=992765453" (March 18, 2022); MK-0777: https://adisinsight.springer.com/drugs/800024505 (March 18, 2022); Encenicline: https://adisinsight.springer.com/drugs/800027229 (March 18, 2022); Bradanicline: https://en.wikipedia.org/wiki/Bradanicline (March 18, 2022); Xanomeline: https://adisinsight.springer.com/drugs/800001727 (March 18, 2022)

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

Drug	Dose (mg)	Oral Bio (%)	Half Life (hr)	Metabolism Major Path	Metabolite Activity (T1/2)
Brilaroxazine[1] In clinical development	15 - 50, QD (to be established)	>80	55	CYP3A4/A5	Inactive
Aripiprazole	10 - 30, QD	87	75	CYP2D6	Active (120h)
Lurasidone	80 - 160, QD	9-19	18	CYP3A4	Active (7.5h)
Olanzapine	10 - 20, QD	~60	33	CYP1A2	Inactive
Risperidone	4 – 8, QD	70	2-4	CYP2D6	Active (20h)
Quetiapine	100 - 300, BID	---	6	CYP3A4	Active (12h)
Cariprazine	6, QD	52	48-120	CYP3A4	Active (2-3 wks)
Brexpiprazole	4, QD	95	91	CYP3A4	Active (86h)
Clozapine	150-450, QD	60-70	14	CYP1A2	Active (22h)

Brilaroxazine In vitro Metabolism

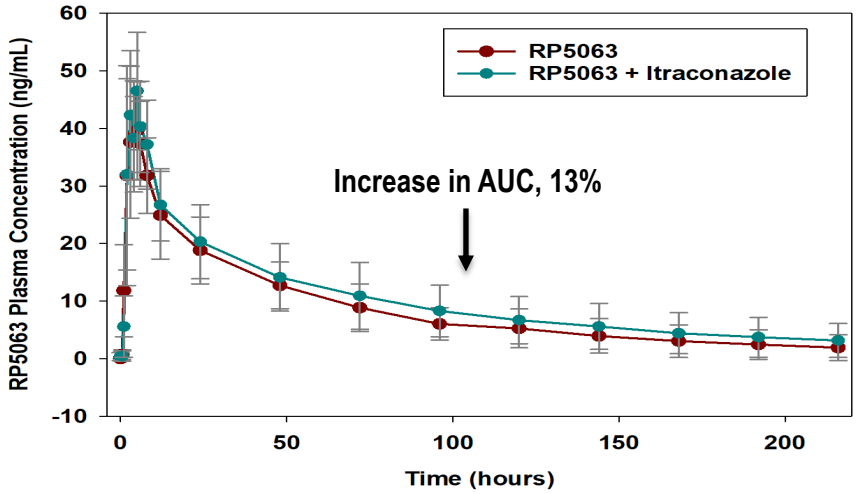


FDA has indicated no DDI studies for CYP2D6 are necessary

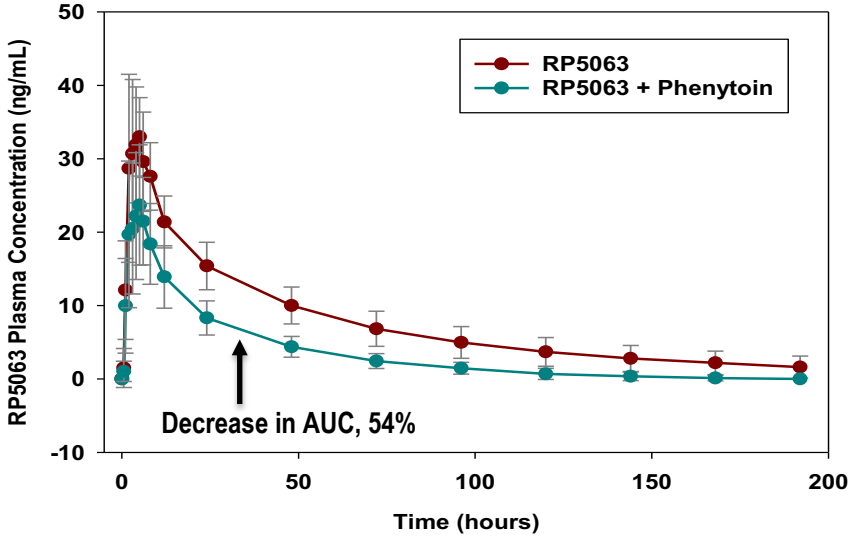
(1) Bhat L. et al, CYP3A inhibition and induction exert limited effects on brilaroxazine pharmacokinetics, ASPET Conference in May 18-21, 2023, Poster: #376,

Brilaroxazine DDI Studies with CYP3A4 Inhibitor, Itraconazole and CYP-Inducer, Phenytoin

Plasma Concentration of RP5063 vs RP5063 + Itraconazole



Plasma Concentration of RP5063 vs RP5063 + Phenytoin



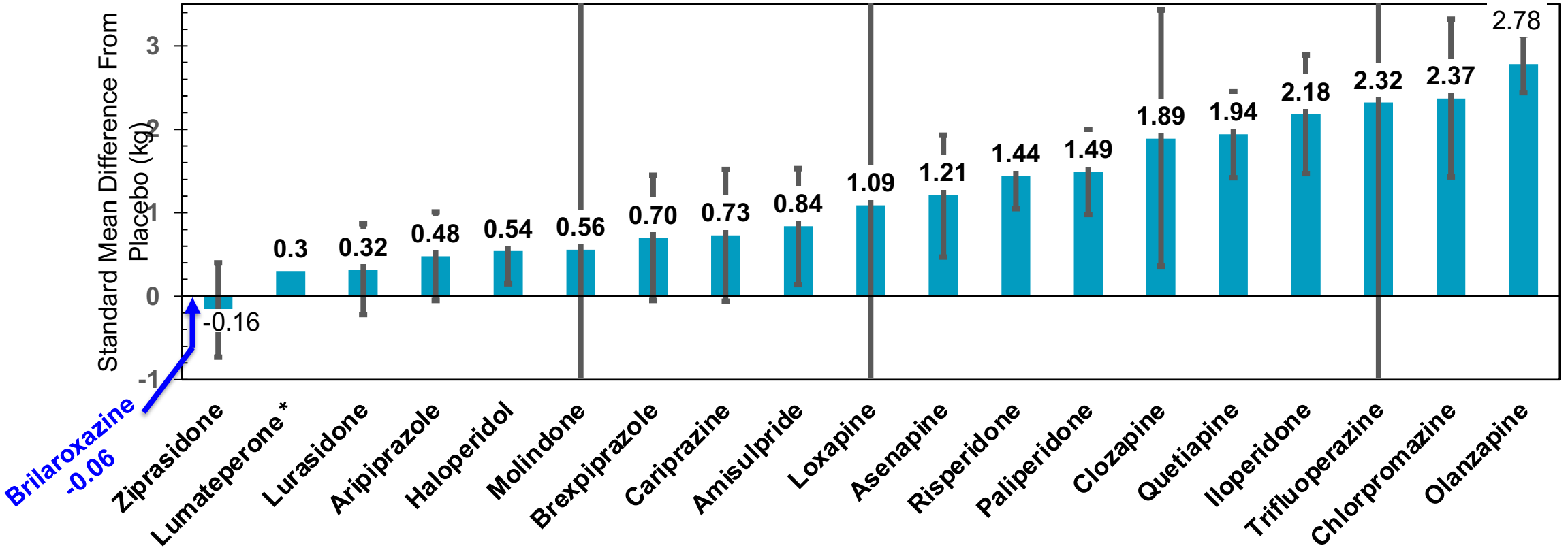
Change in drug concentration with a CYP3A4 Inhibitor	
Antipsychotic	**Fold increase vs brilaroxazine**
Brilaroxazine[1]	< 1.2x
Aripiprazole	4.2x
Risperidone	4.5x
Brexpiprazole	6.5x
Lumetaperone	16.2x
Cariprazine	19.2x
Lurasidone	34.7x
Quetiapine	34.8x

*Olanzapine[9] not evaluated; metabolized by CYP1A2

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

Most Recent Network Meta-analyses of Weight Gain Focusing on Antipsychotics Available in US

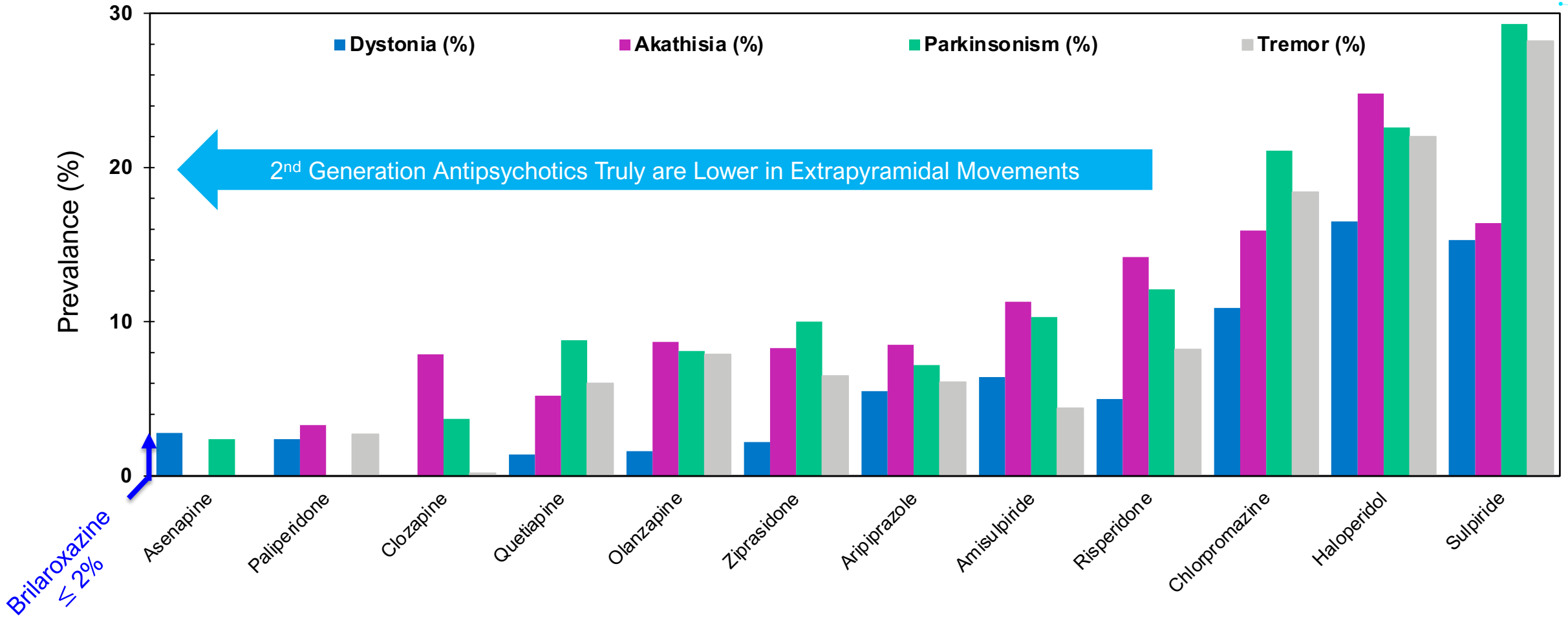
Standard Mean Difference is a parametric effect size calculated in a meta-analysis; similar to Hedges' g



No overlap in 95% CI: there is a significant difference between antipsychotics; Overlap in 95% CI: there may or may not be a significant difference; Brilaroxazine's AE profile is based on the Phase 2 data

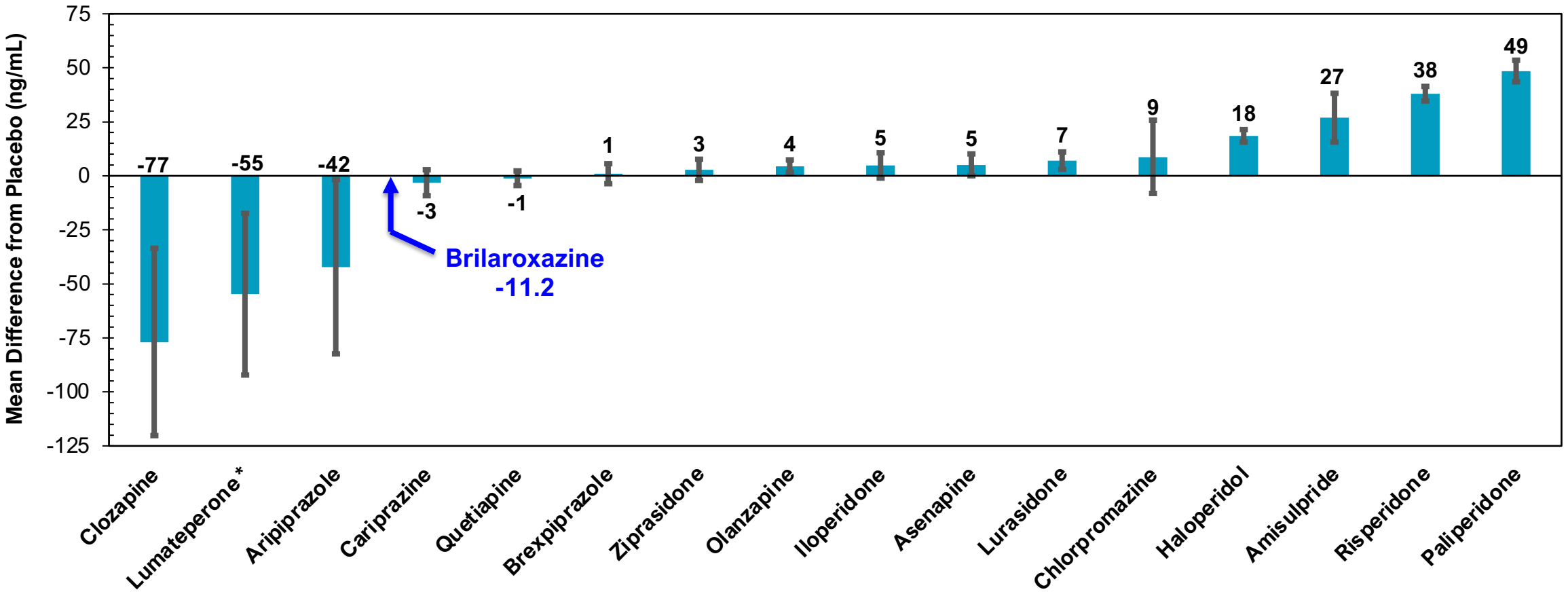
Huhn, M, et al. Lancet 2019;394:939–51. * Rowe W, et al. Poster CPNP 2020

Summary of Extrapyramidal Movement Disorder Prevalence



Marino D, et al. Canadian Journal of Psychiatry 2018;63(11):730-739.

Prolactin Change Varies Widely

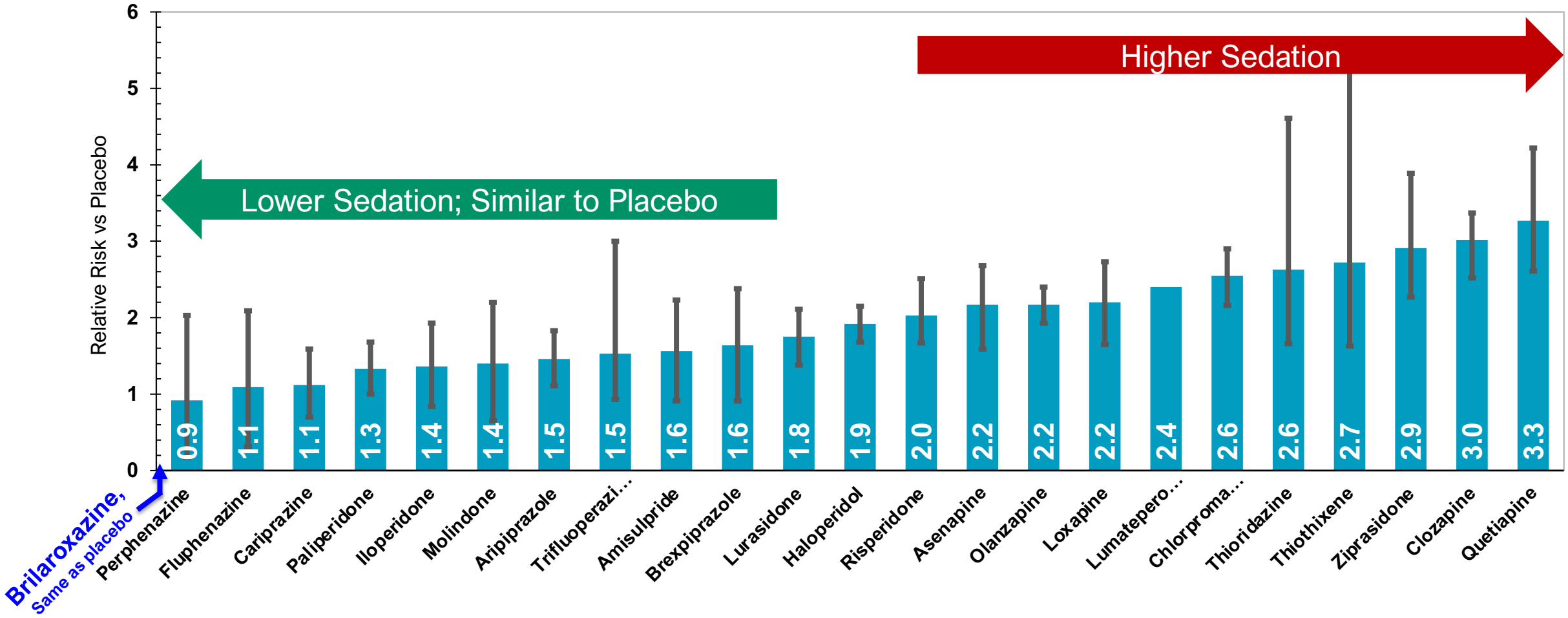


Prolactin clinical assays do not usually distinguish between free prolactin (active) vs macroprolactin (inactive). This accounts for majority of poor correlation between measured prolactin and clinical adverse effects

Huhn, M, et al. Lancet 2019;394:939–51. * Caplyta NDA 209500 12/20/2019 https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/209500Orig1s000TOC.cfm Accessed 02/21/202021
Soh NAAC, et al. Int. J. Environ. Res. Public Health 2020(17):8199 https://doi.org/10.3390/ijerph17218199.

Most Recent Network Meta-analysis of Sedation: US Antipsychotics

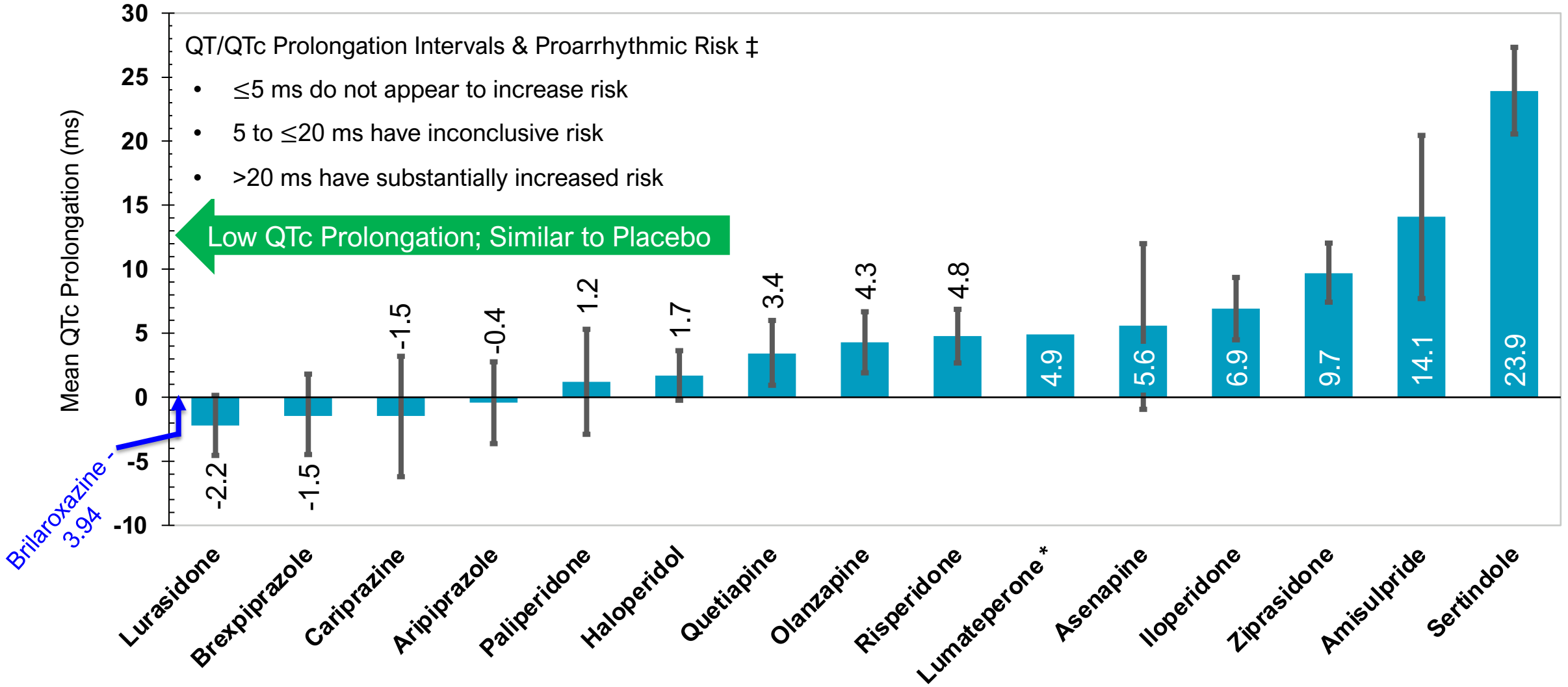
Relative Risk (RR) is the ratio of the listed drug's incidence to placebo's incidence (an RR of 2 is twice as likely as placebo)



Huhn, M, et al. Lancet 2019;394:939–51. * Rowe W. Poster CPNP 2020.

https://doi.org/10.3390/ijerph17218199.

QTc Prolongation in Clinical Trials



Summary: Schizophrenia remains a devastating illness for many patients, despite newer therapies

Treatments ideally should be:

More effective in addressing:

- positive/negative symptoms; cognitive deficits; reduced functional capacity; relapse prevention→ recovery/remission

Less harmful/Less frequent adverse events:

- metabolic syndrome (obesity, high lipids, glucose, and BP); neuroleptic motor (EPS, Tardive Dyskinesia, Akathisia); cardiovascular/autonomic (Dizziness, dry mouth, BP, prolonged QTc, etc); hormonal (hyperprolactinemia, sexual dysfunction)

Less complicated regimens

- Fewer concomitant medications, reduced risk of DDIs
- Increased adherence/compliance

- Brilaroxazine's unique combination of dopamine and serotonin receptor activities and potential anti-inflammatory effects, suggest a well tolerated Rx for patients with schizophrenia, with the potential to improve acute, chronic/life-long symptoms, and disability

- Data from ongoing and planned clinical trials are needed to validate brilaroxazine's potential (based on its pharmacologic and pharmacokinetic profile)

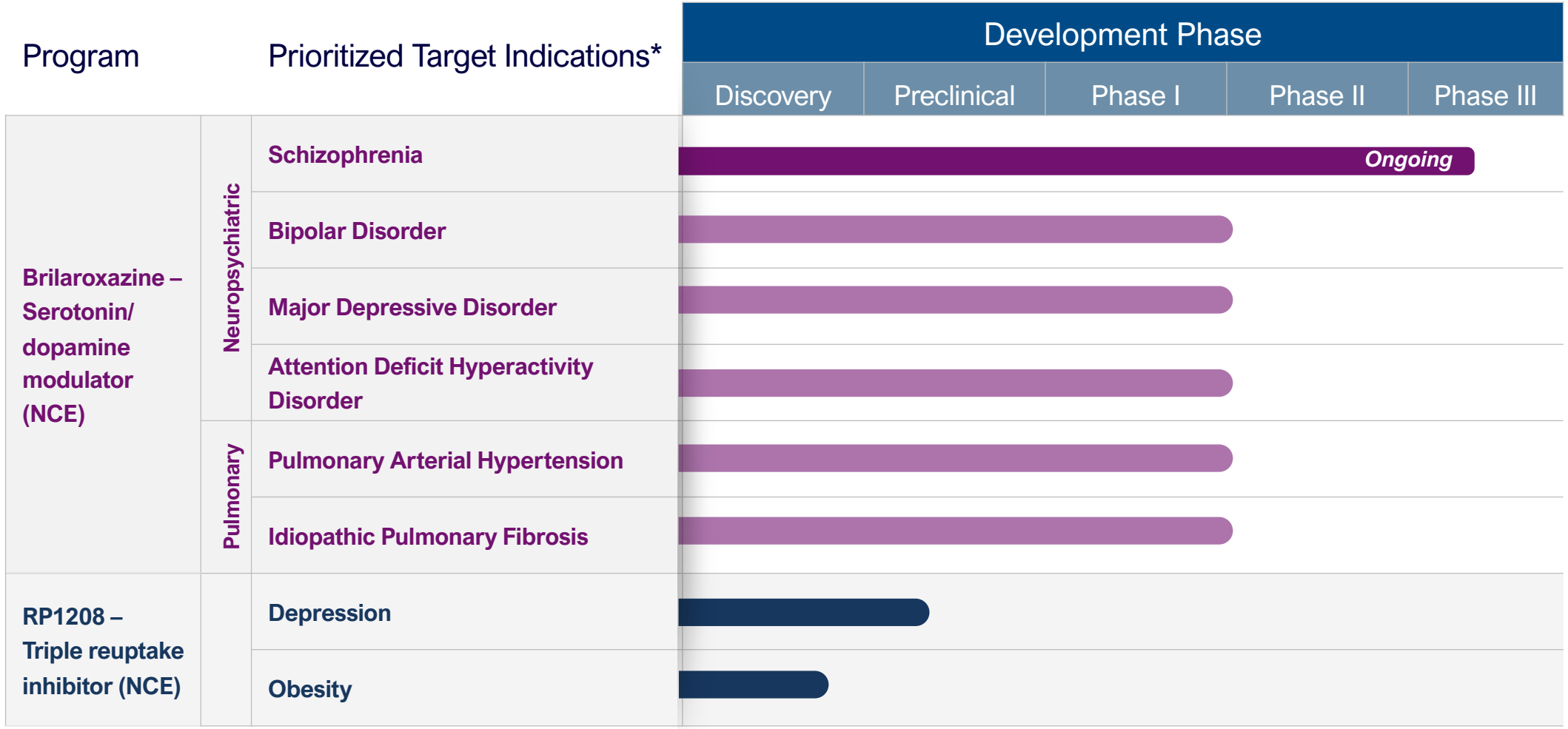
Development of Brilaroxazine for Schizophrenia and other Psychiatric Disorders

Laxminarayan Bhat, PhD

Founder, President & CEO

Reviva Pharmaceuticals

Extensive Clinical Development Pipeline: Platform Therapies

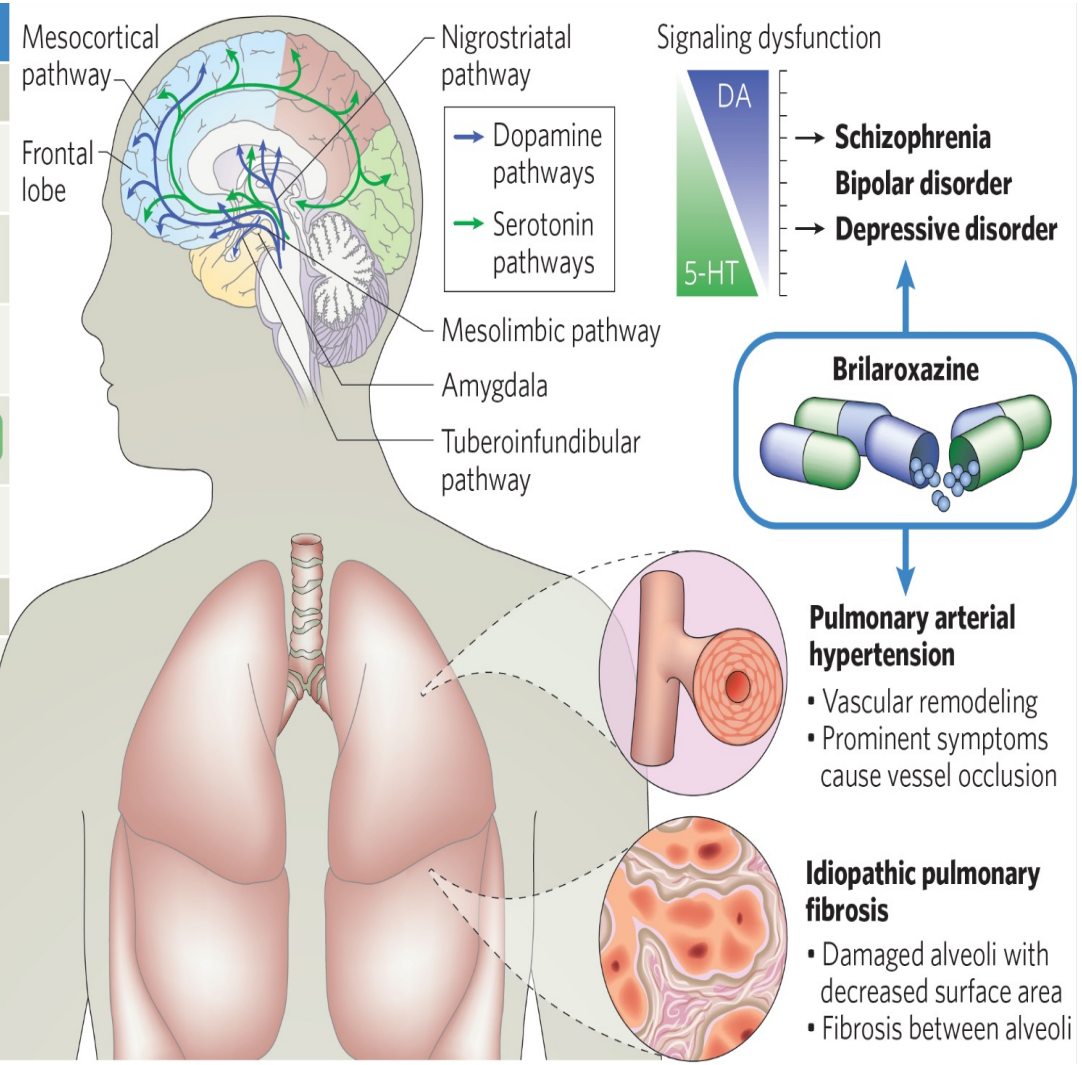


*Opportunity to expand into other indications including Parkinson's Psychosis and Alzheimer's (Psychosis/agitation)

Dysfunctional Serotonin Signaling is Implicated in the Pathobiology of Psychiatric Disorders and Inflammatory Diseases

- Brilaroxazine is a potent modulator of serotonin and dopamine signaling pathways
- Dysfunctional serotonin and dopamine signaling pathways are:
  - implicated in the pathobiology of neuropsychiatric diseases
  - associated with dysregulated immune responses
- Dysfunctional serotonin signaling is implicated in the pathobiology of immune / inflammatory diseases, PAH, IPF and psoriasis

Dysfunction (region)	Receptors involved
Central nervous system disorders	
Positive symptoms (mesolimbic)	D_2 D_3 D_4
Negative symptoms (mesocortical, PFC)	D_4 5-HT_{1A} 5-HT_{2A} 5-HT_{2B}
Cognitive symptoms (dorsolateral PFC)	5-HT_{1A} 5-HT_{2A} 5-HT_6 5-HT_7
Aggressive symptoms (OFC, amygdala)	D_1 D_2 D_4 5-HT_{2A} 5-HT_{2B} 5-HT_7
Affective symptoms (ventromedial PFC)	5-HT_{1A} 5-HT_{2B} 5-HT_7
Pulmonary arterial hypertension	
Vasoconstriction	5-HT_{2A} 5-HT_{2B}
Fibrosis and inflammation	5-HT_{2A} 5-HT_{2B} 5-HT_7
Thrombosis	5-HT_{2A}
Idiopathic pulmonary fibrosis	
Inflammation	5-HT_7
Fibrosis	5-HT_{2A} 5-HT_{2B}



biopharmadealmakers

Bhat L. Nature 2021, 15(2): B24; Bhat L. et al, J Neurology & Neuromedicine 2018, 3(5):39-50; Bhat L. et al, European J Pharmacology 2018, 827:159-166.

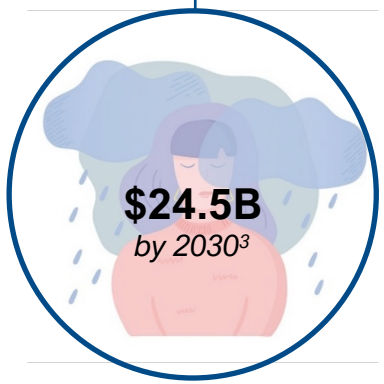
Potential Market Opportunity for Brilaroxazine (RP5063)

Addressing Significant Unmet Medical Needs: Psychiatric Conditions and Immune System Abnormalities

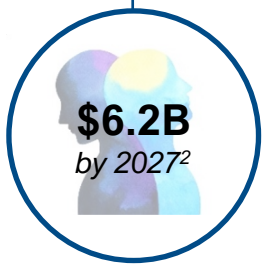
Neuropsychiatric Indications

Schizophrenia

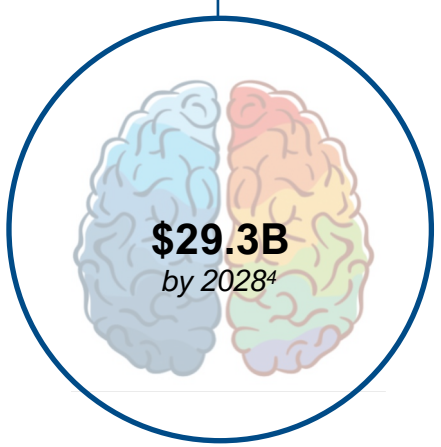
Major Depressive Disorder



Bipolar Disorder

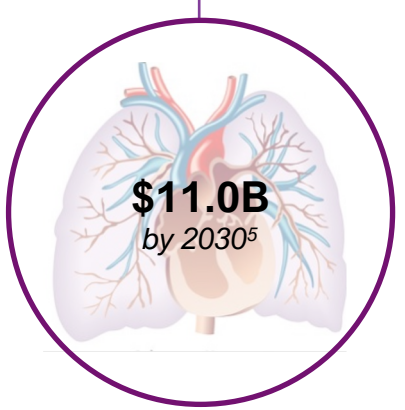


ADHD

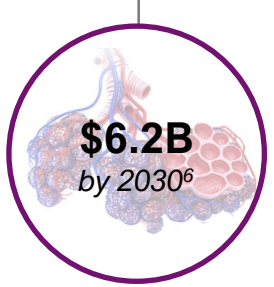


Pulmonary Indications

Pulmonary Arterial Hypertension (PAH)



Idiopathic Pulmonary Fibrosis (IPF)



1.Schizophrenia: Verified Market Research 2021
2.Bipolar Disorder: Maximize Market Research 2021
3. MDD: Research and Markets.Com, 2021
4. ADHD: Verified Market Research, 2022
5. PAH: Grand View Research, 2022
6. IPF: Allied Market Research, 2022

Brilaroxazine (RP5063) in Phase 3 Development for Schizophrenia

Promising Asset In Phase 3 Studies

Differentiated pharmacology profile as modulator of serotonin and dopamine signaling pathways

Prioritizing ongoing pivotal Phase 3 trial in schizophrenia with topline data anticipated in mid-2023

Potential for clinical expansion in additional neuropsychiatric disorders and lung diseases

Positive Results to Date in Phase 2

Met primary endpoint with statistically significant reduction in schizophrenia on total PANSS scores vs placebo

Significantly mitigated positive symptoms, negative symptoms, and social inhibition

Directional improvement in depression and cognitive symptoms

Demonstrated favorable safety profile

Targeting Large Market Opportunity

The global schizophrenia is estimated to reach over $10bn by 2028[1]

Serotonin and dopamine receptors, which are targeted by brilaroxazine, are the primary targets for approved antipsychotics

Brilaroxazine has a favorable efficacy and side effect profile vs. currently approved antipsychotics

1. Schizophrenia: Verified Market Research 2021

Brilaroxazine Schizophrenia Program

Clinical Efficacy, Safety, and Compliance

Brilaroxazine (RP5063) Phase 1 Study Outline

Evaluated Safety and Efficacy in Stable Schizophrenia Patients

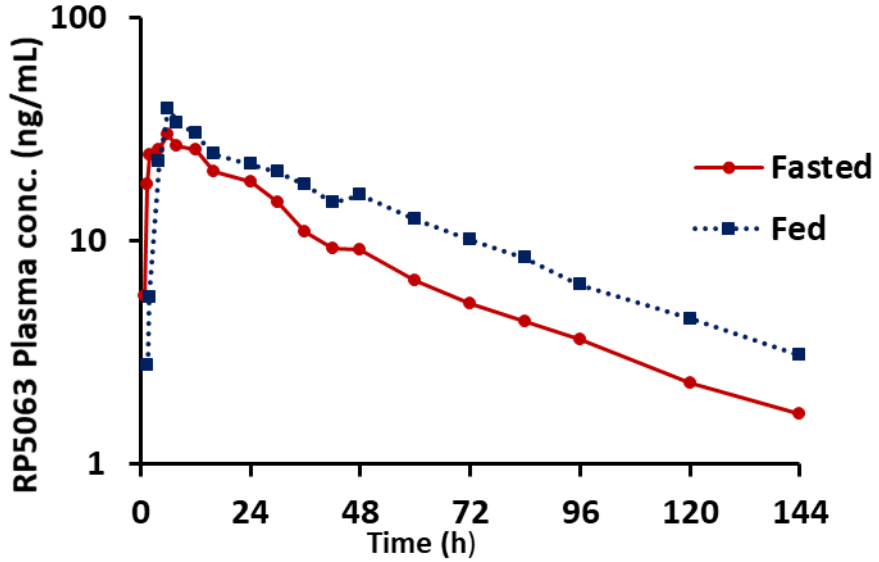
Placebo Controlled Trial

Subjects	Phase 1a: Caucasians (~70%) & Japanese (~30%) healthy males Phase 1b: Schizophrenia Patients (stable)
Phase 1a SAD (n=16)	Single ascending dose (10mg, & 15 mg) to MTD, safety & PK, Double blind, 8-subjects/cohort including 2 placebo
Food Effect	Open-label study (n=8) in healthy male subjects, 15mg dose
Phase 1b MAD (n=32)	Multi ascending dose, once daily for 10 days, safety, PK & PD 10mg, 20mg, 50mg and 100mg, dose per day for 10 days Double blind, 8-subjects/cohort including 2 placebo

Brilaroxazine (RP5063) Phase 1 Study PK and Safety Profile

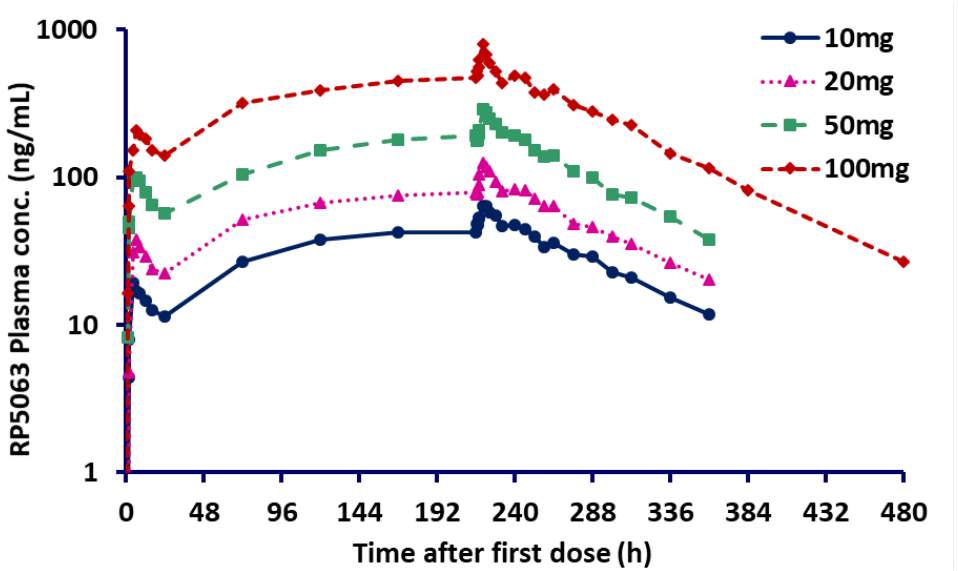
Administered Orally to Volunteers (10 – 100 mg/day)

Single Ascending Dose (15mg, N = 28)
(in healthy subjects)



- Good absorption with reasonable T_{max}
- Dose dependent and proportional increase in C_{max} and AUC_{∞}
- Half-life (T1/2 = 42 h) suitable for once a day dosing
- No significant food effect, brilaroxazine can be administered with or without food.

Multiple Ascending Dose, 10 Days (N = 32)
(in stable schizophrenia subjects)



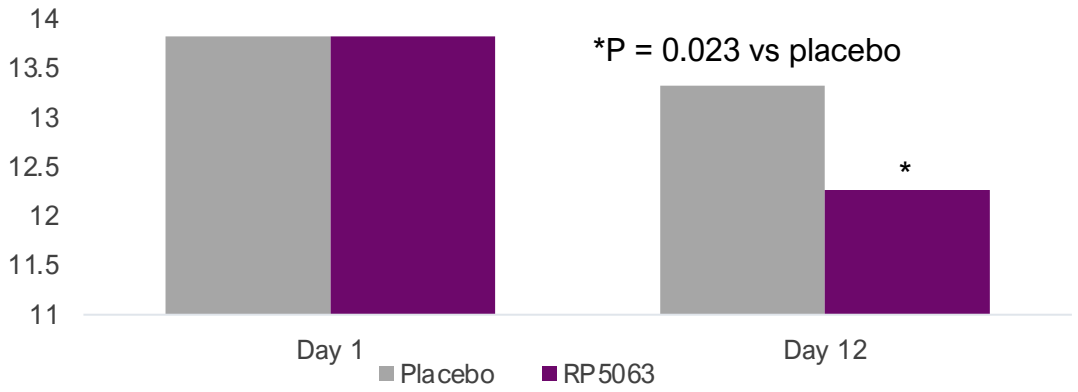
- Brilaroxazine administered once daily for 10 days
- Linear, predictable PK across all doses and time
- Relatively long half-life (~60 hrs); good for compliance, if dose missed
- Steady state in 5 days (120 hrs)
- Well tolerated, no dose limiting safety signals in ECG, clinical lab, vital signs, and physical exams

Bhat et al. J Neurology & Neuromedicine 2018, 3(5): 39-50. Cantillon M. et al. *Clinical & Translational Science 2018, 11: 387-396.*
Cantillon M. et al. *Clinical & Translational Science 2018, 11: 378-386.*

Brilaroxazine Phase 1B MAD Study Efficacy Data in Stable Schizophrenia

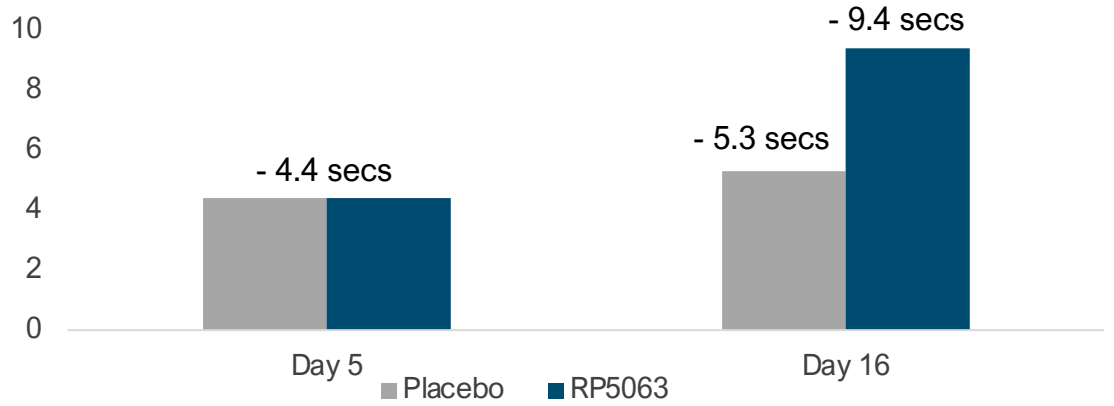
Decrease in Positive Symptoms and Improvement in Cognition (10 Days Treatment)

Efficacy for Schizophrenia
PANSS Positive Data



- PANSS Baseline for sub-analysis: ≥50
- Pooled data of RP5063 (10-100mg), N = 19

Improvement in Cognition
Trails A & B Data



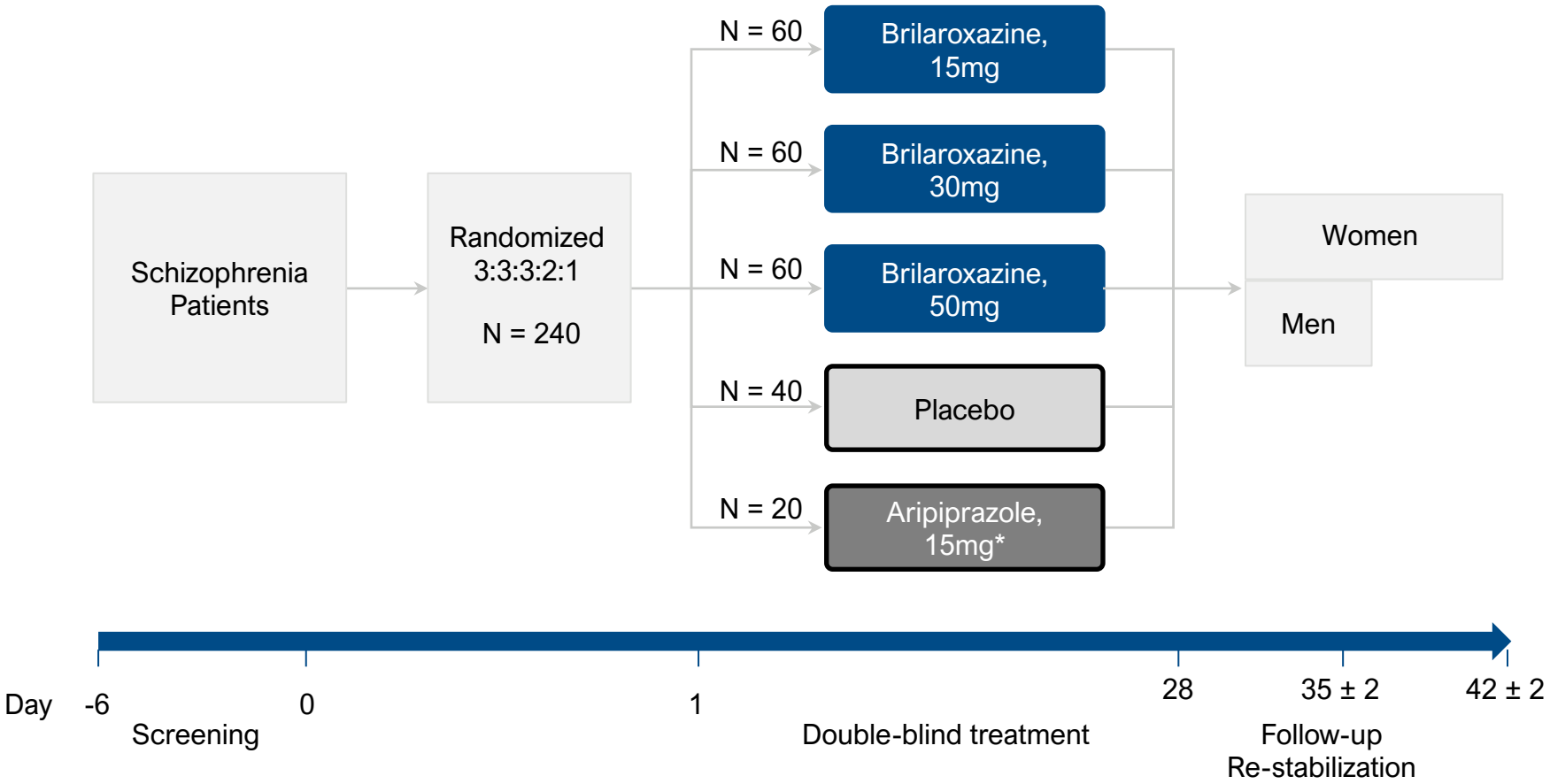
- PANSS Baseline Scores: 39-69
- Pooled data of RP5063 (10-100mg), N=32

✓ Efficacy further supported by the phase 2 study in acute schizophrenia patients[1]
✓ Cognition improvement supported by pharmacology profile, and translational studies data in rodents[2]

(1) Bhat et al. J Neurology & Neuromedicine 2018, 3(5): 39-50 ; (2) Rajagopal, L. et al. Behavioral Brain Research 2017, 332: 180-199.

Brilaroxazine: Successfully Completed Phase 2 Schizophrenia Trial Design

Randomized, double-blind, placebo-controlled, multicenter (USA, EU, Asia) trial to assess the safety and efficacy of brilaroxazine in acute exacerbation of schizophrenia or schizoaffective disorder



Study Overview

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

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

Pharmacokinetics:
Population pharmacokinetics

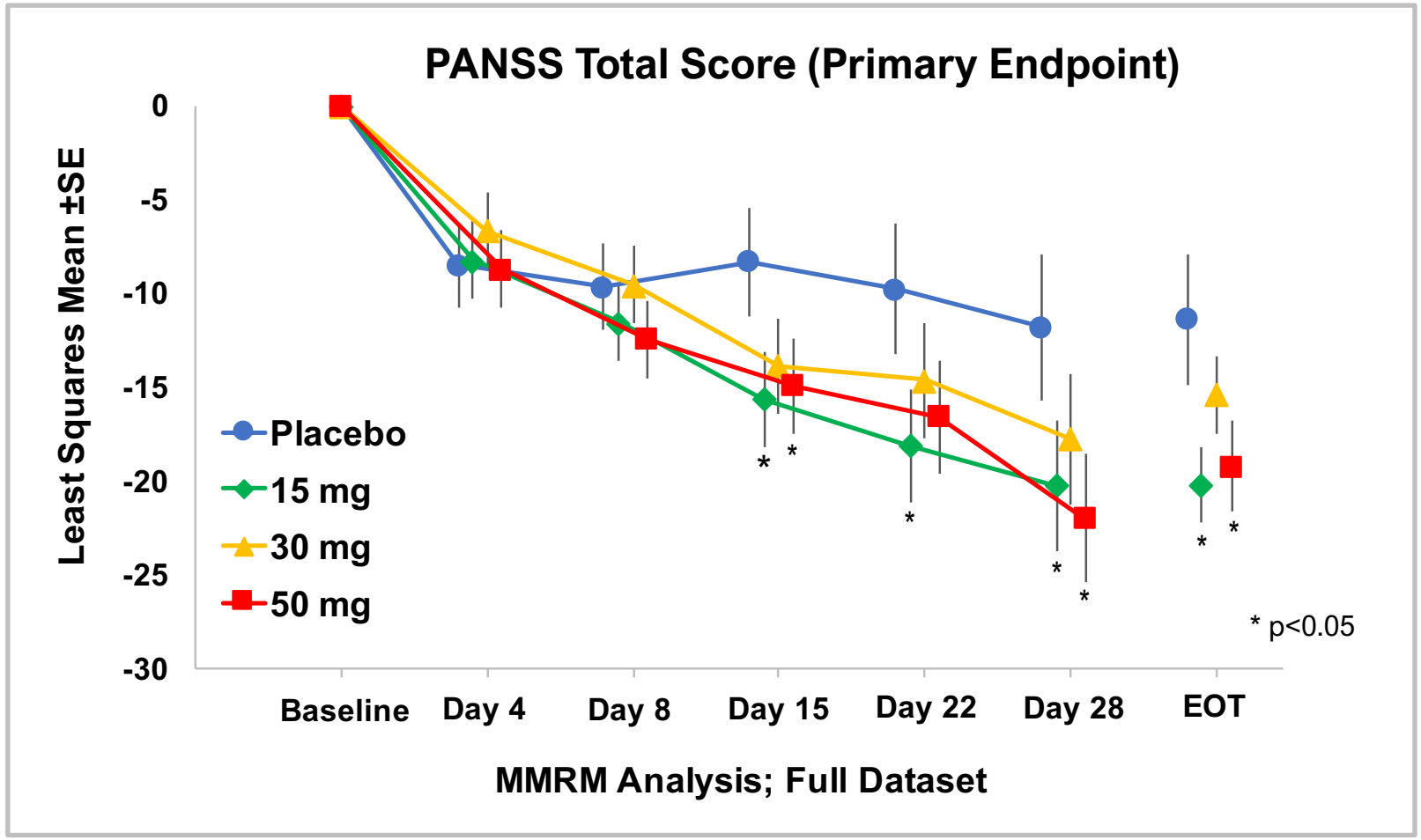
*The aripiprazole arm was included solely to show assay sensitivity and was not powered to show efficacy.

Schizophrenia Phase 2 Study: Significant Treatment Difference from Placebo

Brilaroxazine demonstrated improved PANSS total score across all dose levels (N=234)

Efficacy Data for Schizophrenia

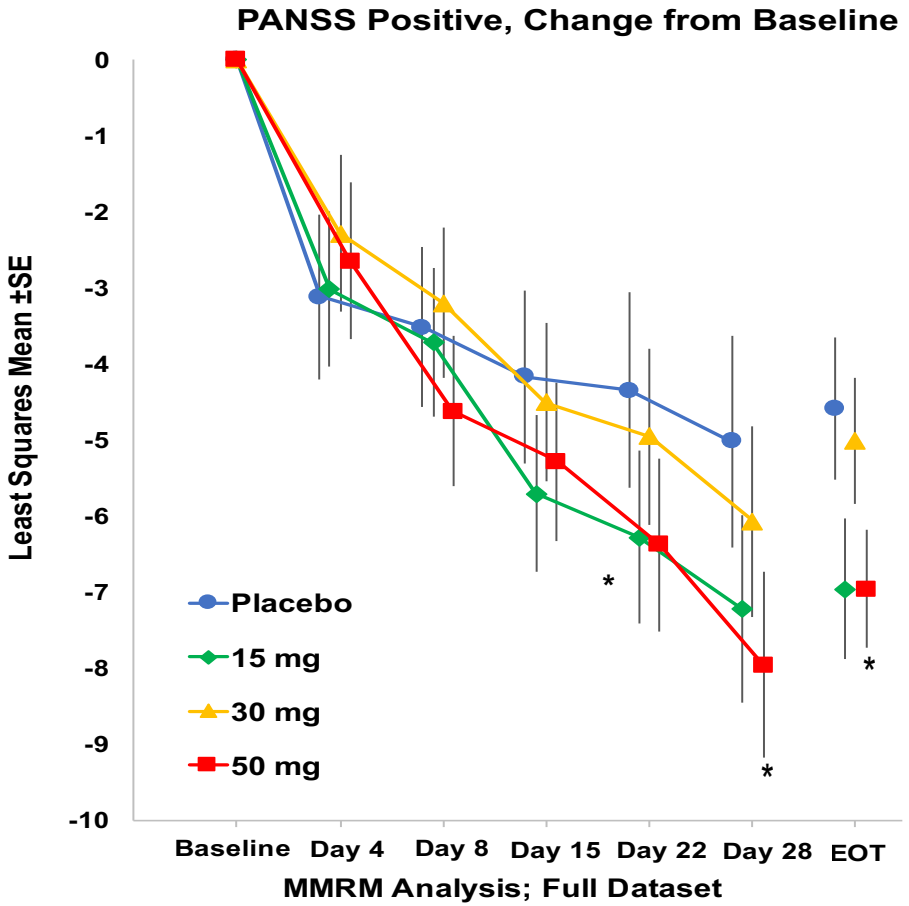
- Study met the safety and efficacy endpoints
- Statistically significant, sustained treatment effect with decrease in PANSS scores
- Treatment effects started separating from placebo within a week



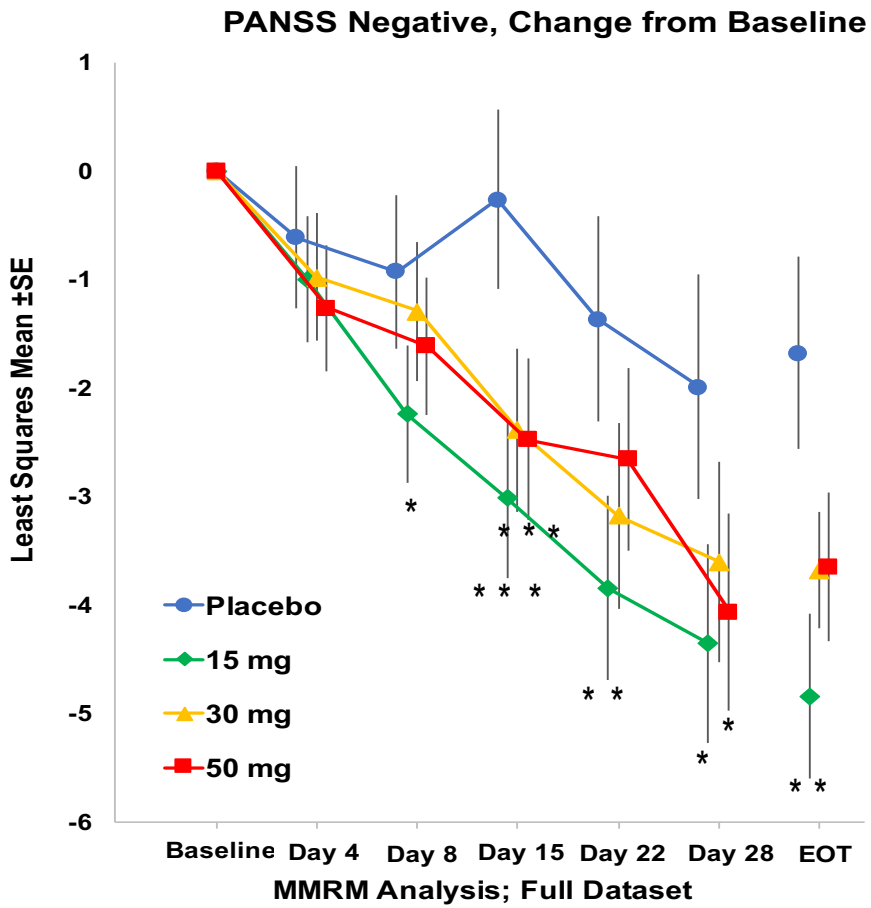
Brilaroxazine Mitigated Positive and Negative Symptoms

Phase 2 Study in Schizophrenia

Decrease in Positive Symptoms



Decrease in Negative Symptoms



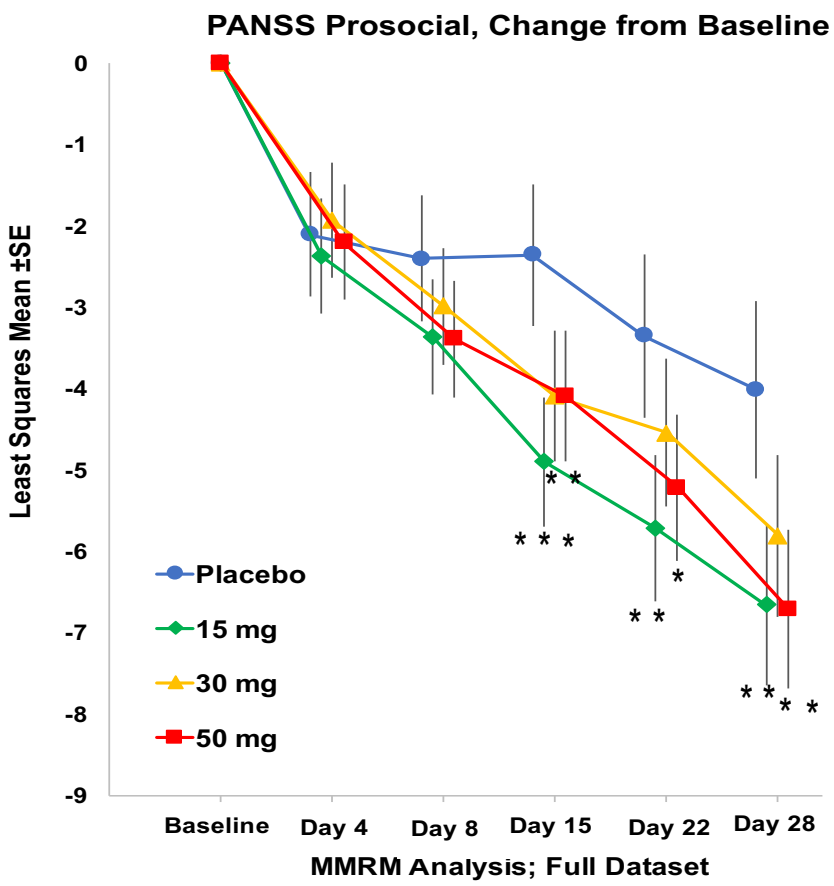
* p<0.05, ** p<0.01, *** p<0.001

Bhat et al. J Neurology & Neuromedicine 2018, 3(5): 39-50 ; Cantillon, M. et al. Schizophrenia Research 2017, 189: 126-133

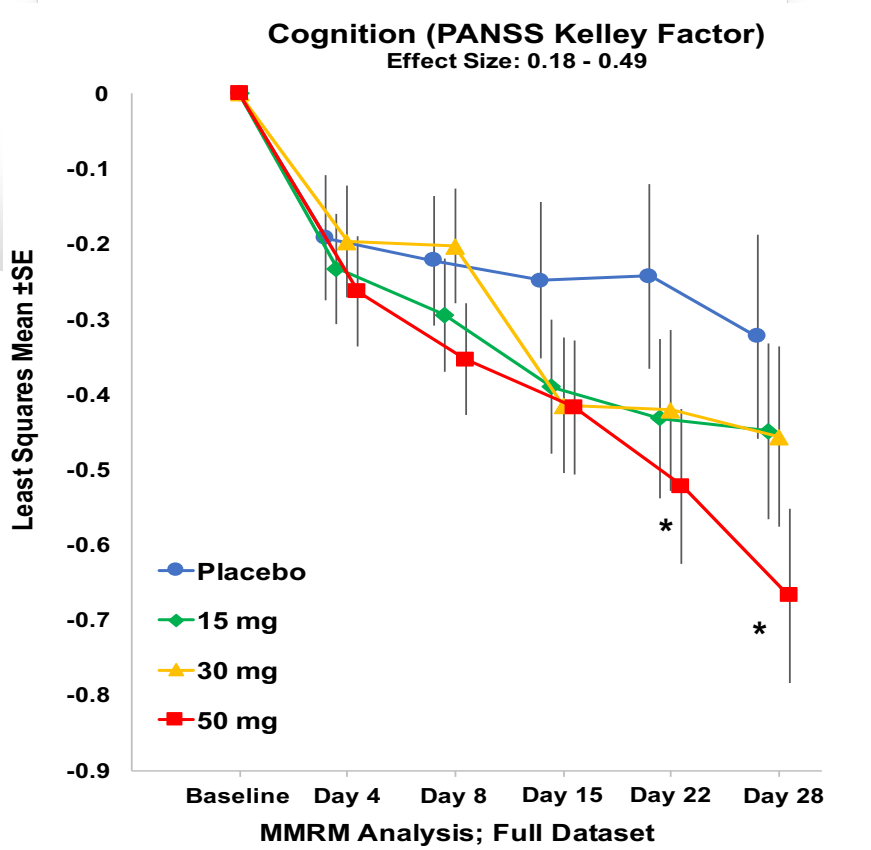
Brilaroxazine Improved Social Functioning and Cognition

Phase 2 Study in Schizophrenia

Improvement in Social Functioning



Improvement in Cognition



* p<0.05, ** p<0.01, *** p<0.001

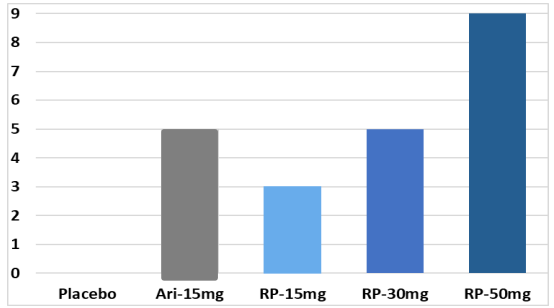
Bhat et al. J Neurology & Neuromedicine 2018, 3(5): 39-50 ; Cantillon, M. et al. Schizophrenia Research 2017, 189: 126-133

Schizophrenia Phase 2 Study: Brilaroxazine Side Effect Profile

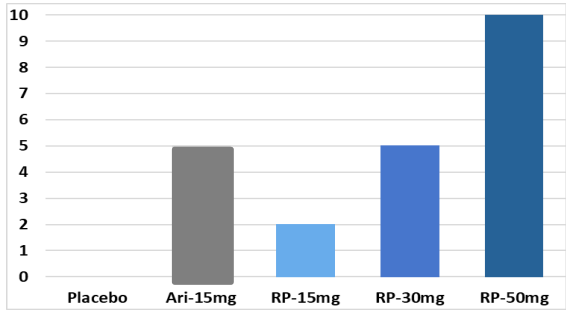
Neuroleptic, Endocrine and Metabolic Side Effects of Brilaroxazine Comparable to Placebo (N=234)

CNS / Neuroleptic Side Effects

Extrapyramidal Side Effect (%)

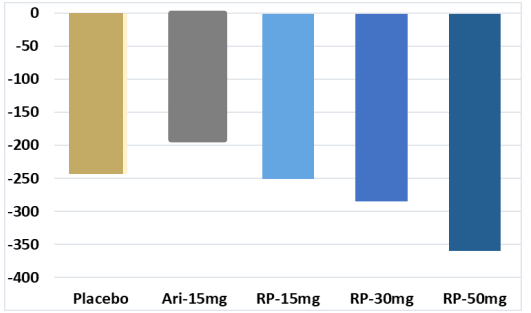


Akathisia (%)

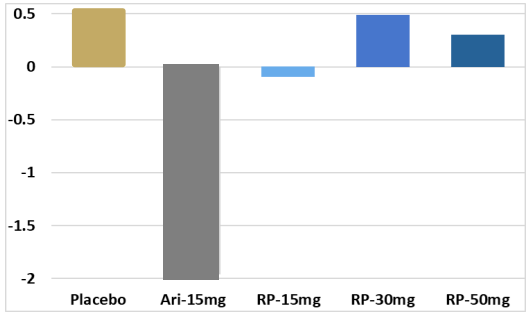


Endocrine Side Effects

Change in Prolactin (mIU/L)

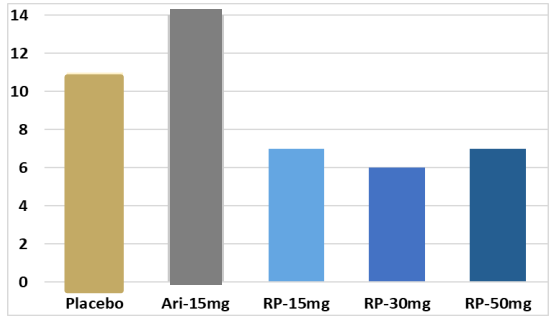


Change in Thyroid-T4 (pmol/L)

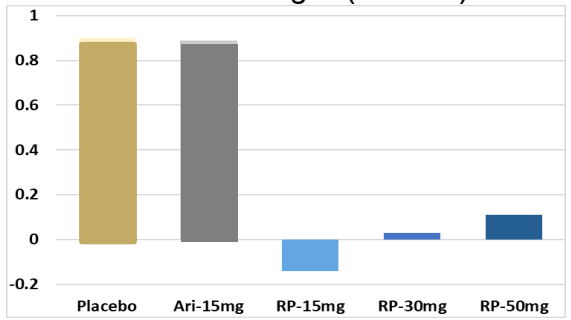


Metabolic Side Effects

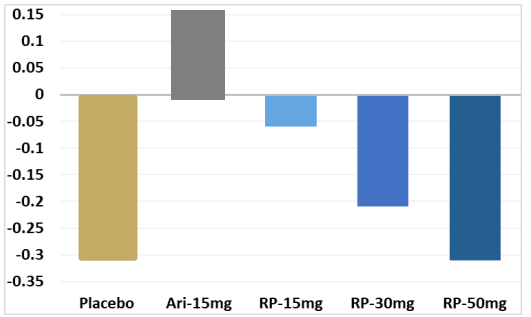
Body Weight Increase (%)



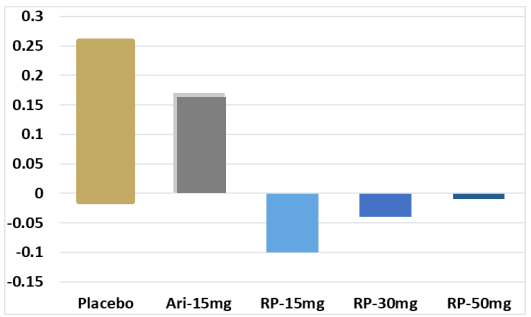
Diabetes/Blood Sugar (mmol/L)



Cholesterol (mmol/L)



Lipids/Triglycerides (mmol/L)



RP: 15mg projected, widely used dose

Ari: Aripiprazole; RP: Brilaroxazine (RP5063)

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

Lower Clinical Drug-Drug Interactions with Brilaroxazine vs Standards of Care

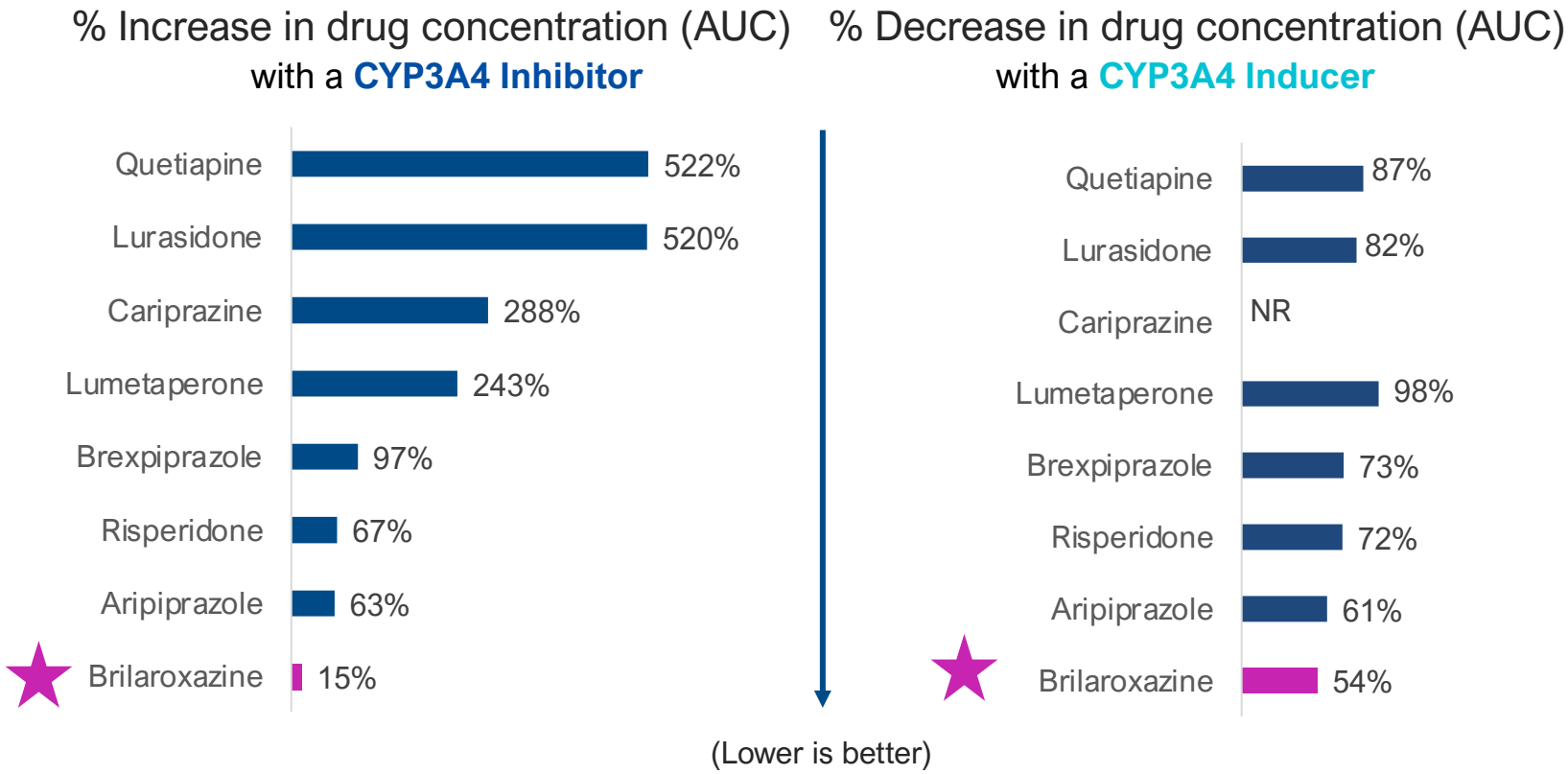
Up to 34x higher drug plasma concentration with standard of care antipsychotics over brilaroxazine in presence of a strong CYP3A4 inhibitor: A Clinical Differentiation Factor

Drug-drug interactions alter plasma drug concentrations, and can impact efficacy and side effect profiles of a drug

~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

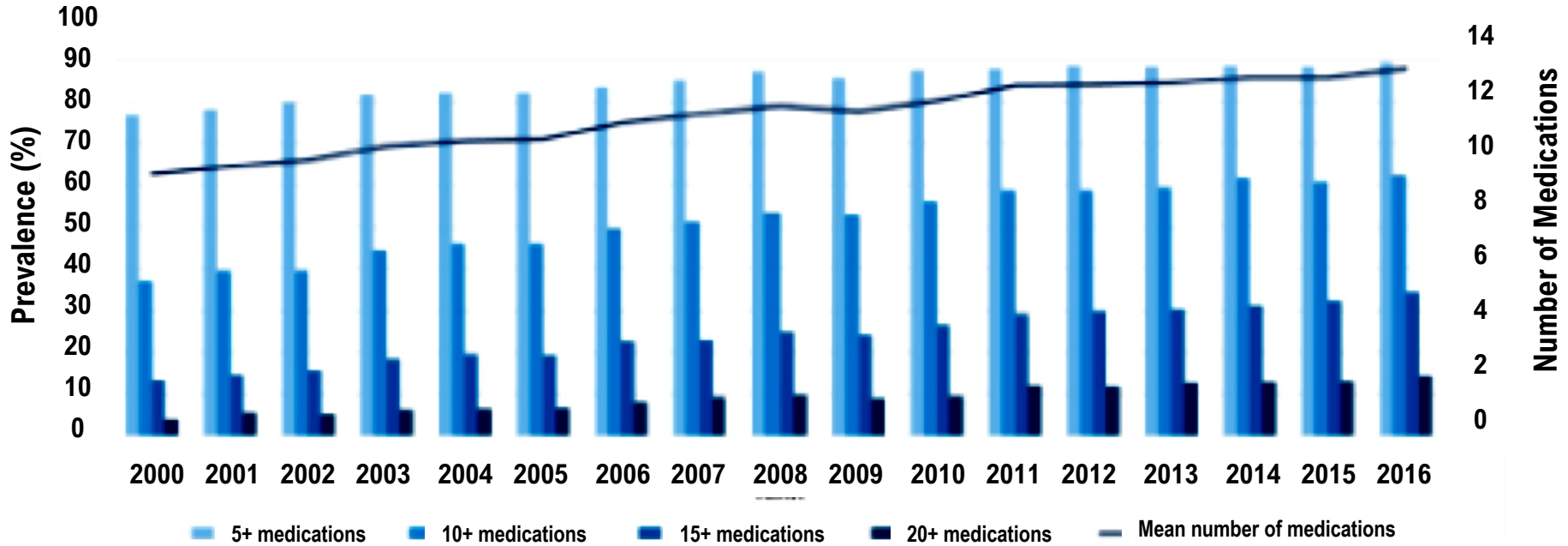
*Olanzapine[9] not evaluated; metabolized by CYP1A2[10]



(1) RVP-10-004 study data 2023 (unpublished); (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; NR: not reported

Polypharmacy Among Older Adults with Schizophrenia

Clinical significance of drug-drug interactions



Age-standardized proportions of older adults with schizophrenia exposed to different classes of medications between 2000 and 2016.

- Polypharmacy increases the risk of potential drug–drug interactions (pDDIs).
- 58% of patients received >1 antipsychotic medications or combination of antipsychotic and other psychiatric medications.
- Median number of medications consumed yearly rose from 8 in 2000 to 11 in 2016: 5+drugs: 76.6%–89.3%; 10+ drugs: 36.9%–62.2%; 15+drugs: 13.3%–34.4%; 20+ drugs: 3.9%–14.4%.

Lunghi C et al., Frontiers in Pharmacology 2023, 14:1080073.

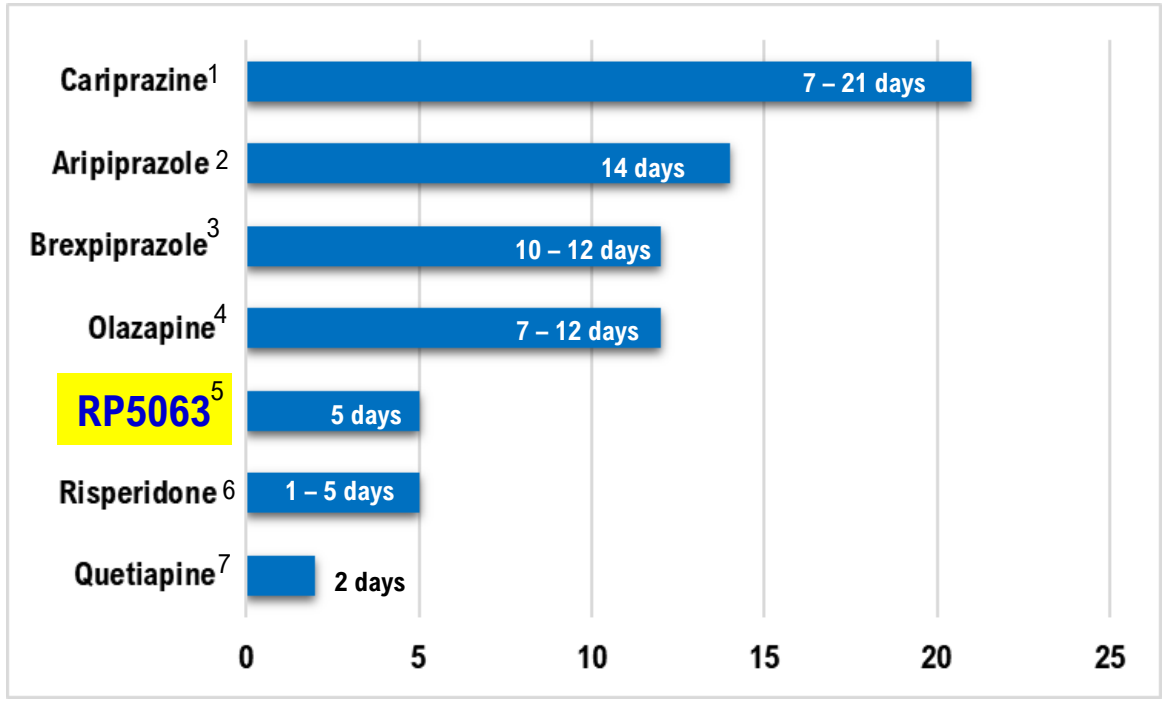
Comparison of Steady State and Onset of Treatment Response

Brilaroxazine (RP5063) vs Standard of Care Antipsychotics: Contributing Factors for Clinical Differentiation

Early time to steady state is critical for enhanced treatment compliance in acute schizophrenia

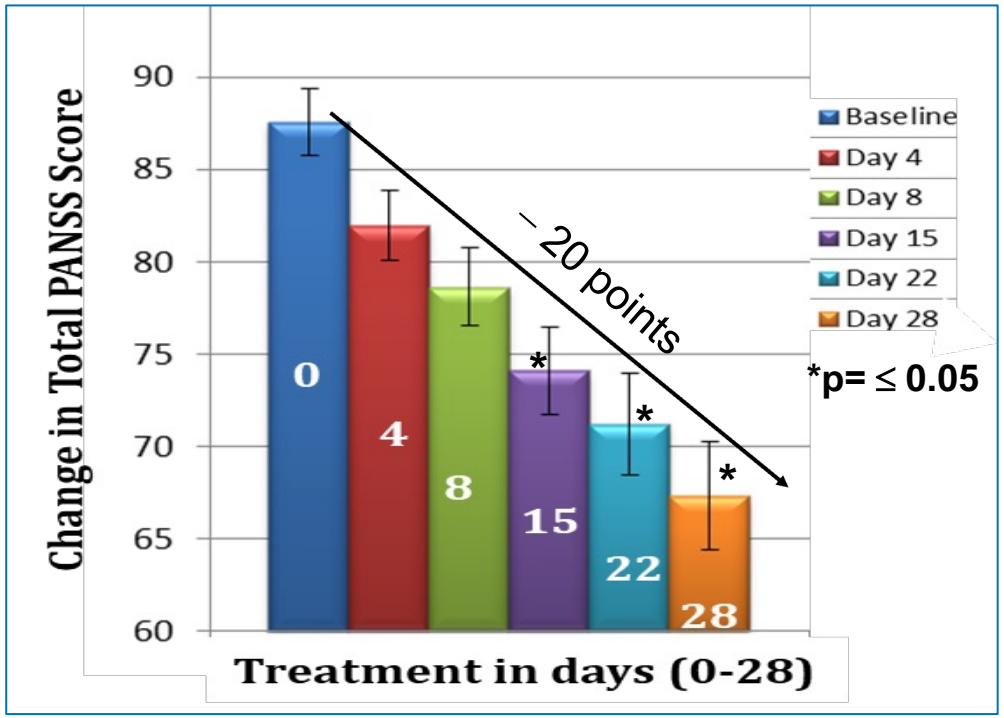
Early onset / treatment response is critical for enhanced treatment compliance and faster recovery in acute schizophrenia

Time to Steady State



1. Eur J DMPK 2021, 46:53-69
2. FDA label insert, 2003
3. Clin Mass Spectrometry 2017, 6:21-24
4. EMEA Dossier 2004
5. Brilaroxazine phase 1 and 2 data
6. FDA Dossier 1996
7. FDA Dossier 2003

Brilaroxazine Treatment effect (15mg)

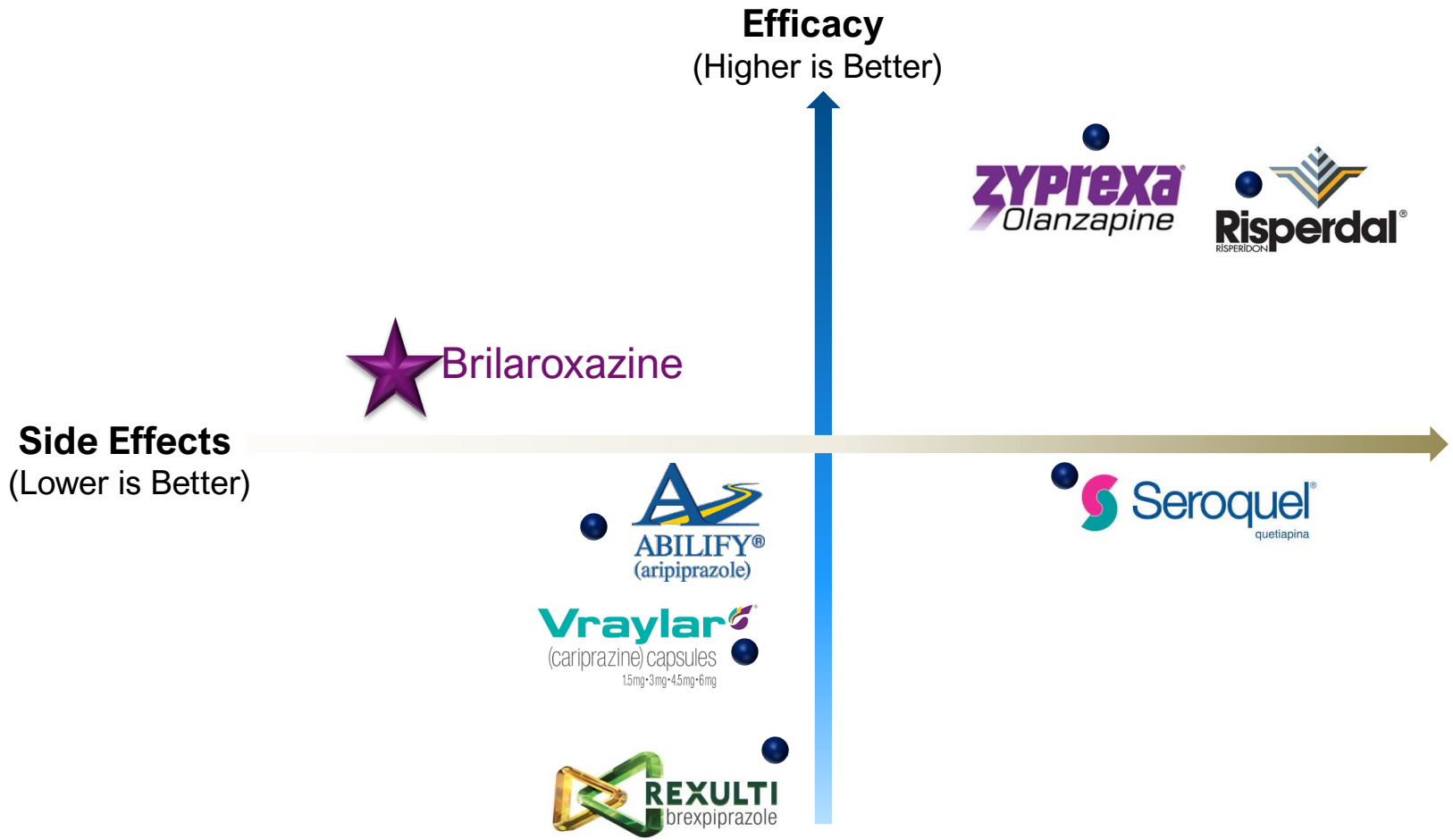


☞ Placebo adjusted score: 10.5 points

Current Positioning of Brilaroxazine (RP5063) vs. Major Antipsychotics

Meta-Analysis of Clinical Data of Antipsychotics

Current data suggests that brilaroxazine may have a favorable efficacy and side effect profile vs. currently approved antipsychotics



Reviva Sponsored Research from Zacks SC Research, April 2021; Lancet 2019, 394:939-951.

Bridging the Therapeutic Gap in Schizophrenia

Acute Phase

- Robust clinical efficacy with early onset of action, superior safety and tolerability, and high treatment compliance
- Strong and sustained efficacy for major symptom domains (positive, negative, mood and cognitive symptoms)
- Once daily oral (tablets) dosing regimen with no dose titration

Transition

Maintenance/Stable Phase

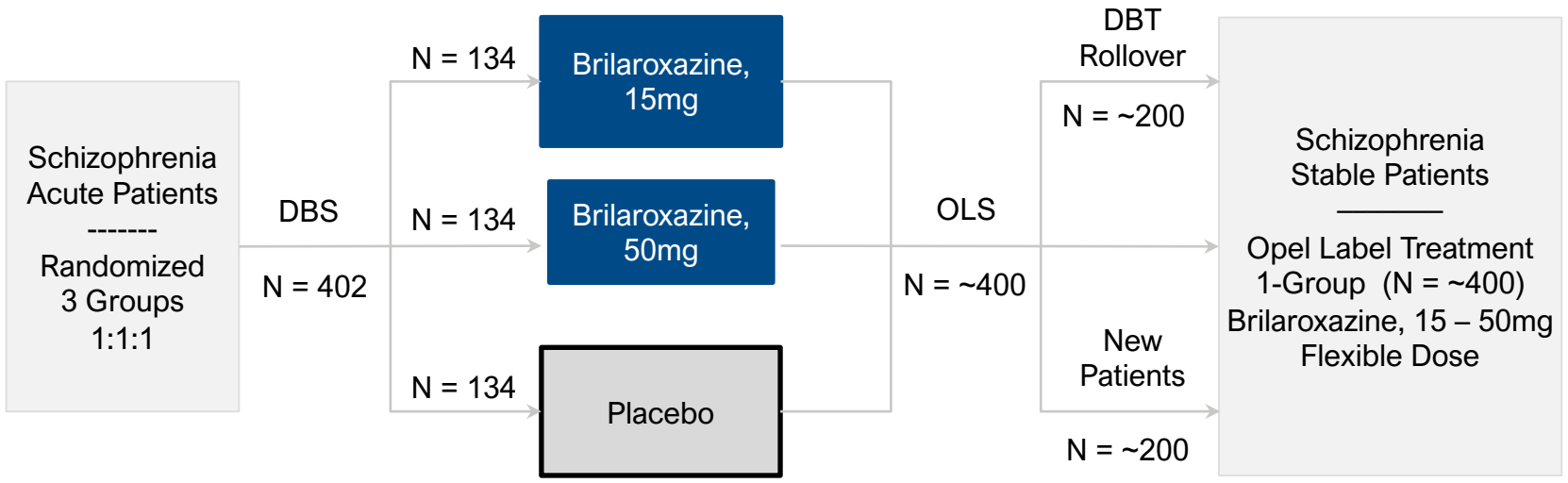
- Strong and sustained efficacy for major symptom domains (positive, negative, mood and cognitive symptoms) potential benefit from antiinfmmatory effect with superior long-term safety to achieve high remission rate, to improve treatment compliance and avoid relapse incidences
- Flexible dosing regimens: once daily dose (tablets) or Long-acting i.m./depot once 60-90 days dose formulations

Estimated 40% patients reported to discontinue treatment and/or experience relapse incidences while transitioning from acute to maintenance treatment with current standard of care antipsychotics*

*Source: The British Journal of Psychiatry 2006, 189:433-440.

Brilaroxazine Phase 3 RECOVER Trial For Schizophrenia (ongoing)

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



Part 1:
Double-blind Study (DBS)
28 Days

1-Week follow up and stabilization for patients discontinue treatment or not rolling over to OLS

Part 2:
Open Label Study (OLS)
52 Weeks

1-Week follow up and stabilization for patients discontinue or complete the OLS

Study Overview

Primary Endpoint (DBS):
Reduction in total PANSS at the end of treatment in a brilaroxazine arm from baseline versus placebo

Safety (DBS, OLS):
Clinical, labs, body weight, lipids, fasting glucose, prolactin

Pharmacokinetics:
Population pharmacokinetics

For details see: www.clinicaltrials.gov (search key word, RP5063)

Reviva to Present at the Scientific Conferences in Q2-2023

Society of Biological Psychiatry (SOBP) Annual Meeting in San Diego, April 27-29, 2023
Brilaroxazine (RP5063), a novel serotonin-dopamine stabilizer, displays antipsychotic efficacy in rodents (Poster #S242)
Laxminarayan Bhat, Kouacou Adiey, Seema R Bhat, Prabhu Mohapatra.

International Societies for Investigative Dermatology (ISID) Meeting in Tokyo, Japan, May 10-13, 2023
Brilaroxazine topical liposomal-gel formulation displays efficacy in the imiquimod-induced psoriatic BALB/c mouse model.
Laxminarayan Bhat, Seema R Bhat, Arulprakash Ramakrishna, Muthukumar Amirthalingam

American Society for Pharmacology and Experimental Therapeutics (ASPET) Annual Meeting in St. Louis, May 18-21, 2023

- CYP3A inhibition and induction exert limited effects on brilaroxazine pharmacokinetics (Poster #376)
  Laxminarayan Bhat, Seema R Bhat, Arulprakash Ramakrishna, and Palaniappan Kulanthaivel
- Single-dose brilaroxazine pharmacokinetics, metabolism and excretion profile in animals and humans (Poster #579)
  Laxminarayan Bhat, Seema R Bhat, and Palaniappan Kulanthaivel

American Thoracic Society (ATS) Annual Meeting in Washington, D.C. May 19-24, 2023
Brilaroxazine efficacy in a bleomycin-induced rodent model of idiopathic pulmonary fibrosis (poster #623)
Laxminarayan Bhat, Seema R Bhat, Marie-Claude Nault, Marzena Biernat and Sabastien M. Labbe

Publications on Brilaroxazine for Neuropsychiatry/Neurology

https://revivapharma.com/publications/

1. Laxminarayan Bhat, Kouacou Adiey, Seema R Bhat, Prabhu Mohapatra. RP5063, a novel dopamine-serotonin stabilizer displays antipsychotic efficacy in rodents. Medical Research Archives 2023 (in print)
2. Laxminarayan Bhat, Marc Cantillon, and Robert Ings. Brilaroxazine Clinical Experience in Schizophrenia: A New Option to Address Unmet Needs. J Neurology & Neuromedicine 2018, 3(5): 39-50. **Invited Review**
3. Marc Cantillon, Robert Ings, and Laxminarayan Bhat; A population pharmacokinetic and pharmacodynamic analysis of phase 2 study data evaluating RP5063 in patients with schizophrenia or schizoaffective disorder. European Journal of Drug Metabolism and Pharmacokinetics 2018, 43(5):573-585.
4. Marc Cantillon, Robert Ings, Laxminarayan Bhat. Initial clinical experience of RP5063 following single doses in normal healthy volunteers and multiple doses in patients with stable schizophrenia. Clinical & Translational Science 2018, 11: 387-396.
5. Marc Cantillon, Robert Ings, Laxminarayan Bhat. Pharmacokinetics of RP5063 following single-doses to normal healthy volunteers and multiple doses over 10 days to stable schizophrenic patients. Clinical & Translational Science 2018, 11:378-386.
6. Marc Cantillon, Arulprakash R, Ajay Alexander, Robert Ings, Dennis Sweitzer, Laxminarayan Bhat; Dopamine Serotonin Stabilizer RP5063: A Randomized, Double-blind, Placebo-controlled Multicenter Trial of Safety and Efficacy in Exacerbation of Schizophrenia or Schizoaffective Disorder; Schizophrenia Research 2017, 189:126-133.
7. Lakshmi Rajagopal, Sunoh Kwon, Mei Huang, Eric Michael, Laxminaryan Bhat, Marc Cantillon, Herbert Y. Meltzer; RP5063, an atypical antipsychotic drug with a novel mechanism of action, improves cognition and psychosis in mouse models of schizophrenia; Behavioral Brain Research 2017, 332:180-199.

Reviva Pharmaceuticals Holdings, Inc.

General Inquiries

info@Revivapharma.com

Business Inquiries

busdev.rp@Revivapharma.com

Investor Relations Contact

IR@Revivapharma.com

Q&A