Zacks Small-Cap Research
Sponsored – Impartial – Comprehensive
January 13, 2021
John D. Vandermosten, CFA
312-265-9588 / jvandermosten@zacks.com
scr.zacks.com
10 S. Riverside Plaza, Suite 1600, Chicago, IL 60606

Reviva Pharmaceutical Holdings, Inc. (RVPH - NASDAQ)

Brilaroxazine: Multi-receptor Modulator on Deck

Based on our DCF model and a 15% discount rate, Reviva is valued at approximately $21.00 per share. Our model applies a 50% probability of ultimate approval and commercialization for RP5063 in schizophrenia. The model includes contributions from the United States and rest of world.

Current Price (1/12/2021)	$9.11
Valuation	**$21.00**

INITIATION

Reviva is a research and development pharmaceutical company with two portfolio compounds targeting ten indications. The candidates address multiple related mental disorders, rare diseases & other categories of unmet need. Reviva's lead indication in schizophrenia with Brilaroxazine (RP5063) will begin a Phase III trial in 2021. Complementary Phase II work with RP5063 in bipolar disorder and depression may also begin.

Brilaroxazine is a novel, multimodal serotonin, dopamine & nicotinic receptors modulator with an improved efficacy & side effect profile compared to other antipsychotics. The drug class is established with over $10 billion in revenues. Unmet needs persist, related to efficacy, side effects & discontinuation. A new offering with an improved profile is expected to carve material share from the existing market and expand into untreated patients. Secondary candidate, RP1208, is in preclinical studies for depression and obesity.

We expect launch of three Phase III trials for RP5063 starting in mid-2021, generating registrational data by 2024. After agency review in the US and other jurisdictions, we anticipate approval to be granted by the FDA in 2025 followed by other territories. Our valuation assumes commercialization in the US and rest of world in 2025 and 2026 respectively.

SUMMARY DATA

52-Week High	**13.00**
52-Week Low	**7.31**
One-Year Return (%)	**N/A**
Beta	**N/A**
Average Daily Volume (sh)	**28,973**
Shares Outstanding (mil)	**9.23**
Market Capitalization ($mil)	**84.1**
Short Interest Ratio (days)	**4.99**
Institutional Ownership (%)	**70.1**
Insider Ownership (%)	**120**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2020 Estimate	**N/A**
P/E using 2021 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of USD)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	$0.0 A	$0.0 A	$0.0 A	$0.0 A	$0.0 A
2020	$0.0 A	$0.0 A	$0.0 A	$0.0 E	$0.0 E
2021					$0.0 E
2022					$0.0 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2019	-$0.02 A	-$0.02 A	-$0.01 A	$0.00 A	-$0.05 A
2020	-$0.04 A	-$0.05 A	-$0.04 A	-$0.06 E	-$0.17 E
2021					-$1.11 E
2022					-$1.63 E

INITIATION

We are initiating coverage of Reviva Pharmaceutical Holdings, Inc. (NASDAQ: RVPH) with a current valuation of $21.00 per share. This present value is based on our estimates for successful Phase III trials in schizophrenia and subsequent approval by the FDA of Brilaroxazine (RP5063). We anticipate that the required trials will be complete by 2024 and receive regulatory approval in the US by 2025. In parallel with regulatory submission in the US, we also see similar efforts in other selected geographies. Reviva's lead indication targets schizophrenia, a serious mental disorder characterized by the subject suffering hallucinations, delusions and disordered thinking and behavior that impairs normal function.

An estimated 0.25% to 1% of the global population suffers from schizophrenia. Other sources, such as the World Health Organization, estimate there to be 20 million persons with the chronic disorder.

Reviva plans Phase II work in several indications associated with schizophrenia including bipolar disorder, depression, ADHD and psychosis related to neurodegenerative disease. Two orphan conditions may also be pursued in pulmonary arterial hypertension and idiopathic pulmonary fibrosis. These indications are amenable to RP5063's mechanism of action which relies on various states of binding to and modulation of multiple serotonin, dopamine and nicotinic receptors where it has antagonist and partial agonist activity.

There are numerous antipsychotics approved for use; however, a high discontinuation rate due to suboptimal efficacy and serious side effects reveal an unmet need. Commonly prescribed antipsychotics leave many patients suffering from neuroleptic, endocrine and metabolic side effects that frequently lead to discontinuation. These therapies do not provide efficacy uniformly across the spectrum of symptoms. Many of these agents are prescribed at a lower than medically needed level in order to limit the severity of side effects but fail to provide a therapeutic effect at that dose leading patients to discontinue therapy.

RP5063, with its better balance of receptor activity, may allow for therapeutic doses to be used in difficult to treat patients while limiting the impact of the common neurological, metabolic and endocrine side effects associated with commonly prescribed agents.

Reviva will soon launch registrational studies addressing acute and maintenance treatment for schizophrenia that will be completed over the next few years. Pivotal studies are expected to be complete by 2024, after which a new drug application (NDA) will be filed in the United States and other geographies. Assuming customary review periods, approval is anticipated in 2025 followed by near immediate commercialization in the United States and following a short delay in other areas. Pricing is forecast to be in line with other newly launched branded antipsychotics and penetration is modeled to be in the low single digit range of the addressable market. If the drug profile is better than expected, we anticipate higher penetration levels to occur.

As of December 2020, Reviva holds approximately $9 million in cash and will target the raise of additional funds to support its development projects. The once private firm combined with the special purpose acquisition company Tenzing Acquisition Corp. on December 14, 2020. The merger is expected to provide the capital necessary to advance its development programs. With no debt on balance sheet and a capital raise planned for the near term, we expect Reviva to launch the first of its schizophrenia programs in mid-2021 which include two $20 million Phase III trials, one $25 million maintenance study and a $10 million safety study.

We anticipate that pivotal data will be available for the schizophrenia indication by 2024 followed shortly after by a new drug application (NDA) to the FDA and other regulatory agencies. Approval in the US and other regions is anticipated in 2025 and 2026 respectively followed by commercial launch. If successful, RP5063 or Brilaroxazine will address several shortcomings of approved schizophrenia treatments and expand the therapeutic armamentarium for this chronic and debilitating mental disorder.

Key reasons to own Reviva Pharmaceuticals shares:

- **RP5063 Phase III asset may address an unmet need in schizophrenia and other mental disorders vs. existing therapies**
  - **Greater degree of efficacy**
  - **Lower level of side effects**
  - **Improved discontinuation rate**
  - **Addresses negative symptoms**
  - **Improved social functioning**
  - **Opportunity for approval in multiple mental disorders**
  - **Faster onset of action vs. standard of care**
  - **Binding to multiple serotonin and dopamine receptors implicated in schizophrenia**
- **Additional RP5063 Phase II ready programs in multiple indications**
  - **Bipolar Disorder**
  - **Depression**
  - **Attention Deficit Hyperactivity Disorder (ADHD)**
  - **Alzheimer's Psychosis/Behavior**
  - **Parkinson's Psychosis**
  - **Pulmonary Arterial Hypertension (Group 1)**
  - **Idiopathic Pulmonary Fibrosis**
- **RP1208 preclinical programs in development**
  - **Depression**
  - **Obesity**
- **Potential for intellectual property protection until 2037 for RP5063**

In the following sections we review Reviva's lead indication in schizophrenia, the structure behind RP5063 and compare it with other products on the market recognized to treat the condition. Our review of schizophrenia is presented along with discussion of the disease's pathophysiology, prevalence, treatment and risk factors. We report on relevant preclinical and clinical data, trial design and development history for RP5063 in schizophrenia and provide a summary of other treatments for the condition. The report also explores RP5063's secondary indications and the pre-clinical work being done with RP1208. We expect first sales of RP5063 in 2025 following a successful trial outcome, submission of an NDA and regulatory approval. Following an in-depth discussion of our model assumptions, we provide an appraisal of Reviva and generate a valuation of $21.00 per share. RP5063 may address an unmet need for patients with schizophrenia and other mental disorders, providing a safer and more effective treatment than what is now available.

SCIENTIFIC BRIEF

Reviva's lead candidate, RP5063, is pursuing multiple indications and leading with schizophrenia. Commonly mistaken with multiple personality disorder, schizophrenia is a complex, chronic and debilitating mental illness categorized into positive, negative, depression and cognitive symptoms. The labels of positive and negative do not denote whether the symptoms are beneficial or harmful to the patient, but rather to whether the symptoms add or subtract from normal. Positive symptoms are symptoms that present with the illness and include hallucinations and delusions. Negative symptoms describe normal behaviors that lessen or become subdued with onset of the illness such as inability to show emotions, apathy, difficulty speaking and withdrawing from social situations and relationships. Cognitive symptoms include impairments in attention, working memory or executive function. Regardless of the symptom category, schizophrenia is a complex pathology of the brain involving a multitude of brain regions, neural pathways, neurochemistry and receptor/cell biology. Schizophrenia appears to involve genetic factors and hereditary risk as well. Pathophysiology of schizophrenia remains to be fully understood. The theories of pathophysiology generally revolve around neurotransmitters, mainly dopamine and serotonin, and four neural pathways in the brain, mesocortical, nigrostriatal, mesolimbic and tuberoinfundibular.[1]

Prevalence and Incidence

Estimates of global prevalence and incidence of schizophrenia vary. In a systematic review, Saha *et al.*[2] found median point prevalence 4.6 per 1,000 or 0.46% but it ranged across its 23 studies from 1.9 to 10.0 per 1,000. Furthermore, median period and lifetime prevalence varied at 3.3 and 4.0 per 1,000, respectively. Based on current US and global population estimates,[3] the number of individuals with schizophrenia could be 1.5 million in the US, and 35.6 million globally. In 2019, the World Health Organization estimated that schizophrenia affects 20 million people worldwide.[4] In materials cited by the National Institute of Mental Health, domestic prevalence of schizophrenia and related psychotic disorders is from 0.25% to 0.64%[5,6,7] and internationally from 0.33% to 0.75%.[8,9]

Standard of Care

The goals of schizophrenia treatment are symptom reduction, relapse prevention and helping the patient to adapt so they can function as normally as possible. Both pharmacological and nonpharmacological approaches are used. Psychotherapy is implemented in schizophrenia management and includes individual, group and cognitive behavioral variants, but antipsychotic drugs form the predominant basis for schizophrenia management.

Antipsychotics Background

In 1951, the surprisingly effective trial of chlorpromazine in psychiatric patients was a breakthrough and catalyst for psychotropic drugs.[10] In addition, recognition of the chemical mediation at the site of the synapse along with advances and evolution in laboratory chemistry allowed the demonstration of chlorpromazine blockade of dopamine receptors. The surprising efficacy and laboratory results identified dopamine as the primary therapeutic target. Chlorpromazine's development sparked the development of numerous psychotropic drugs, blockers of dopamine receptors in accordance with the dopaminergic hypothesis. These so-called "typical"[11] antipsychotics shared dopamine D_2 antagonism, but had considerable side effects including extrapyramidal side effects related to involuntary

[1] Patel, K. R., Cherian, J., Gohil, K., & Atkinson, D. (2014). Schizophrenia: overview and treatment options. *P & T : a peer-reviewed journal for formulary management*, *39*(9), 638–645.
[2] Saha, S., Chant, D., Welham, J., & McGrath, J. (2005). A systematic review of the prevalence of schizophrenia. *PLoS Med*, *2*(5), e141.
[3] https://www.census.gov/popclock/
[4] https://www.who.int/news-room/fact-sheets/detail/schizophrenia
[5] Kessler RC, Birnbaum H, Demler O, Falloon IR, Gagnon E, Guyer M, Howes MJ, Kendler KS, Shi L, Walters E, Wu EQ. The prevalence and correlates of nonaffective psychosis in the National Comorbidity Survey Replication (NCS-R). Biol Psychiatry. 2005 Oct 15;58(8):668-76.
[6] Wu EQ, Shi L, Birnbaum H, Hudson T, Kessler R. Annual prevalence of diagnosed schizophrenia in the USA: a claims data analysis approach. Psychol Med. 2006 Nov;36(11):1535-40. PMID: 16907994
[7] Desai, PR, Lawson, KA, Barner, JC, Rascati, KL. Estimating the direct and indirect costs for community-dwelling patients with schizophrenia. Journal of Pharmaceutical Health Services Research, 2013 Jul;4(4):187-194. doi/10.1111/jphs.12027/epdf
[8] Saha S, Chant D, Welham J, McGrath J. A systematic review of the prevalence of schizophrenia. PLoS Med. 2005 May;2(5):e141. PMID: 15916472
[9] Moreno-Küstner B, Martín C, Pastor L. Prevalence of psychotic disorders and its association with methodological issues. A systematic review and meta-analyses. PLoS One. 2018;13(4):e0195687. PMID: 29649252
[10] Ban T. A. (2007). Fifty years chlorpromazine: a historical perspective. *Neuropsychiatric disease and treatment*, *3*(4), 495–500.
[11] The term "typical" refers to the first generation of antipsychotics developed in the 1950s which are dopamine antagonists that have a high incidence of side effects relative to newer treatments. These have largely been replaced by "atypical" antipsychotics which have an improved extrapyramidal side effect profile.

movements as in Parkinson's disease.[12] Antagonism of D_2 receptors in one area of the brain helped to control symptoms but the same activity in other parts of the brain produced the unwanted side effects. The first generation, typical antipsychotics not only modulated dopamine but also impacted other receptor classes, explaining the diverse side effect profile. This non-specificity is a challenge that has prompted further inquiry into localizable targets.

The brain is made up of an intricate and highly complex network of neurons and their axonal pathways which coordinate various motor, behavioral, emotional, endocrine and cognitive functions, via an orchestrated organization of various areas with specific functions in the cortical and deep cortical gray matter. Each region of the brain contains neurons which are cells that have a specific function to propagate electrical signals. The neurons communicate with one another via neurotransmitters and receptors. A neuron can trigger an action potential in another neuron by releasing neurotransmitters at a point where the two neurons meet, known as a synapse.

Neurotransmitters are prolific molecules, the most common of which include adrenaline, noradrenaline, dopamine, serotonin, gamma-aminobutyric acid (GABA), acetylcholine, glutamate and endorphins. The neurotransmitters with their particular chemical structure have unique binding characteristics with receptors. Because the brain is complex and is mostly composed of neurons that communicate with neurotransmitters, pathology of the brain is likewise complex. However, drugs that modulate one or more neurotransmitter receptors can have varied effects in many or multiple neurological disorders, including bipolar disorder and major depressive disorder, indications Reviva is also pursuing with RP5063. Since these other disorders are also pathologies of the brain with neurotransmitter relevance, even psychosis in Alzheimer's and Parkinson's Disease are relevant targets.

With typical antipsychotics presenting a set of side effects almost as diverse as the underlying schizophrenia symptomatology, and the realization that the antipsychotics modulate not only dopamine but multiple receptor classes throughout the brain, atypical antipsychotics took another step to refine which and to what extent receptors were modulated. As the drugs' receptor binding properties relate to chemical structure, through modifying the structure one can tune the receptor modulation profile, and by extension, attempt to maximize efficacy while minimizing side effects. While D_2 dopamine was the focus of first generation antipsychotics, second generation antipsychotics supplied greater antagonism of 5-HT_{2A} versus D_2 dopaminergic receptors. Lower D_2 antagonism reduced extrapyramidal side effects. Third generation antipsychotics include aripiprazole, brexpiprazole and cariprazine which are differentiated by their partial agonism for dopamine and serotonin receptors. Aripiprazole is a D_2 partial agonist[13] and contrasts with earlier generations characterized by D_2 antagonism. In addition to D_2 and 5-HT_{2A}, there are many receptors that now must be considered when developing small molecule antipsychotics.

Developing antipsychotics now requires selectivity and control in which receptors are modulated and to what extent and in what areas while maintaining the ultimate goal of maximizing efficacy while minimizing side effects.

As an example, the introduction of clozapine marked the beginning of the second generation of antipsychotics, its binding profile provided evidence of the evolution of binding profile tuning. It binds to dopamine $D_{1\text{-}5}$ receptors with tenfold higher affinity to D_4 than D_2.[14] Its D_4 and 5-HT_{2A} antagonism as well as 5-HT_{1A} partial antagonism decreased negative symptoms. Histaminic effects caused sedation. Additionally, Clozapine's muscarinic modulation produced excessive salivation and weight gain as side effects, as its metabolite was an allosteric modulator of M1 and M4-muscarinic receptors. Thus, not only is the receptor binding profile of the drug important but its metabolites also require consideration.

Exhibit I – Receptor-Target Effect Relationship[15]

Receptor	Symptoms
D_2	Positive
D_4	Depression/Cognition
5-HT_{1A}	Negative
5-HT_{2A}	Negative
5-HT_{2B}	Excitement/Agitation
5-HT_6	Depression/Cognition
5-HT_7	Depression/Cognition

[12] First generation antipsychotics had extrapyramidal side effects resembling Parkinson's Disease, a disease characterized by lack of dopamine.
[13] Agonists activate receptors when bound, antagonists do not activate the receptor when bound and block other compounds from activating.
[14] Stępnicki P, Kondej M, Kaczor AA. Current Concepts and Treatments of Schizophrenia. Molecules. 2018 Aug 20;23(8):2087. doi: 10.3390/molecules23082087. PMID: 30127324; PMCID: PMC6222385.
[15] Compiled from Zacks analyst research

Antipsychotics can be extensively and uniquely metabolized in the body and the metabolites can help to explain the variation in efficacy and side effects. Quetiapine, one of the most metabolized antipsychotics, had less than 1% of the drug recoverable in its native state.[16] It is eliminated by the liver (cytochrome P450 metabolism) or excreted via filtration through kidneys. The potential effects of drug metabolites should be considered as well as possible drug interactions when used in combination with other therapeutic agents and appropriate dose arrangements must be considered in patients with impaired kidney or liver functions.

Adverse reactions of antipsychotics include extrapyramidal side effects due to blockage of D_2 receptors in the nigro-striatal pathway including dyskinesia, dystonia, akathisia, tremors, rigidity and, restlessness. At high doses typical antipsychotics may cause off-target antagonism in the mesocortical pathway resulting in negative symptoms and cognitive decline while causing agonistic effects on the tuberoinfundibular pathway and resulting in hyperprolactinemia which may be associated with sexual dysfunction and galactorrhea. Metabolic side effects such as weight gain, type 2 diabetes, hypertriglyceridemia, glucose dysregulation, dyslipidemia can lead to long term cardiovascular health risks. These risks are associated with the serotonin 5-HT_{2C}, adrenergic α 2, muscarinic M3 receptors. Antihistaminic activity can lead to sedation, drowsiness, vertigo, disturbed sleep, agitation, nightmares, dementia, loss of memory or depression. Adrenergic blockade may cause hypotension, while anticholinergic side effects result in blurred vision, constipation and dry mouth. Other side effects outside the central nervous system include various organ systems including cardiovascular, gastro-intestinal, genitourinary and hematopoietic systems. One of the most significant of the hematopoietic related side effects is agranulocytosis which can be fatal.

Both efficacy and side effects depend on the drug's structure and binding affinity to the various receptors. These side effects have been addressed to a certain extent in subsequent generations of antipsychotics mostly at the expense of efficacy.

Exhibit II – Receptor Pharmacology of Antipsychotics[17,18]

	RECEPTOR BINDING PROFILE																			
	D_1	D_2	D_3	D_4	H_1	H_2	H_3	5-HT_{1A}	5-HT_{1B}	5-HT_{2A}	5-HT_{2B}	5-HT_{2C}	5-HT_6	5-HT_7	M_1	M_3	α_1	α_{2A}	α_{2B}	α_{2C}	Transporter
Olanzapine	++	++	++	++	+++	++	+		+	+++	++	++	+++	++	++	++	++	+	++	++	
Zotepine	++	+++	+++	+	+++	+		+	++	+++		+++	+++	++	+	+	+++	+	+++	++	SERT, NET
Clozapine	+	+	+	++	+++	+		+	+	++	+++	++	++	++	+++	++	+++	++	++	++	
Chlorpromazine	++	+++	+++	+++	+++	+	+			+++	+++	++	+++	+++	++	++	+++	+	++	++	
Sertindole		+++	+++	+++	+			+	++	++++		+++		++			+++	+	+	+	
Iloperidone	+	+++	+++	++	+			++	++	+++		++	+	+			+++	+	+	++	
Risperidone	+	+++	+++	+++	+++	+		+	++	++++	++	++		+++			+++	++	++	+++	
(Nor)quetiapine	+	+	+		+++			++		++		+	+	++	+	+	++	+	+	++	NET
Paliperidone	+	+++	+++	+++	++	+		+	++	+++		++	+	+++			+++	+++	+++	+++	
Asenapine	+++	+++	++++	+++	+++	+++		+++	+++	++++	++++	++++	++++	++++			+++	+++	++++	+++	
Amisulpride		+++	+++	+++							++			++							
Aripiprazole		+++	+++	+	++			+++	+	++	++++	++	+	++			++	++	++	++	SERT
Brexpiprazole	+	++++	+++	+++	++			++++	++	++++	+++	+	++	+++			+++	++	++	++++	SERT, NET
Cariprazine		++++	++++		++			+++		++	++++	+		+			+				
Haloperidol	+	+++	+++	+++		+			+	+				+			++	+	+	+	
Lurasidone	+	+++						+++		+++		+		++++			++	++		+++	
Ziprasidone	+	+++	+++	++	++			+++	+++	++++	++	++++	++	+++			++	+	++	++	SERT, NET

[16] Sheeham JJ, Sliwa JK, Amatniek JC, Grinspan A, Canuso CM. Atypical Antipsychotic Metabolism and Excretion. 2010. *Current Drug Metabolism*

[17] Siafis, S., Tzachanis, D., Samara, M., & Papazisis, G. (2018). Antipsychotic Drugs: From Receptor-binding Profiles to Metabolic Side Effects. *Current neuropharmacology*, *16*(8), 1210–1223. https://doi.org/10.2174/1570159X15666170630163616

[18] Antagonism and inverse agonism are indicated by blue color whereas partial agonism by yellow. The number of crosses and color intensity are correlated to binding affinity.

As indicated in the preceding table, the antipsychotics approved for use differ in their binding affinity, their agonism and antagonism to various receptors and vary in their therapeutic benefit and side effects.

Most antipsychotics are administered orally or peripherally and doses and efficacy are measured in milligrams. An important consideration is the availability of the drug in the brain which relies on the crucial step of crossing the blood brain barrier (BBB). The BBB is an important cellular boundary that controls access to the central nervous system (CNS) to allow for proper neuronal function. The semipermeable barrier that lines blood vessels in the nervous system is comprised of endothelial cells that form tight junctions preventing many harmful blood components from passing into the cerebrospinal fluid. Small molecules including antipsychotics can, to varying degrees, pass through the barrier. They must pass through the BBB in order to enter the brain and act therapeutically. The degree to which the antipsychotic is able to cross into the brain will affect its efficacy and only the drug that is present in the brain can act. Only limited data exists regarding the permeability of antipsychotic compounds through the BBB; however, antipsychotics have, in the past, been compared to chlorpromazine in their dose-dependent efficacy, known as chlorpromazine equivalence (CPZE).

To assess the clinical efficacy of an antipsychotic, frameworks have been established such as the Positive and Negative Syndrome Scale (PANSS), the Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS). Together these are the most widely used schizophrenia symptom rating tools. The scales are used in the evaluation of schizophrenia patients and their response to therapy. PANSS is an interval scale consisting of 30 items with the patient scoring on a range from one to seven for each item. The items quantify the experience of the patient and include positive, negative and general symptoms.

Exhibit III – PANSS Criteria[19]

Positive	**General**
Delusions	Somatic concern
Conceptual disorganization	Anxiety
Hallucinatory behavior	Guilt feelings
Excitement	Tension
Grandiosity	Mannerisms and posturing
Suspiciousness/persecution	Depression
Hostility	Motor retardation
Negative	Uncooperativeness
Blunted affect	Unusual thought content
Emotional withdrawal	Disorientation
Poor rapport	Poor attention
Passivity	Lack of judgment and insight
Apathetic social withdrawal	Disturbance of volition
Difficulty in abstract thinking	Poor impulse control
Lack of spontaneity and conversational flow	Preoccupation
Stereotyped thinking	Active social avoidance

Antipsychotics reduce both positive and negative symptoms and present a side effect profile which requires consideration. Because the small molecule treatments are administered orally, they can have unwanted off-target effects. Second generation atypical antipsychotics have improved on the efficacy of the class and reduced the side effects relative to first generation offerings via more selective engineering of receptor binding and modulation. Antipsychotics still have room for improvement as a drug class because many patients discontinue therapy due to the side effects. A study by Liu-Seifert, Adams and Kinon in 2005 found that 53% of patients halted atypical antipsychotic treatment at an early stage with 36% citing poor response and worsening symptoms.[20] Schizophrenia research and understanding of shortcomings continues to advance with currently available treatments guiding toward refined receptor pharmacological profiles. Reviva's RP5063 aims to improve the efficacy and side effect profile entirely with its finely tuned receptor modulation profile.

[19] Compiled from Zacks analyst research

[20] Liu-Seifert, H., Adams, D.H. & Kinon, B.J. Discontinuation of treatment of schizophrenic patients is driven by poor symptom response: a pooled post-hoc analysis of four atypical antipsychotic drugs.*BMC Med* **3,** 21 (2005). https://doi.org/10.1186/1741-7015-3-21

INDICATIONS, PIPELINE & CANDIDATES

Indications

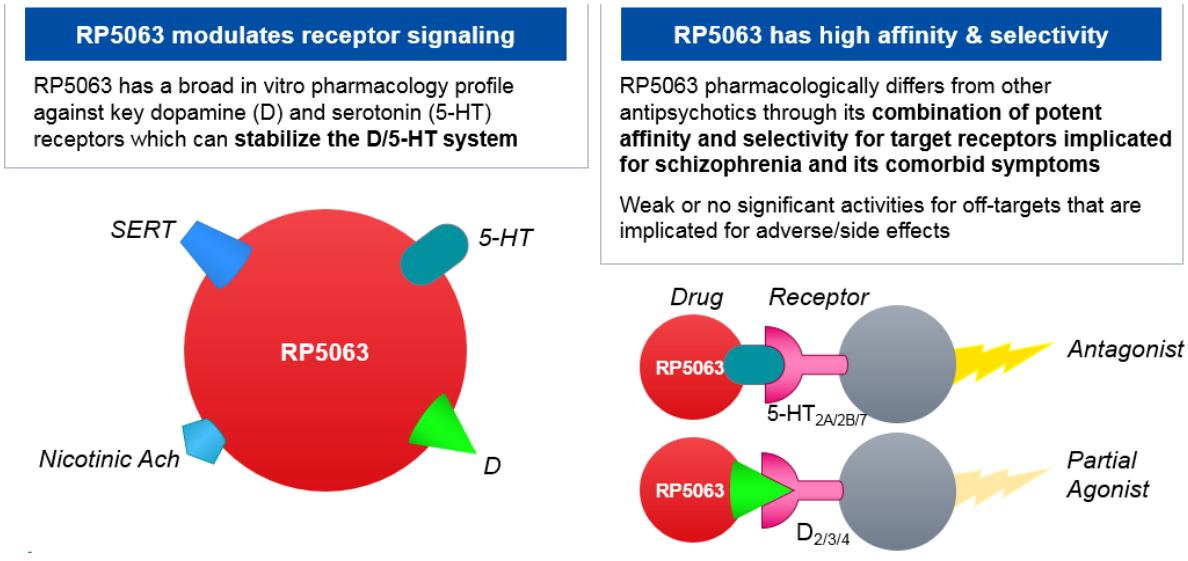
RP5063 was engineered based on the latest understanding in receptor efficacy and side effect relationships guided by the shortcomings and data generated by preceding therapies. RP5063 possesses a high binding affinity for the $D_{2/3/4}$ and 5-$HT_{1A/2A/2B/7}$ receptors, moderate affinity for 5-HT_6 and nicotinic acetylcholine ($\alpha_4\beta_2$) receptors and the serotonin transporter, a partial agonist of $D_{2/3/4}$ and 5-$HT_{1A/2A}$ receptors and antagonist of 5-$HT_{2B/6/7}$ receptors. RP5063 have either very weak activity or no activity for off target 5-HT_{2C}, adrenergic $\alpha_{1,2}$ or muscarinic receptors.

Exhibit IV – RP5063 Receptor Binding Affinities[21]

Receptor	Functional Activity	RP5063 Binding Affinity (nM)
D_{2L}	Partial agonist	0.45
D_{2S}	Partial agonist	0.62
D_3	Partial agonist	3.7
D_4	Partial agonist	6
5-HT_{1A}	Partial agonist	1.5
5-HT_{2A}	Partial agonist	2.5
5-HT_{2B}	Antagonist	0.19
5-HT_7	Antagonist	2.7
5-HT_6	Antagonist	51
5-HT_3	Not Determined	78
Serotonin transporter (SERT)	N/A	107
D_1	Not Determined	100
Nicotine-nAChRα4β2	Agonist	36.3

RP5063 development was guided by not only which targets were critical to efficacy, but also the binding strength and activity among receptors. Analysis of prior therapies found that successful second generation antipsychotics presented receptor activity ratio between 5-HT_{2A} and D_2 of less than 10. Furthermore, atypical antipsychotic Calyp-ta, which was seen as relatively ineffective, presented a 5-HT_{2A}:D_2 binding ratio of about 64. RP5063 has a 5-HT_{2A}:D_2 ratio of just over 6x, which is anticipated to provide balanced efficacy for both positive and negative symp-toms that is in line with other blockbuster products.

Exhibit V – Multimodal Modulator of Serotonin and Dopamine Receptors[22]



[21] Cantillon M, *et al.* Meltzer H. Dopamine Serotonin Stabilizer RP5063: A Randomized, Double-blind, Placebo-controlled Multicenter Trial of Safety and Efficacy in Exacerbation of Schiz-ophrenia or Schizoaffective Disorder. Schizophrenia Research 2017, 189: 126-133.
[22] Source: January 2021 Reviva Pharmaceuticals Corporate Presentation

Preclinical and Clinical Work

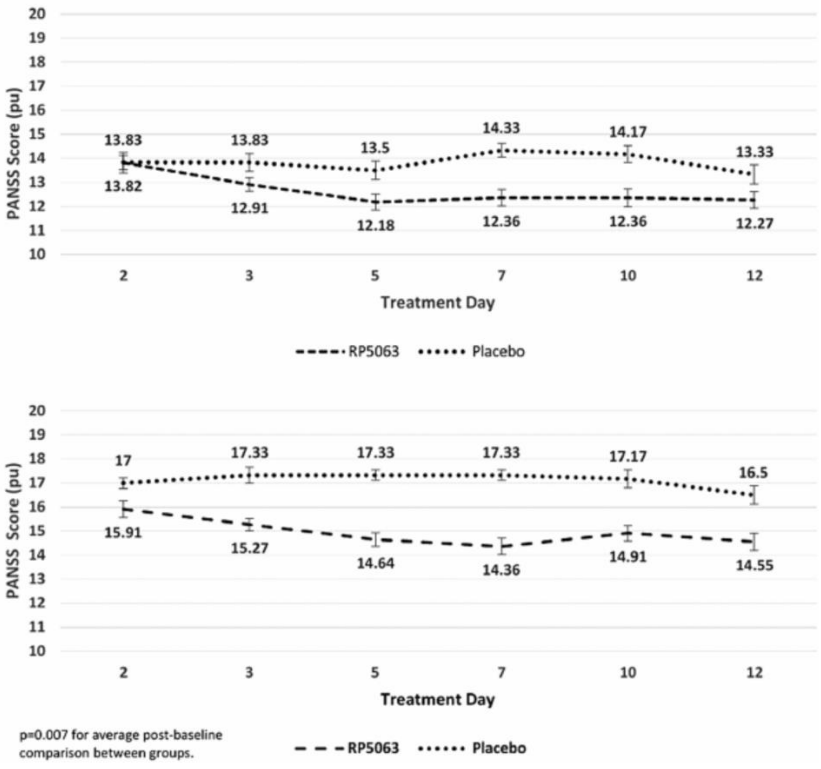
Work to vet RP5063 began in a murine model where the compound was shown to efflux dopamine and glutamate in the prefrontal cortex, a cue that suggested improved cognition and memory enhancement when translated to clinical studies in humans. Further rodent work showed reduced NMDA induced stereotypy, reversed apomorphine induced prepulse inhibition (PPI), reduced phencyclidine (PCP) induced locomotor activity and attenuated apomorphine induced climbing, the results suggesting efficacy in reducing positive motor symptoms. Rodent models exhibited restored cognitive function, thought to be a function of RP5063's balanced multi-receptor modulation.[23] Finally, BBB penetration of RP5063 was quantified with a brain:plasma ratio of 3.4 compared to aripiprazole's ratio of 1.5. This result demonstrates higher BBB penetration thereby allowing more compound to enter the brain and act therapeutically with less peripheral, off-target modulation.

In addition to preclinical *in vivo* studies, RP5063 has completed Phase Ia (SAD), Phase Ib (MAD) and Phase II (REFRESH) studies. The candidate is in preparation for Phase III studies anticipated to begin in mid-2021.

The Phase Ia in healthy subjects confirmed the safety profile of the drug while Phase Ib was conducted in stable schizophrenia patients. Acute schizophrenia patients are actively experiencing symptoms while stable patients have less severe, even absent symptoms.

The intent of the Phase Ia[24] study was to assess the pharmacokinetics and safety of RP5063. The drug was administered to test subjects orally at doses between 10 and 100 mg/day. Healthy subjects (n=28) were analyzed in both fasted and fed states with a single ascending dose. RP5063 behaved in typical fashion, with good absorption and reasonable T_{max}[25] and half-life of 42 hours. No significant effect from food was observed allowing the flexibility of RP5063 administered with or without food. There were 32 treatment-emergent adverse events (TEAE) observed with orthostatic hypotension (n=6), nausea (n=5) and dizziness (n=4) the most common. One serious adverse event was observed; however, the patient was later found to have a history of seizures.

Exhibit VI – RP5063 vs Placebo, PANSS vs Days[26]



[23] Rajagopal L, Kwon S, Huang M, Michael E, Bhat L, Cantillon M, Meltzer H. RP5063, an atypical antipsychotic drug with a unique pharmacologic profile, improves declarative memory and psychosis in mouse models of schizophrenia. 2017. Behavioral Brain Research

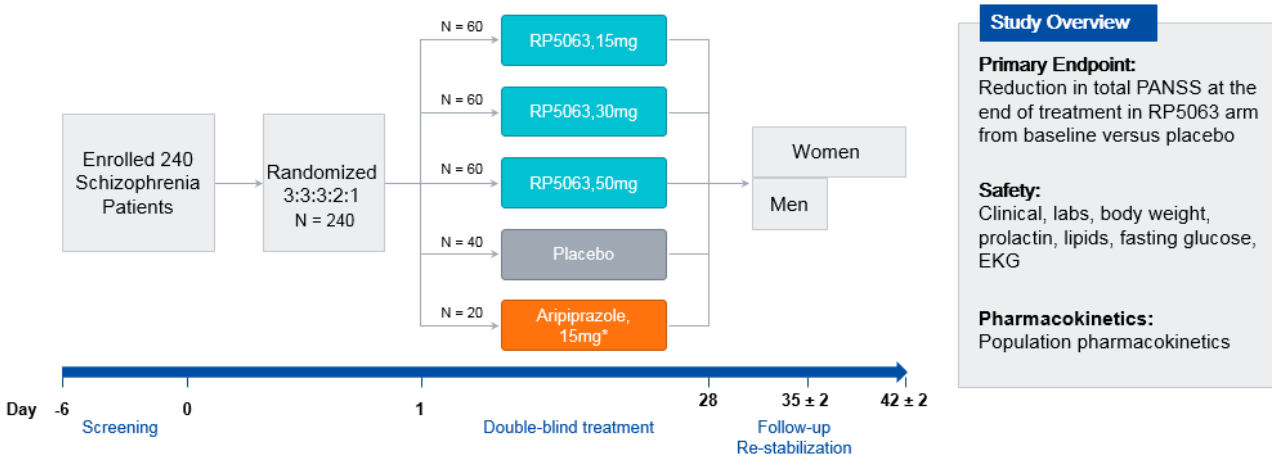
[24] Cantillon, M., Ings, R. and Bhat, L. (2018), Initial Clinical Experience of RP5063 Following Single Doses in Normal Healthy Volunteers and Multiple Doses in Patients with Stable Schizophrenia. Clinical And Translational Science, 11: 387-396. https://doi.org/10.1111/cts.12545

[25] Time taken to reach maximum concentration

[26] Cantillon, M., Ings, R. and Bhat, L. (2018), Initial Clinical Experience of RP5063 Following Single Doses in Normal Healthy Volunteers and Multiple Doses in Patients with Stable Schizophrenia. Clinical And Translational Science, 11: 387-396. https://doi.org/10.1111/cts.12545

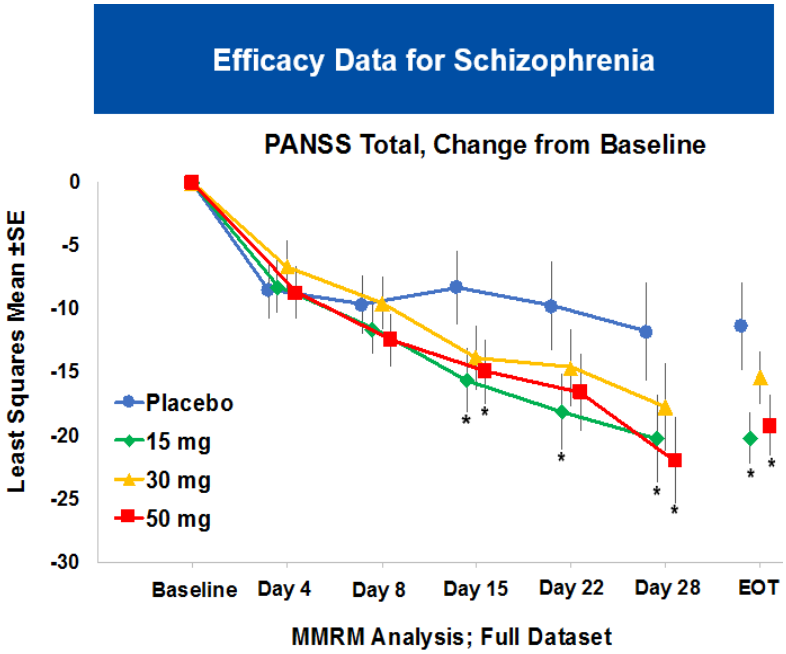
In Phase Ib,[27] stable schizophrenia subjects (n=32) were assessed in multiple ascending doses over a 10-day period. RP5063 was administered once daily and pharmacokinetics were observed to be linear and behaved predictably across all doses at all points in the measured period. Steady state was reached in 5 days (120 hours). Most importantly, RP5063 was well tolerated and no dose-limiting safety signals were observed. 75 TEAEs were reported with akathisia (n=20) and somnolence (n=14) the most frequent. Preliminary results from Phase Ib showed statistically significant improvement over placebo in patients with baseline PANSS of greater than 50 in positive subscale scores. Trail Making Test[28] results, a measure of cognition, were directionally favorable. The results in the preliminary trials were a foundation for Phase II.

Exhibit VII – REFRESH Phase II Structure[29]



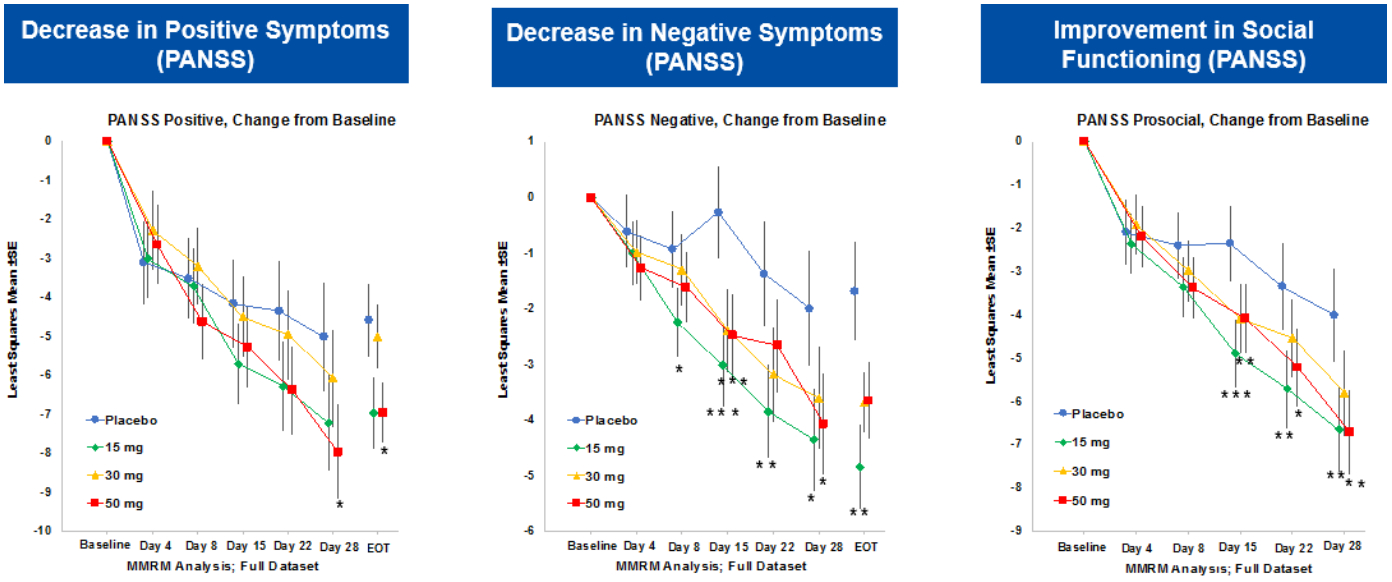
Phase II (REFRESH) was a randomized, double blind, placebo controlled, multi-center trial intended to assess safety and efficacy of RP-5063 in acute exacerbation of schizophrenia or schizoaffective disorder.[31] 22 clinical sites located in the Philippines, India, Malaysia, Moldova and the United States participated in the trial. The primary endpoint for the study was reduction in total PANSS at end of treatment from baseline vs placebo. Secondary endpoints included change from baseline to day 4, 8 15, 22 and 28 on PANSS total, positive and negative subscales, 20% improvement in PANSS total and one-point improvement on the clinical global impressions scale severity (CGI-S).[32] 234 subjects were enrolled. Patients were randomized into five arms including 15 mg (n=60), 30 mg (n=60) and 50 mg (n=60) doses as well as placebo (n=40) and aripiprazole 15 mg (n=20). Approximately one week of screening was followed by 28 days of dosing and follow up afterward of one and two weeks for men and women, respectively. Pharmacokinetic analysis was also performed. 186 of 234 enrolled subjects completed the study.

Exhibit VIII – Phase II Change from baseline PANSS Total[30]



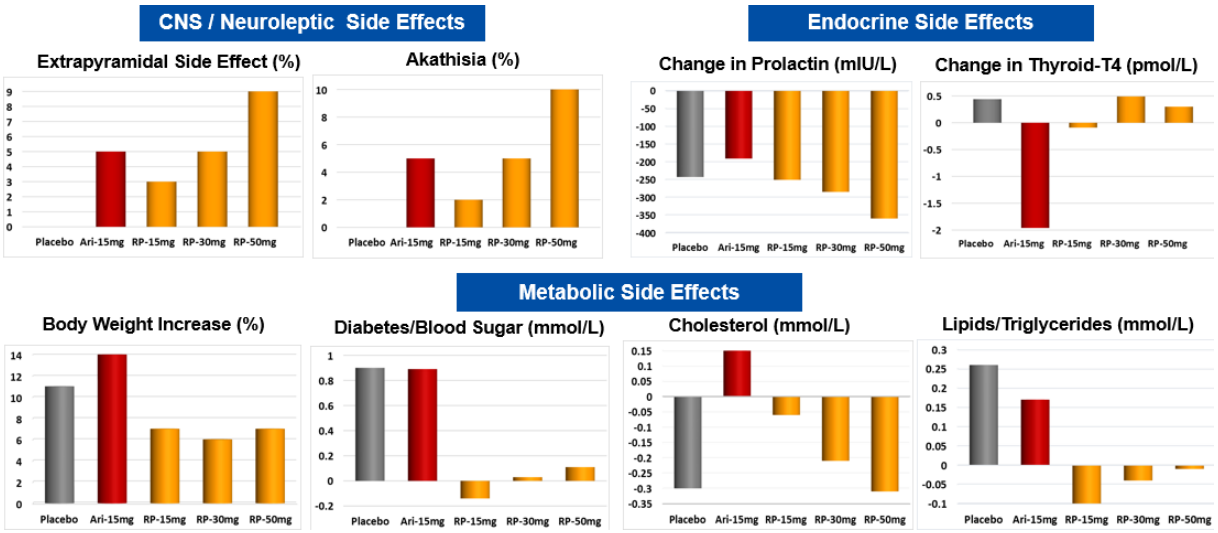
[27] Cantillon, M., Ings, R. and Bhat, L. (2018), Initial Clinical Experience of RP5063 Following Single Doses in Normal Healthy Volunteers and Multiple Doses in Patients with Stable Schizophrenia. Clinical And Translational Science, 11: 387-396. https://doi.org/10.1111/cts.12545
[28] The Trail Making Test is used to measure frontal lobe function and is a neuropsychological test of visual attention and task switching.
[29] Cantillon M, Prakash A, Alexander A, Ings R, Sweitzer D, Bhat L. Dopamine serotonin stabilizer RP5063: A randomized, double-blind, placebo-controlled multicenter trial of safety and efficacy in exacerbation of schizophrenia or schizoaffective disorder. Schizophr Res. 2017 Nov;189:126-133. doi: 10.1016/j.schres.2017.01.043. Epub 2017 Feb 16. PMID: 28215471.
[30] Cantillon M, Prakash A, Alexander A, Ings R, Sweitzer D, Bhat L. Dopamine serotonin stabilizer RP5063: A randomized, double-blind, placebo-controlled multicenter trial of safety and efficacy in exacerbation of schizophrenia or schizoaffective disorder. Schizophr Res. 2017 Nov;189:126-133. doi: 10.1016/j.schres.2017.01.043. Epub 2017 Feb 16. PMID: 28215471.
[31] Schizoaffective disorder is a combination of schizophrenia symptoms and mood disorder symptoms
[32] The CGI-S is a measure of clinician's view of patient's global functioning

Exhibit IX – Phase II, Positive, Negative and Social Functioning PANSS[33]



PANSS total score demonstrated a statistically significant decrease in 15 mg and 50 mg RP5063 arms vs placebo ($p = 0.0212$ and $p = 0.0167$) at the end of treatment at day 28 and with statistical significance starting as early as day 15. Although numerically superior, the 30 mg arm did not reach statistical significance ($p = 0.27$) due to non-treatment related discontinuation. Differences between the RP5063 treatment arms were not statistically significant. When broken into subscores, RP5063 showed greater improvement in negative and prosocial symptoms compared to positive symptoms. Approved therapies are relatively ineffective at reducing negative symptoms, which shifts the balance towards RP5063 if it maintains its profile in registrational trials. At the end of the dosing period, 41%, 26% and 39% of patients in the treatment arms experienced 30% improvement or greater from baseline in total PANSS. Subjects improved by two points or greater on CGI-S at day 28 at twice the frequency versus placebo and 73%, 58% and 72% improved by one point or greater. CGI-S changes from baseline were statistically superior to placebo for 15 mg and 50 mg arms with 30 mg numerically superior. Note, the study was not designed as a head-to-head study against aripiprazole and lacked the power to draw conclusions between the two in terms of efficacy and timing based on data from this study alone. TEAEs were reported for 129 subjects. Most frequently reported TEAEs were extrapyramidal symptoms, akathisia and increased levels of alanine aminotransferase (ALT) and aspartate transaminase (AST). Elevated ALT and AST levels were observed in both placebo and active group and were attributable to preexisting conditions.

Exhibit X – Neuroleptic, Endocrine and Metabolic Side Effects vs. Placebo[34]



[33] Cantillon M, Prakash A, Alexander A, Ings R, Sweitzer D, Bhat L. Dopamine serotonin stabilizer RP5063: A randomized, double-blind, placebo-controlled multicenter trial of safety and efficacy in exacerbation of schizophrenia or schizoaffective disorder. Schizophr Res. 2017 Nov;189:126-133. doi: 10.1016/j.schres.2017.01.043. Epub 2017 Feb 16. PMID: 28215471.

[34] Reviva Pharmaceuticals January 2021 Corporate Presentation

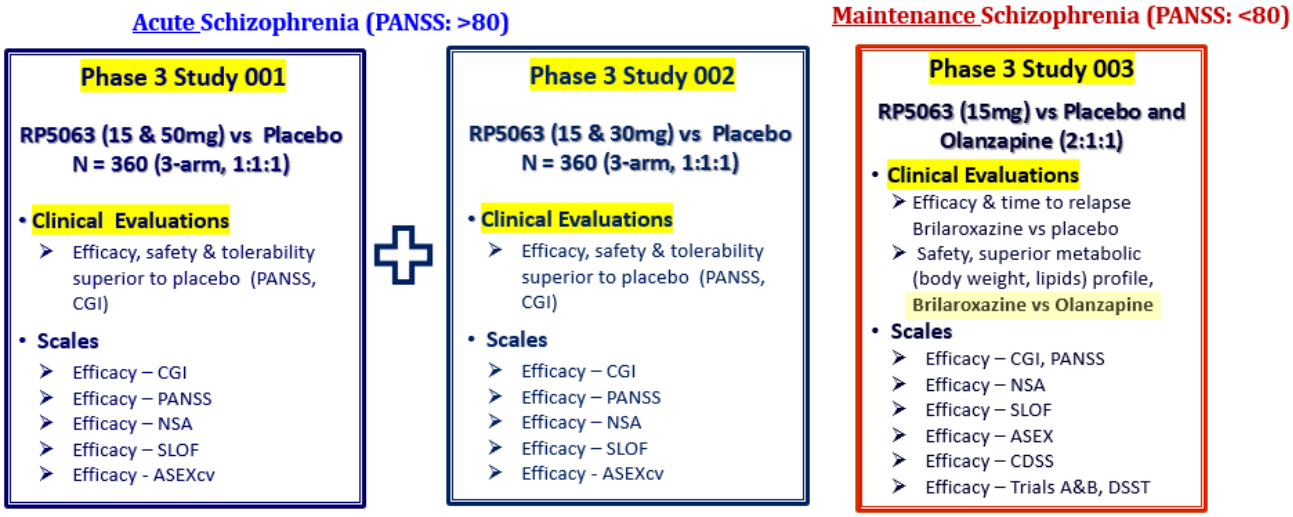
Despite reflecting the results from a relatively short term assessment, there was a notable lack of clinically relevant changes from baseline in body mass or body mass index, a side effect typical of second generation antipsychotics. Likewise there were no clinically meaningful trends in laboratory parameters (glucose, cholesterol, triglycerides), ECG or vital signs, no metabolic, endocrine or cardiac side effects. There was a small decrease in prolactin and no reports of sexual side effects. Antipsychotics as a class are plagued by side effects that can diminish patient adherence and RP5063 demonstrated a low intensity side effect profile as illustrated in the previous exhibit. The 15 mg and 50 mg arms in the Phase II RP5063 trial displayed robust compliance with low discontinuation of 14% and 12%, respectively, and no side-effect related discontinuation in 15 mg and 30 mg arms. Only one patient presenting extrapyramidal symptoms dropped out in the 50 mg arm. RP5063's favorable safety profile extended into long term toxicology studies, which are now completed. Summary of Phase II conclusions:

- Total PANSS reduction of 20.2 (15 mg), 15.4 (30 mg) and 19.2 (50 mg)[35]
- PANSS reduction achieved over 4 week (28-day) duration
- 14%, 25% & 12% discontinuation for the 15, 30 & 50 mg doses vs. 26% for placebo & 35% for aripiprazole
- No cardiometabolic, cardiovascular, prolactin or neurologic complications.
- Lack of systemic accumulation implies no need for dose titration
- Early onset of action; steady state drug levels achieved 120 hours after dosing

Phase III Schizophrenia Trial Design

Management has announced its intent to pursue initiation of Phase III trials for RP5063 after completing the public listing via the Tenzing special purpose acquisition company (SPAC) transaction. Phase III studies will be in acute and stable schizophrenia patients. Dosing is anticipated to be once-daily with the potential to develop once-monthly depot (implant) dose to mitigate compliance risk. Reviva has completed an end-of-Phase II meeting with the FDA, and the agency has guided for a "superior safety" label claim, with implications for individual patient safety and economic advantage for population coverage. The FDA has waived the cytochrome (CYP) 2D6 (liver enzyme) drug interaction study. Based on discussions with management, we anticipate two Phase III studies in 360 patients each for the acute schizophrenic population and one 400 patient Phase III in the maintenance population.

Exhibit XI – Phase III Trial Design[36]



Bipolar Disorder I & II, Major Depressive Disorder

In addition to schizophrenia, RP5063 is targeting Bipolar Disorder (BD) I and II, and Major Depressive Disorder (MDD). Phase I safety work conducted for schizophrenia is also relevant for other psychotic disorders and will allow Phase II work for BD and MDD to begin. RP5063 is broadly applicable in multiple indications because these diseases are often comorbid and exist on a continuum of dopamine and serotonin dysfunction, with schizophrenia on the dopamine end, MDD on the serotonin end and BD in between.

[35] Statistical significance was achieved at the 5% level for both the 15 and 50 mg arms.
[36] Reviva Pharmaceuticals January 2021 Corporate Presentation

In general, bipolar disorder (BD) is a life-long mental health condition characterized by extreme mood swings. It is treated typically with a combination of psychotherapy and medication. Classification of Bipolar I differs from Bipolar II in symptomatology. The current criteria for classification into Bipolar I is a patient with at least one manic episode that may be preceded or followed by hypomanic or major depressive episodes. BD II is a milder form of mood volatility where episodes of hypomania alternate with periods of severe depression.

Major Depressive Disorder (MDD), also referred to as clinical depression, is characterized by intense feelings of sadness for extended periods of time. It is a significant medical condition that can impact not only mood and behavior, but even physiological functions such as appetite and sleep. MDD is common with an estimated prevalence among US adults 18 or older of 17.3 million, or 7.1% of US adults.[37] MDD is defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) according to criteria related to the duration and intensity of various behavioral, mood and physiological changes. Typically, these changes and symptoms need to be relatively constant, intense and persist for at least two weeks. The exact cause of MDD is unknown. It is believed that genetics and environmental factors such as stress are risk factors for the condition. Environmental triggers can include alcohol and drug use, other medical conditions or medications and childhood abuse. Standard of care for MDD includes pharmacotherapy as well as psychotherapy. There are several classes of antidepressants including selective serotonin reuptake inhibitors (SSRI), serotonin-norepinephrine reuptake inhibitors (SNRI) and tricyclic antidepressants.

Pulmonary Arterial Hypertension and Idiopathic Pulmonary Fibrosis

Neurotransmitters have a ubiquitous role in body homeostasis leading Reviva to explore RP5063's efficacy in Pulmonary Arterial Hypertension (PAH) and Idiopathic Pulmonary Fibrosis (IPF). Both are orphan diseases[38] in preparation for Phase II trials. The FDA granted orphan status to RP5063 for PAH in 2016 and IPF in 2018.

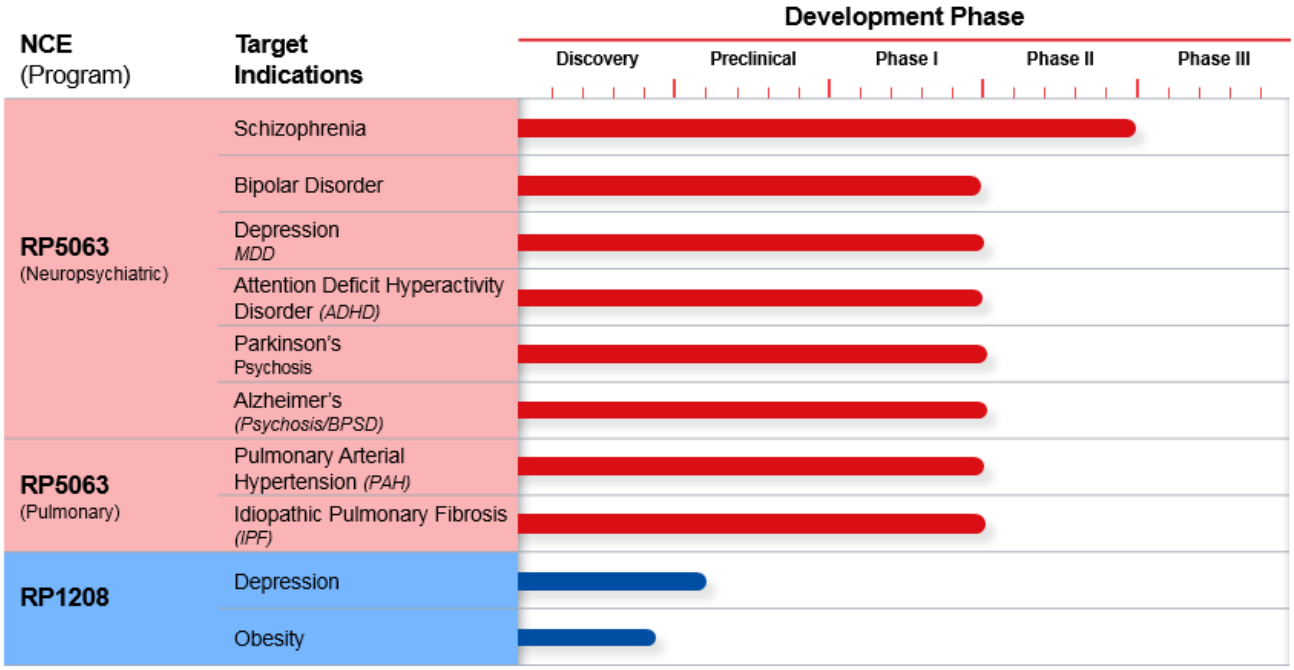
Because the route of administration, dosing frequency and compound are the same, the safety data generated in the Phase Ib and II human studies in schizophrenia are sufficient to support PAH and IPF trials. RP5063 was well tolerated, even at the maximum 100 mg dose, and has already completed long term regulatory toxicology studies. For the pulmonary applications (PAH & IPF), a once-daily inhaler is being considered.

Pathophysiology of PAH and IPF is characterized by lung tissue remodeling due to inflammation, proliferation of fibrosis, microthrombi and pulmonary hypertension. As it pertains to neurotransmitters, elevated plasma serotonin (5-HT) levels, increased expression of 5-$HT_{2A/2B/7}$ and increased inflammatory cytokines in the lungs of PAH and IPF patients have been observed. 5-HT receptors have been associated with fibrosis and their antagonism of 5-HT_{2B} has been shown, *in vitro* and *in vivo*, to attenuate myofibroblast differentiation.[39] These myofibroblasts are cells that are responsible for pulmonary fibrosis observed in PAH and IPF. 5-HT_{2A} activation has been implicated in vasoconstriction, blood clot formation and proliferation and 5-HT_7 activation is thought to lead to inflammation and fibrosis as well. As an antagonist of 5-$HT_{2A/2B/7}$, RP5063 has been evaluated for its ability to counteract vasoconstriction, thrombosis, inflammation and fibrosis that contribute to vascular remodeling.

RP5063 has demonstrated equivalent or even superior efficacy compared to first line treatments with a notable lack of cardiac side effects across multiple *in vivo* evaluations. Tissue analysis of a Sugen Hypoxia (SuHx)-induced rat model showed lack of pulmonary vascular fibrosis. RP5063 also mitigates inflammation reducing tumor necrosis factor (TNF) α, interleukin (IL)-β, IL-6 and chemokine leukotriene beta (LTB)-4 in the rat model of PAH. When alone and co-administered with standard of care nintedanib and pirfenidone, RP5063 reduced hydroxyproline, a proxy for collagen deposition and lung fibrosis. Histopathology data identified a statistical improvement in bleomycin-induced lung damage, a chemotherapeutic known to cause lung fibrosis that is used to simulate IPF. In these models, respiratory resistance, O_2 saturation and survival rate were shown to be statistically improved or directionally correct.

[37] National Institute of Mental Health. Major Depression. 2017 Data. https://www.nimh.nih.gov/health/statistics/major-depression.shtml
[38] Orphan indications are those diseases where the afflicted population is fewer than 200,000 in the US.
[39] Löfdahl A, *et al.*. 5-HT2B receptor antagonists attenuate myofibroblast differentiation and subsequent fibrotic responses in vitro and in vivo. Physiol Rep. 2016 Aug;4(15):e12873. doi: 10.14814/phy2.12873. PMID: 27482070; PMCID: PMC4985542.

Exhibit XII – Reviva Drug Pipeline[40]



[40] Source: January 2021 Reviva Pharmaceuticals Corporate Presentation

PEERS & COMPETITORS

Reviva's primary indication is in schizophrenia. As a result, companies and therapies targeting schizophrenia are considered peers and competitors of Reviva. There is no cure for schizophrenia, only treatment and symptom management. Current standard of care employs medications and psychosocial therapy. Electroconvulsive therapy (ECT) may also be considered.[41] Antipsychotics commonly modulate the neurotransmitter dopamine. Second generation antipsychotics address some of the side effects experienced in the first generation but have not demonstrated materially improved efficacy compared to first generation offerings. Aripiprazole, fluphenazine and haloperidol are also available as long-acting injectables.

The invention of chlorpromazine in 1951 was a breakthrough and catalyst for psychotropic drugs.[42] Recognition of the chemical mediation at the site of the synapse along with advances and evolution in laboratory chemistry allowed the demonstration that chlorpromazine blocked dopamine receptors. Chlorpromazine's development catalyzed the development of future psychotropic drugs. Chlorpromazine, fluphenazine, haloperidol and perphenazine are considered first generation, also called typical antipsychotics. While the exact therapeutic mechanism of first generation antipsychotics is not completely understood, it is primarily driven by antagonism of the D_2 dopamine receptor, a trait that all first generation antipsychotics share. The compounds can modulate other receptors to varying degrees. Chlorpromazine and fluphenazine are phenothiazine class first generation antipsychotics.

Antipsychotics can be categorized into those that target primarily dopamine receptors (first generation or typical antipsychotics), and those that target selective dopamine and serotonin receptors (second generation or atypical antipsychotics). In the last two decades, allosteric modulator of dopamine receptor antipsychotic drug candidates targeting downstream receptors such as glutamate, GABA, nicotinic and muscarinic receptors have been developed but none have shown clinically significant efficacy for schizophrenia in pivotal trials. For example, Haldol was a first-generation antipsychotic, an antagonist of D_2 and was effective at reducing positive symptoms. Second generation antipsychotics such as Risperdal, Zyprexa and Seroquel are D_2 and 5-HT_{2A} antagonists, primarily effective against positive symptoms but with limited efficacy against negative symptoms. The primary benefit of second generation antipsychotics over first generation offerings stemmed from an improved side effect profile. Abilify, a third-generation antipsychotic, is a partial agonist of dopamine and serotonin and antagonist activity at 5-HT_{2A} and provided improved efficacy in both negative and positive symptoms.

Atypical antipsychotics, also considered as second generation antipsychotics, are reported to be more effective than their first generation counterparts in addressing cognitive dysfunction and negative symptoms.[43] Unlike first generation antipsychotics whose therapeutic effect is largely explained by D_2 dopamine antagonism, second generation antipsychotics are more complex, interacting with multiple receptors, though they are thought to share low affinity for D_2 dopamine receptors and have relatively high affinities for 5-HT_{2A} serotonin receptors. Aripiprazole is an exception, which is reported to be a high-affinity D_2 dopamine receptor partial agonist.[44] RP5063 interacts with a multitude of dopamine and 5-HT target receptors implicated in schizophrenia. Many of the available therapies also modulate multiple receptors with varying degrees of selectivity whereas RP5063 appears to have balanced selectivity and functional activity for target receptors for treating schizophrenia and schizoaffective disorders. While the pathophysiology of schizophrenia remains to be fully understood, it appears that symptom relief best comes from the proper mix of neuromodulation.

Excluding several of the most recent second generation entries, most antipsychotics have matured past patent protection and are now offered as generics. If approved, RP5063 will compete with all existing therapies on the market, generic and branded. Ranking antipsychotics in terms of efficacy and side effects is difficult. The mechanism of action for these drugs is multifaceted making it difficult to predict efficacy. Recognizing this difficulty, the physician guidance provided by the American Psychiatric Association (APA) does not directly compare antipsychotics due to the limited and inconsistent head-to-head clinical trials and emphasizes the individuality in patient response. Clozapine has often been considered the most effective antipsychotic. However, it is also typically reserved only for treatment resistant schizophrenia as its side effect profile can be fatal.[45] Thus, the clinical need is not for increasingly effective antipsychotics, but developing those that minimize side effects while also addressing negative symp-

[41] https://www.mayoclinic.org/diseases-conditions/schizophrenia/diagnosis-treatment/drc-20354449
[42] Ban T. A. (2007). Fifty years chlorpromazine: a historical perspective. *Neuropsychiatric disease and treatment*, *3*(4), 495–500.
[43] Kusumi, I., Boku, S. & Takahashi, Y. (2015), Atypical antipsychotics. Psychiatry Clin Neurosci, 69: 243-258. https://doi.org/10.1111/pcn.12242
[44] Agonists bind and activate the receptor whereas antagonists
[45] De Fazio, P., Gaetano, R., Caroleo, M., Cerminara, G., Maida, F., Bruno, A., Muscatello, M. R., Moreno, M. J., Russo, E., & Segura-García, C. (2015). Rare and very rare adverse effects of clozapine. *Neuropsychiatric disease and treatment*, *11*, 1995–2003. https://doi.org/10.2147/NDT.S83989

toms and cognitive dysfunction. The APA withholds recommendation favoring either first or second generation antipsychotics and makes no definitive prescription guidance in the treatment of schizophrenia, but instead provides a patient-centric, personalized and holistic framework.

Exhibit XIII – Common Antipsychotics[46]

Generic	Brand	Generation
chlorpromazine	Thorazine	First (typical)
fluphenazine	Prolixin	First (typical)
haloperidol	Haldol	First (typical)
perphenazine	Trilafon	First (typical)
aripiprazole	Abilify	Second (atypical)
asenapine	Saphris	Second (atypical)
brexpiprazole	Rexulti	Second (atypical)
cariprazine	Vraylar	Second (atypical)
clozapine	Clozaril	Second (atypical)
iloperidone	Fanapt	Second (atypical)
lurasidone	Latuda	Second (atypical)
olanzapine	Zyprexa	Second (atypical)
paliperidone	Invega	Second (atypical)
quetiapine	Seroquel	Second (atypical)
risperidone	Risperdal	Second (atypical)
ziprasidone	Geodon	Second (atypical)
lumateperone	Caplyta	Second (atypical)

Comparative Efficacy: Schizophrenia

Apart from the broad guidance offered by the APA, prescription trends emerge. Sources that allow insight into prescription patterns include sales data, forecasts and studies directly evaluating prescriptions. Still, the trends and insights are inconclusive. First, the adoption of new antipsychotics, as evidenced by the arc in sales over patent protected life, is likely an indicator of the still unmet need for the schizophrenic patient population. Based on data from EvaluatePharma, the antipsychotic with the highest cumulative sales over the past decade was Abilify, followed by Invega Sustenna and Zyprexa. However, in terms of peak annual sales, Abilify and Zyprexa approached ~$5 billion in peak annual global sales while newer drugs Invega Sustenna and Latuda appear to be approaching ~$3 billion and ~$2 billion, respectively. Invega Sustenna and Latuda do not appear to be as commercially successful as the most recent predecessors. This may be an indication of the lasting efficacy of formerly branded antipsychotics that patients continue to use. It may be that the early antipsychotics are more effective or have struck a better balance in terms of efficacy and side effects than these newer options.

Exhibit XIV – Antipsychotic Global Sales[47]

			Annual Sales (Indication) - WW										
			Sales										
Rank	Product	Company	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
1	Invega Sustenna	Johnson & Johnson	152	378	796	1,248	1,588	1,791	1,978	2,210	2,440	2,696	2,836
2	Latuda	Sumitomo Dainippon Pharma	-	87	195	421	754	1,004	1,257	1,612	1,664	1,743	1,837
3	Abilify MAINTENA	Otsuka Holdings	-	-	-	43	135	334	527	632	797	934	1,086
4	Invega Trinza	Johnson & Johnson	-	-	-	-	-	39	236	359	488	634	790
5	Risperdal Consta	Johnson & Johnson	1,500	1,583	1,425	1,318	1,190	970	893	805	737	688	619
6	Rexulti	Otsuka Holdings	-	-	-	-	-	15	113	178	281	373	465
7	Vraylar	AbbVie	-	-	-	-	-	-	-	-	-	-	398
8	Zyprexa	Eli Lilly	5,026	4,622	1,701	1,195	1,037	940	725	581	471	419	398
9	Abilify	Otsuka Holdings	4,593	5,216	5,305	5,749	4,762	2,872	879	600	463	344	299
10	Aristada	Alkermes	-	-	-	-	-	5	47	94	148	189	229
Total			19414	20740	14602	13623	12723	11019	9267	9078	9446	10020	10255

[46] Compiled from Zacks analyst research
[47] Evaluate Pharma, January 2021, Evaluate, Ltd. Indication > Psychiatry > Psychotic disorders | Schizophrenia, Worldwide

Exhibit XV – Top Antipsychotics by 2026 Forecasted Worldwide Sales[48]

Brand Name	Generic Name	Company	Mechanism of Action	2026 Sales
Invega	Paliperidone palmitate	Johnson & Johnson	5-HT2 antagonist, D2 antagonist	$4,856 m
Vraylar	Cariprazine hydrochloride	AbbVie	5-HT2A antagonist, 5-HT1A partial agonist, D2 agonist, D3 agonist	$1,307 m
Abilify	Aripiprazole	Otsuka Holdings	5-HT2 antagonist, 5-HT1A partial agonist, D2 partial agonist	$1,080 m
Rexulti	Brexpiprazole	Otsuka Holdings	5-HT2 antagonist, 5-HT1A partial agonist, D2 partial agonist	$852 m
KarXT	Trospium chloride; xanomeline	Karuna Therapeutics	Selectively activates muscarinic acetylcholine receptors in the brain to improve the therapeutic potential of xanomeline	$746 m
Caplyta	Lumateperone tosylate	Intra-Cellular Therapies	Unknown, but efficacy could be mediated through a combination of antagonist activity at central serotonin 5-HT_{2A} receptors and postsynaptic antagonist activity at central dopamine D_2 receptors.	$705 m

RP5063 is structurally most similar to Abilify but makes important, key chemical modifications. These modifications tune not only receptor pharmacology, but also provide the key innovation of ensuring metabolites are innocuous and do not cause side effects. RP5063 also has early onset of action and better penetration of the blood-brain barrier as compared with Abilify. This profile supports higher efficacy at lower oral doses and with potentially fewer peripheral side effects.

In preliminary evaluation, RP5063 has demonstrated not only superior efficacy, but does so in a shorter time frame. This faster efficacy is expected to support patient treatment adherence and improve discontinuation rates.

Exhibit XVI – Decrease in Total PANSS[49]

Antipsychotic Drug	Total PANSS	Weeks	Source
RP5063	-20	4	Bhat L., et al. J Neurology and Neuromedicine. 2018
Olanzapine (Zyprexa)	≤-17.7	6	Tollefson G., et al. Am J Psychiatry. 1997
Risperidone (Risperdal)	-15.7	4	Potkin S., et al. Arch Gen Psychiatry. 2003
Brexpiprazole (Rexulti)	≤-16	6	Correll C., et al. Schizophr Res. 2016
Aripiprazole (Abilify)	-14.5	4	Potkin S., et al. Arch Gen Psychiatry. 2003
Cariprazine (Vraylar)	≤-14	6	Durgam S., et al. Int Clin Psychopharmacol. 2016
Lumateperone (Caplyta)	-13.2	4	Lieberman J., et al. Biological Psychiatry. 2015

With further refined receptor pharmacology, RP5063 aims to have greater efficacy in the historically challenging negative symptoms and alleviate cognition and depression symptoms.

[48] Evaluate Pharma, Indication > Psychiatry > Psychotic disorders | Schizophrenia – Worldwide
[49] Compiled from Zacks analyst research

Exhibit XVII – Peers and Competitors[50]

Ticker	Company	Price	MktCap (MM)	EV (MM)	Therapeutic Area
ABBV	AbbVie	$109.02	$192,472	$266,804	Saphris, Vraylar
AXSM	Axsome Tx	$77.94	$2,911	$2,756	MDD, AD agitation in Ph3
AZN	AstraZeneca	$50.56	$132,699	$142,487	Seroquel
BHVN	Biohaven Pharma	$86.31	$5,173	$4,891	Obsessive Disorder
BMY	Bristol-Myers	$64.97	$147,007	$167,216	Abilify
CNCE	Concert Pharma	$12.34	$378	$251	CTP-692 Ph2 for Schizophrenia
HLTRF	HLS Tx	$13.05	$419	$514	Clozaril
HLUYY	H. Lundbeck A/S	$34.86	$6,942	$7,780	Abilify, Rexulti
ITCI	Intra-Cellular Ther	$32.02	$2,567	$1,843	Schizophrenia
JNJ	J&J / Janssen	$159.37	$419,548	$421,447	Invega, Risperdal
KRTX	Karuna Tx	$107.59	$2,884	$2,539	Schizophrenia, KarXT
LLY	Eli Lilly	$185.94	$177,867	$190,571	Zyprexa
MRK	Merck	$85.00	$215,053	$234,018	Saphris
NERV	Minerva Neuro	$2.56	$109	$77	MIN-101 Ph3 for Schizophrenia
NVS	Novartis	$94.39	$216,030	$231,657	Clozaril
OTSKY	Otsuka Pharma	$21.13	$23,054	$21,500	Abilify, Rexulti
PFE	Pfizer	$37.77	$209,941	$237,814	Geodon
SAGE	Sage Tx	$91.03	$4,738	$4,069	Depression
SMFG	Sumitomo	$6.75	$46,345	$68,503	Latuda
VNDA	Vanda Pharma	$13.96	$763	$415	Fanapt
private	Sunovion				Latuda
RVPH	Reviva Pharma	$9.11	$84	$75	Brilaroxazine for Schizophrenia & other neuropsychiatric

Intellectual Property (IP)

As Reviva's candidates are molecules, much of its IP surrounds the protection of the candidates' specific structures and derivatives. The IP is broadly categorized into arylpiperazine and cycloalkylmethylamine derivatives for the treatment of schizophrenia and obesity and their related conditions. The arylpiperazine IP supports Reviva's RP5063 candidate, while the cyloalkylmethylamine IP supports candidate RP1208. Reviva also has IP related to indanone-based cholinesterase inhibitors and quinolinone-based atypical antipsychotic agents. As of year-end 2020, Reviva holds 57 granted patents and 21 patents pending in the US and foreign countries.

Exhibit XVIII – Arylpiperazine and Derivatives Patents[51]

Pat. No.	Title	Indication[52]
10,441,590	Methods for treating pulmonary hypertension	Pulmonary Hypertension
9,975,862	Arylpiperazine derivatives and methods of utilizing same	Schizophrenia
9,907,803	Methods for treating attention deficit hyperactivity disorder	ADHD
9,604,944	Arylpiperazine derivatives and methods of utilizing same	Schizophrenia
9,255,076	Arylpiperazine derivatives and methods of utilizing same	Schizophrenia
8,980,883	Arylpiperazine derivatives and methods of utilizing same	Schizophrenia
8,859,552	Methods of utilizing arylpiperazine derivatives	Schizophrenia
8,461,154	Methods of utilizing arylpiperazine derivatives	Schizophrenia
8,431,570	Methods of utilizing arylpiperazine derivatives	Schizophrenia
8,188,076	Compositions, synthesis, and methods of utilizing arylpiperazine derivatives	Schizophrenia
8,207,163	Compositions, synthesis, and methods of using piperazine based antipsychotic agents	Schizophrenia

[50] Price and market capitalization data is as of January 12, 2020.
[51] Sourced from the US Patent and Trademark Office Database
[52] Includes related psychoses or related co-morbid indications, please refer to patent for details

Reviva has 11 patents related to arylpiperazine, its derivatives, their synthesis and their uses, primarily targeting schizophrenia and related psychoses, including acute manic, bipolar disorder, autistic disorder and depression, and also targeting pulmonary hypertension and attention deficit hyperactivity disorder (ADHD). Reviva also has one patent application for arylpiperazine and derivatives, application number 20140155392 entitled Methods of Utilizing Arylpiperazine Derivatives in schizophrenia and related psychoses.

Exhibit XIX – Cycloalkylmethylamine and Derivatives Patents[53]

Pat. No.	Title	Indication[54]
9,695,116	Compositions, synthesis, and methods of using phenylcycloalkylmethylamine derivatives	Obesity, Depression
9,302,981	Synthesis, methods of using, and compositions of cycloalkylmethylamines	Obesity
9,296,681	Cycloalkylmethylamines	Obesity, Depression
9,238,625	Compositions, synthesis, and methods of using phenylcycloalkylmethylamine derivatives	Obesity, Depression
9,096,515	Methods of using cycloalkylmethylamine derivatives	Obesity, Depression
8,669,285	Synthesis, methods of using, and compositions of cycloalkylmethylamines	Obesity
8,604,244	Compositions, synthesis, and methods of using cycloalkylmethylamine derivatives	Obesity, Depression
8,445,714	Cycloalkylmethylamines	Obesity
8,372,883	Methods of using cycloalkylmethylamines	Obesity
8,338,632	Cycloalkylmethylamines	Obesity
7,989,500	Synthesis, methods of using, and compositions of cycloalkylmethylamines	Obesity

Similar to RP5063, RP1208 is protected by 11 patents for cycloalkylmethylamines, phenylcyclomethylamines, their derivatives, and their synthesis and use. The primary indications targeted are obesity and depression, and related comorbid indications.

Exhibit XX – Cycloalkylmethylamine and Derivatives Patent Applications[55]

App. No.	Title	Indication[56]
20140194508	Synthesis, methods of use & compositions of cycloalkylmethylamines	Obesity
20140066500	Cycloalkylmethylamines	Obesity, Depression
20140024709	Methods of using cycloalkylmethylamine derivatives	Obesity, Depression
20140024679	Compositions, synthesis & methods of using phenylcycloalkylmethylamine derivatives	Obesity, Depression
20130231386	Synthesis, methods of use & compositions of cycloalkylmethylamines	Obesity
20120172426	Compositions, synthesis & methods of using cycloalkylmethylamine derivatives	Obesity, Depression
20110263888	Cycloalkylmethylamines	Obesity
20110263877	Cycloalkylmethylamines	Obesity
20110263704	Methods of Using Cycloalkylmethylamines	Obesity
20140194508	Synthesis, methods of use & compositions of cycloalkylmethylamines	Obesity
20140066500	Cycloalkylmethylamines	Obesity, Depression

[53] Sourced from the US Patent and Trademark Office Database
[54] Includes related psychoses or related co-morbid indications, please refer to patent for details
[55] Sourced from the US Patent and Trademark Office Database
[56] Includes related psychoses or related co-morbid indications, please refer to patent for details

Recent Operational Achievements

Reviva completed its Phase II study of Brilaroxazine for schizophrenia in 2018, which was followed by consultation with the FDA in an end-of-Phase II meeting which guided Phase III trial design. Activities necessary to begin the Phase III trial include safety and toxicology studies, manufacturing of drug substance (API) and drug products, stability data in oral tablets, Phase III feasibility assessments in the US, Europe and Asia and submission of Phase III protocols and regulatory documents to the FDA.

There are additional studies in addition to the Phase III which must also be completed. These include a mandatory two year carcinogenicity study in rodents, a mandatory, standard human metabolism profiling with radiolabeled RP5063 and a mandatory, standard drug-drug interaction study. A special protocol assessment (SPA) has been accepted by the FDA for the carcinogenicity study. A QTc prolongation study and registration of commercial batches of drug substance and drug products must also be completed.

2020 was spent in preparation for the Phase III trial and consummating the combination with Tenzing Acquisition Corp. In July 2020, Reviva announced that it had entered into a definitive agreement to merge with Tenzing, in an agreement that was approved by Tenzing's shareholders. In November, Narayan Prabhu was appointed as Chief Financial Officer, effective following the completion of the combination with Tenzing.

On December 14, 2020, Reviva completed the merger with Tenzing. The company raised approximately $10.5 million as a result of the transaction and is preparing to launch its Phase III study in mid-2021.

MANAGEMENT PROFILES

Laxminarayan Bhat, Ph.D., Founder, President and Chief Executive Officer

Dr. Bhat founded Reviva Pharmaceuticals in 2006. Since the company's inception, Dr. Bhat has advanced a portfolio of proprietary compounds at varying stages of development, including chronic diseases in major therapeutic areas such as CNS, metabolic, cardiovascular and pain. Dr. Bhat brings over 20 years of experience in drug discovery and development to Reviva and has held research positions at XenoPort, ARYx Therapeutics and Higuchi Biosciences Center. He is the author of over 25 published papers, inventor of over 100 granted patents and was selected for the Alexander von Humboldt fellowship. Dr. Bhat received his Ph.D. in synthetic organic chemistry from Central University (NEHU), India and postdoctoral training in France, Germany and United States.

Marc Cantillon, M.D., Chief Medical Officer

Dr. Cantillon has over 20 years of drug development experience, gained at the NIH, in academia and in industry. He has held roles at AstraZeneca, Sanofi-Aventis, Wyeth/Pfizer, Schering-Plough/Merck Sharp & Dohme Corp, and has engaged in consultancy for pharmaceutical, biotech and venture investment firms. Dr. Cantillon's expertise is in translational proof of mechanism and proof of concept and global clinical trials, with specialization in central nervous system anesthesiology, neurology and psychiatry. He has initiated and built collaborative strategic partnerships such as Coalition for Major Diseases CAMD, QIBA DCE-MRI and FDG-PET steering committees of Radiology Society of North America (RSNA), Alzheimer Disease Neuroimaging (ADNI), Parkinson's Progression Markers Initiative, Michael J. Fox Foundation and International Society to Advance Alzheimer Research and Treatment. He is board certified by the American Board of Neurology and Psychiatry (ABPN) and an author/coauthor of over 40 research articles and two books. Dr. Cantillon received his M.D. from the Karolinska Institute and did his residency at both Cornell University and Icahn School of Medicine at Mount Sinai.

Narayan Prabhu, CPA, Chief Financial Officer

Mr. Prabhu joined the Company as Chief Financial Officer in December 2020. Since May 2019, Mr. Prabhu served as an independent consultant providing Interim Chief Financial Officer and Controller services to life science companies. Mr. Prabhu previously served as the Chief Financial Officer of Sony Biotechnology Inc., a biotechnology company focused on reagents, flow cytometry and spectral imaging from November 2014 to April 2019. From September 2009 to October 2014, Mr. Prabhu served as the M&A Controller at Cisco Systems, Inc. (NASDAQ: CSCO). Mr. Prabhu is a CPA and received his B.S. in Accounting & Finance from Indiana University at Bloomington Kelley School of Business and MBA from the University of California at Berkeley Haas School of Business.

RISKS

All investments contain an element of risk which reflects business uncertainty and opportunity. Some investments exhibit higher predictability, with current cash flows and established sales. These enterprises will have a lower level of perceived risk while other companies that are developing an undefined, new technology have a much higher level of perceived risk.

The biotechnology space includes companies at both ends of the spectrum, from mega-cap pharmaceutical and device powerhouses that have dozens of established products, to small operations with a handful of employees conducting pre-clinical studies. Many of the risks faced by the large and small firms are similar; however, there are some hazards that are particular to smaller companies that have not yet established themselves or their products. The typical risks faced by companies operating in the biotechnology space include risks related to liquidity, financing & trading, clinical trials, regulatory, personnel, intellectual property, marketing, and geopolitics.

Pandemic Risk

The pandemic has disrupted economic and other activity in the United States and around the globe. It has also caused significant volatility in financial markets. Economic activity worldwide has contracted and may take many quarters to reverse. While the financial markets have not declined in tandem with economic growth, risk perception may increase and financial markets may begin to reflect a lower level of economic activity and decreased availability of capital. Early stage clinical firms lacking revenues rely on capital markets to sustain development efforts and may be sensitive to changes in risk perception and trading dynamics.

Reviva is at a clinical stage of development, has been in between studies and largely remained untroubled by the pandemic. However, as clinical trials resume for the company, patient recruitment and the ability for patients and physicians to meet could be affected by social distancing and quarantine measures.

Liquidity, Financing & Trading

Access to financing comes and goes in cycles. During periods of improving confidence and plentiful liquidity, capital may be easy to obtain; however, during a crisis or a period of heightened risk perception, even companies with bright prospects may be in trouble if they depend on the financial markets to fund their work. Pre-revenue biotech firms rely primarily on equity issuance to fund their operations. The duration of drug development is considerable, and can last as long as 12 to 15 years before product revenues come in the door. Funds can be sourced through debt or grants and tax credits; however, these sources may reduce the flexibility of the company and can create difficulties if debt is unable to be repaid.

If capital is not readily available when needed, a company may be forced to suspend research and development, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising therapies without a viable route forward or force a company to accept onerous terms.

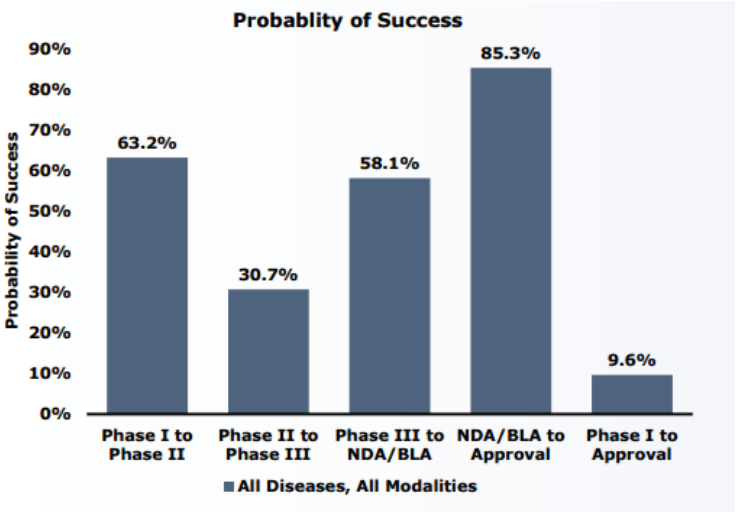
Trading volumes are lower for smaller biotech firms, creating liquidity risk for the investor and large transactions may have a material impact on share price. In periods of crisis or heightened risk perception, share price may be volatile. Companies with smaller capitalizations are typically considered riskier and changes in sentiment may adversely affect their trading prices and volumes. Smaller firms may also have less visibility, compete for investor dollars in a shallow market and be excluded from market indices.

Reviva has not generated revenues since inception and is not expected to produce them until its lead candidate is approved. The company's candidates are in various states of preclinical and clinical development and several years of investment are required before Brilaroxazine can be commercialized. Through its reverse merger with Tenzing, Reviva has acquired funds to advance its clinical candidates.

Clinical Trials

For smaller early-stage companies, investing in drug development is a lengthy process. The timeframe for conducting pre-clinical research to eventually commercializing a drug frequently takes from 12 to 15 years depending on market and company-specific conditions. On average, only one in a thousand compounds in discovery is eventually approved, creating a high hurdle for success.

Exhibit XXI – Success of Phased Trials and Regulatory Approval[57]



The future of a drug development company is largely dependent on the data produced from clinical trials. Due to the cost, magnitude and complexity typical of this work, partners are often sought to share risk. Reviva is seeking partnerships in Asia, Europe and Latin America. If successful, the deals would provide upfronts, milestones and royalties would further support development efforts. Partners may have competing demands which can adversely affect the work they are managing on behalf of the firm. Contract research organizations (CROs) and subcontractors must abide by strict execution and trial parameters that if violated can jeopardize trial success. Subcontractors supervise and execute research, biometric and pharmacovigilance, which are complex tasks. Patient recruitment may be difficult. Clinical investigational centers need sufficient capacity and the candidate drug needs to be manufactured according to current Good Manufacturing Practices (cGMP) and available to administer. Finally, clinical endpoints need to reach statistical significance to justify regulatory approval.

Development and Commercialization

Some firms have performed well during the pandemic with relatively unfettered access to financing despite the economic contraction; however, many clinical trials have also been delayed and disrupted due to restrictions and reallocation of trial site resources. Biotechnology firms frequently have global aspirations and must navigate clinical trial, regulatory approval and marketing regulations in multiple geographies. Companies that have a long history of research success and experience in drug development, with opinion leaders and experts advocating for the product in the field will hold a more favorable position compared to those that do not.

Reviva's candidates are at the both the preclinical and clinical stage with the most advanced candidate, Brilaroxazine, preparing to start Phase III trials in schizophrenia. Reviva is expected to launch the first of three Phase III schizophrenia trials in mid-2021, two in acute patient populations and one in maintenance therapy. It will bear risk related to enrollment, site selection, drug manufacturing, CROs and subcontractors. The process for many of these has already begun.

Regulatory and Legislative

Regulatory risk centers on a sponsor's interactions with regulatory authorities such as the FDA and EMA related to clinical trial requirements, marketing approval of the candidate, expedited pathways and the associated oversight. Previous success with the FDA or other regulatory agencies is another attractive attribute for a sponsor. Success is uncertain and may take years depending upon the needs and desires of the determining authority. Substantial expense is undertaken to bring a molecule or compound through clinical trials and address all of the regulatory agencies' concerns. Some accelerated pathways to approval are available such as those outlined in the Orphan Drug Act and the Breakthrough Therapy designation; however, changes in sentiment or perceived safety of drugs approved through these routes could influence the regulatory environment to demand a more rigorous process and the duration of the approval process may be extended or additional requirements may be put in place.

Companies with exposure to the United States' healthcare system have experienced legislative disruption with the Patient Protection and Affordable Care Act (PPACA) of 2010 and the Health Care and Education Reconciliation Act. These legislative actions impose non-deductible excise taxes on pharmaceutical manufacturers or importers that

[57] Thomas, D.W. *et al.* Clinical Development Success Rates 2006-2015. Bio, Biomedtracker, Amplion. June 2016.

sell branded prescription drugs to government programs, which can increase drug prices as levies are passed through to consumers. Under the PPACA, some firms are required to provide a discount on branded prescription drugs equal to 50% of the government-negotiated price, for drugs provided to certain patients who fall in the Medicare coverage gap. PPACA increases the level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1% and requires collection of rebates for drugs paid by Medicaid managed care organizations. The PPACA also introduced changes to the 340B drug discount program that expanded the patient population with access to the drugs, though at a discounted price. Prior to the PPACA, Congress had adopted the Medicare Prescription Drug, Improvement and Modernization Act of 2003. The Act modified Medicare reimbursement and coverage policies for prescription drugs.

Personnel

Biotechnology companies rely on the expertise and leadership of their executives to make both technical and strategic decisions and investments. Due to the highly competitive nature of the industry, many talented personnel are sought after and firms with the best resources are in the strongest position to attract talented leaders. Leadership turnover can be high in small biotech firms. Change in management is disruptive and can dramatically change the course of a firm. Personnel turnover can place a small company at a disadvantage when compared to larger firms with more specialized employees and executives. Furthermore, there can be risks and challenges associated with adding talent as the firm grows in size, especially with capital constraints. The size of the firm, volatility of stock price and a large component of compensation made up of equity-based compensation can deter certain talent from joining the firm or make it difficult to retain.

As a small firm, Reviva Pharmaceuticals has a limited number of personnel, all of whom play an important role. The loss of either Dr. Laxminarayan Bhat, CEO or Dr. Marc Cantillon, Chief Medical Officer, would severely impact the firm.

Intellectual Property

Intellectual property is the backbone of biotechnology development. Even with government regulation, patent protection is not guaranteed. The patent application process requires time, capital and the disclosure of substantial detail on the company's technology which is eventually made public. Despite submission of an application, patents may not be granted. Patent protection requires legal resources that a startup biotech firm may not have. Furthermore, countries differ in the degree and type of intellectual property protection. Some firms may in- or out-license intellectual property, which exposes parties holding the patent to risk of adherence and litigation regarding the parameters of the licensing. Finally, patent protection is temporary and there is no guarantee that the firm will benefit from the patent protection before it expires. Reviva has intellectual property protection until 2036 and may obtain additional protection from pediatric exclusivity, patent extension or other efforts to protect against competition.

Market Risk

Successful marketing of approved drug candidates relies on adoption by patients and providers. The approved drug must have convincing clinical trial data and maintain a favorable reputation among prescribers. Marketing is expensive and requires an experienced sales force and a presence in the marketing area. Marketed products remain under surveillance and any unexpected adverse effects damage the product's reputation. Furthermore, the risk of a competing or superior therapy is a continuous threat. Insurance coverage is also important. Rapidly obtaining a preferred position on health plan and payor formularies is critical to achieving target penetration rates. If health plans and payors cannot agree on appropriate pricing for the drug and the compound fails to offer a significant benefit above standard of care, the product may not be available on formularies.

Geopolitical

Recent trade tensions between the US and China threaten the world economy and have been exacerbated during the ongoing pandemic. There has been a cross-pollination of capital and drug development between China and North America in recent years which may slow as a result of the trade and political dispute between the countries. This conflict may reduce the availability of capital, partnerships and future development deals between companies in the two nations. The UK seceded from the European Union in 2020, potentially creating additional difficulties for companies seeking to obtain approval and marketing rights throughout Europe. Previously, a drug approved under the centralized procedure in the European Union would be approved in all member states. However, with the withdrawal of the UK, additional efforts and expense may be required to obtain marketing approval in this large European market.

VALUATION

Schizophrenia is a common mental disorder with prevalence ranging from 0.25 to 1% of the world population. Despite over 40 approved products for schizophrenia, unmet needs remain in efficacy and severe side effects, both of which contribute to the high discontinuation rate and lack of treatment. The lack of efficacy and negative side effect profile are a result of the pattern of receptor binding that takes place that is out of balance with the disease. As demonstrated in its Phase II trial, Reviva's Brilaroxazine offers improved efficacy, faster onset of action, a better side effect profile and lower discontinuation rates than other approved antipsychotics. While the drug must continue to show this favorable profile in pivotal trials, early results are promising. We anticipate that Reviva will pursue approval of Brilaroxazine in the US and rest of world following Phase III trials and regulatory approval in 2025 and 2026.

Our model recognizes a population of 328 million in the United States and one billion in developed markets outside the United States as key commercialization regions. Based on our review of schizophrenia prevalence, we assume 0.45% of this identified population presents the disease[58] and that these populations are growing at 0.5% to 0.6% per annum. Further review of resources[59] supports our estimate that 55% of this population receives treatment. About 40% of patients of this group are not responsive.[60] This unresponsive population is the addressable market for Brilaroxazine and represents approximately 330,000 persons in the United States and 1 million persons in the rest of the developed world. The ultimate penetration of the drug will depend on the final data on safety and efficacy from the Phase III trials and we assume a conservative approach based on our interpretation of the Phase II data. Penetration is forecast at 3.1% of the addressable market in 2025 (first year of commercialization) in the United States, rising to 6.0% by year five where it remains until patent and exclusivity expiration. Following the end of intellectual property protection, we forecast a ~10% annual decline. We model the same penetration into global developed addressable markets, but forecast the first year of commercialization in 2026.

Pricing is expected to be $80 per day in the US ($29,000/year) and half this amount ($40 or $15,000/year) outside the US, growing at 3% per year. In the first partial year of commercialization, we anticipate a 5% penetration rate increasing to 33% by year four. Our assumptions for rest-of-world are delayed by a year compared to the United States due to a later start to new drug application and additional time for pricing negotiation. Although Reviva is maintaining the option to commercialize Brilaroxazine itself, our model assumes that a partner will market the product in all regions. We forecast a 30% net royalty rate to be paid which represents the totality of anticipated upfronts, milestones and royalties.

We anticipate a 50% chance of success in 2025 for the candidate when a new drug application is submitted to the FDA with our probability selection guided by cited studies[61,62] and our internal assessment.

Research and development expenses are expected to be $17.5 million in 2021, rising to $28 million in 2022, then declining to $22 and $7.0 million over the subsequent two years as the Phase III trial for RP-5063 ramps up and winds down and generates data to be submitted to the FDA and other regulatory agencies. We assume that no further R&D is incurred following the commercialization of RP-5063. General and administrative expenses are forecasted at $3.6 million in 2021, rising steadily to $6.3 million by 2025 at which time constant 3% annual cost increases are anticipated. The model only reflects revenues and expenses from the development and commercialization of RP-5063 for schizophrenia. Costs and contributions from other indications will be added when they enter trials specific to their advancement. State and federal taxes are anticipated to be 26% and incurred when net operating loss carryovers are exhausted.

Our valuation approach uses a discounted cash flow (DCF) model and assumes a 15% discount rate and a (10%) terminal decline rate. Warrants and options are assumed exercised and proceeds added to the cash balance. We also reflect earn out and additional shares required to obtain additional capital. Our estimates and DCF model generate a valuation of $21.00 per share.

[58] We define this as approximately 1 billion persons who have sufficient government sponsored healthcare or sufficient resources to access needed healthcare in all regions outside the United States. We will refine the geographies pursued as new information is available.
[59] Sources: https://www.nami.org/mhstats & treatmentadvocacycenter.org/evidence-and-research/learn-more-about/25-schizophrenia-fact-sheet.
[60] Source: ncbi.nlm.nih.gov/pmc/articles/PMC5761908/
[61] Thomas, D.W. *et al.* Clinical Development Success Rates 2006-2015. Bio, Biomedtracker, Amplion. June 2016.
[62] Wong, C.H., Siah, K.W. Estimation of Clinical Trial Success Rates and Related Parameters. Biostatistics (2018) 00, 00, pp. 1–14

CONCLUSION

Reviva has designed Brilaroxazine or RP5063 as an improved antipsychotic treatment for schizophrenia and other mental disorders that provides an improved balance of activity for dopamine, serotonin and other receptors. It has shown early promise of improved, accelerated efficacy and lower side effects compared to existing therapies. The candidate has completed Phase II trials and is slated to begin Phase III studies in mid-2021. Studies required for registration are expected to be complete by 2024, allowing for regulatory submission and commercialization in the US and rest of world by 2025 and 2026 respectively.

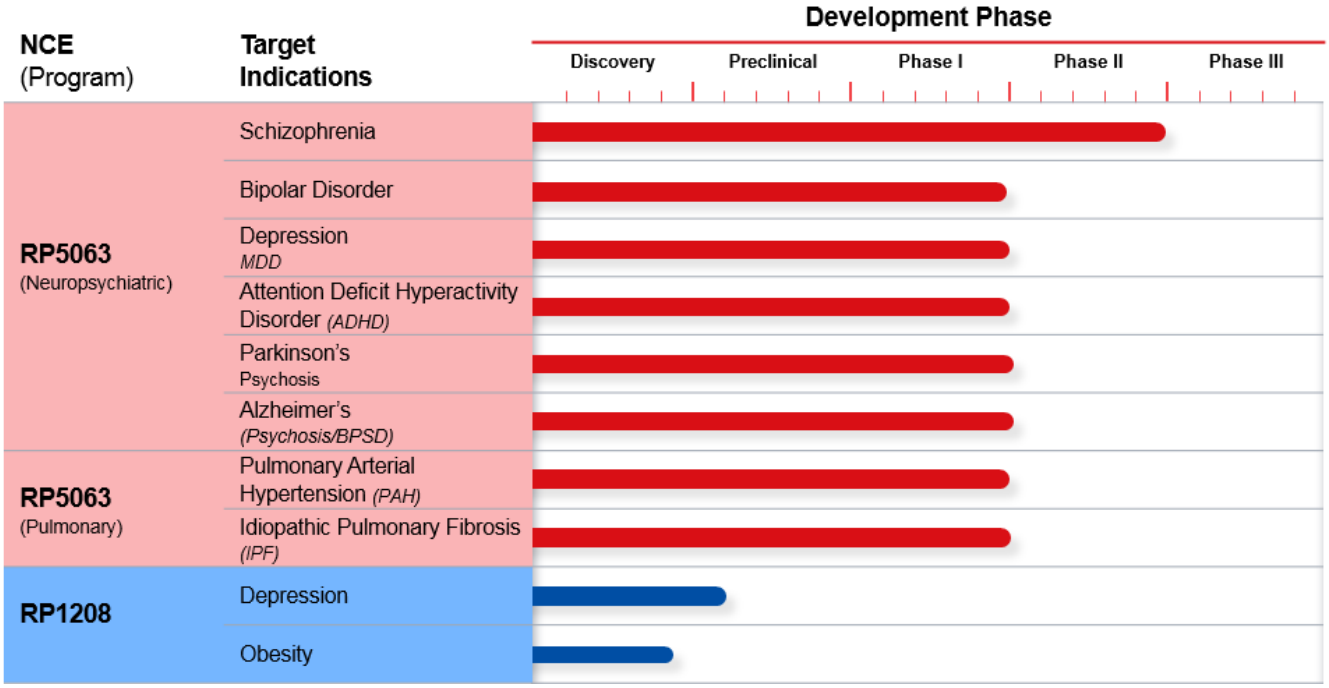
The unmet need in schizophrenia is severe, with up to 1% of the global population presenting the disease, but only about half receiving treatment and 30-50% of patients discontinuing due to lack of efficacy and side effects. Brilaroxazine's improved profile, if validated in pivotal trials, is expected to address the unmet need in individuals who do not tolerate existing antipsychotics. Brilaroxazine has also shown preclinical efficacy in a number of other mental disorders including bipolar disorder, major depressive disorder and psychosis related to neurodegenerative disease. The drug has also shown promise in pulmonary arterial hypertension and idiopathic pulmonary fibrosis.

The market for antipsychotics and schizophrenia treatment is around $10 billion but was double this level in 2011 when several branded competitors including Zyprexa, Abilify and Seroquel were under patent. This demonstrates the market opportunity that exists for a better product.

Our valuation approach anticipates commercialization in the US and developed regions outside the US. The addressable market is the schizophrenic population that is resistant to existing treatments; however, if the drug profile is markedly superior to available offerings, penetration could be higher. We anticipate that a partner will commercialize Brilaroxazine throughout the globe, remitting upfronts, milestones and royalties to Reviva and its shareholders. However, the company may elect to commercialize the product itself in the United States, taking advantage of the relatively small market with a targeted sales force.

After many years as a private company, Reviva Pharmaceuticals Holdings, Inc. is the result of a merger with Tenzing Acquisition Corp., a special purpose acquisition entity. The result of the merger has provided $10.5 million in gross proceeds and a NASDAQ listing which enables easier access to capital. We anticipate a capital raise in the near term which will support the first of two Phase III studies.

Exhibit XXII – Reviva Pipeline[63]



[63] Source: Reviva Pharmaceuticals January 2020 Corporate Presentation.

Key reasons to own Reviva Pharmaceuticals shares:

- **RP5063 Phase III asset to address an unmet need in schizophrenia and other mental disorders vs. existing therapies**
  - **Greater degree of efficacy**
  - **Lower level of side effects**
  - **Improved discontinuation rate**
  - **Addresses negative symptoms**
  - **Improved social functioning**
  - **Opportunity for approval in multiple mental disorders**
  - **Faster onset of action vs. standard of care**
  - **Binding to multiple serotonin and dopamine receptors implicated in schizophrenia**
- **Additional RP5063 Phase II ready programs in multiple indications**
  - **Bipolar Disorder**
  - **Depression**
  - **Attention Deficit Hyperactivity Disorder (ADHD)**
  - **Alzheimer's Psychosis/Behavior**
  - **Parkinson's Psychosis**
  - **Pulmonary Arterial Hypertension (Group 1)**
  - **Idiopathic Pulmonary Fibrosis**
- **RP1208 preclinical programs in development**
  - **Depression**
  - **Obesity**
- **Potential for intellectual property protection until 2037 for RP5063**

Based on our analysis of Brilaroxazine and the clinical trial data generated to date, we see a pathway forward to commercialize the antipsychotic in schizophrenia. Our valuation work takes into account the marketing of the drug in the United States and other developed regions, assuming a 50% probability of ultimate success. The opportunity for Reviva extends beyond schizophrenia and the company has several other programs in mental disorders whose development is complementary to work being done in the lead indication. We will add the costs and benefits of these programs when they enter Phase II trials. As we initiate on Reviva Pharmaceutical Holdings, Inc., our analysis and forecasts generate a valuation of $21.00 per share.

PROJECTED FINANCIALS

Reviva Pharmaceutical Holdings, Inc. - Income Statement[64,65]

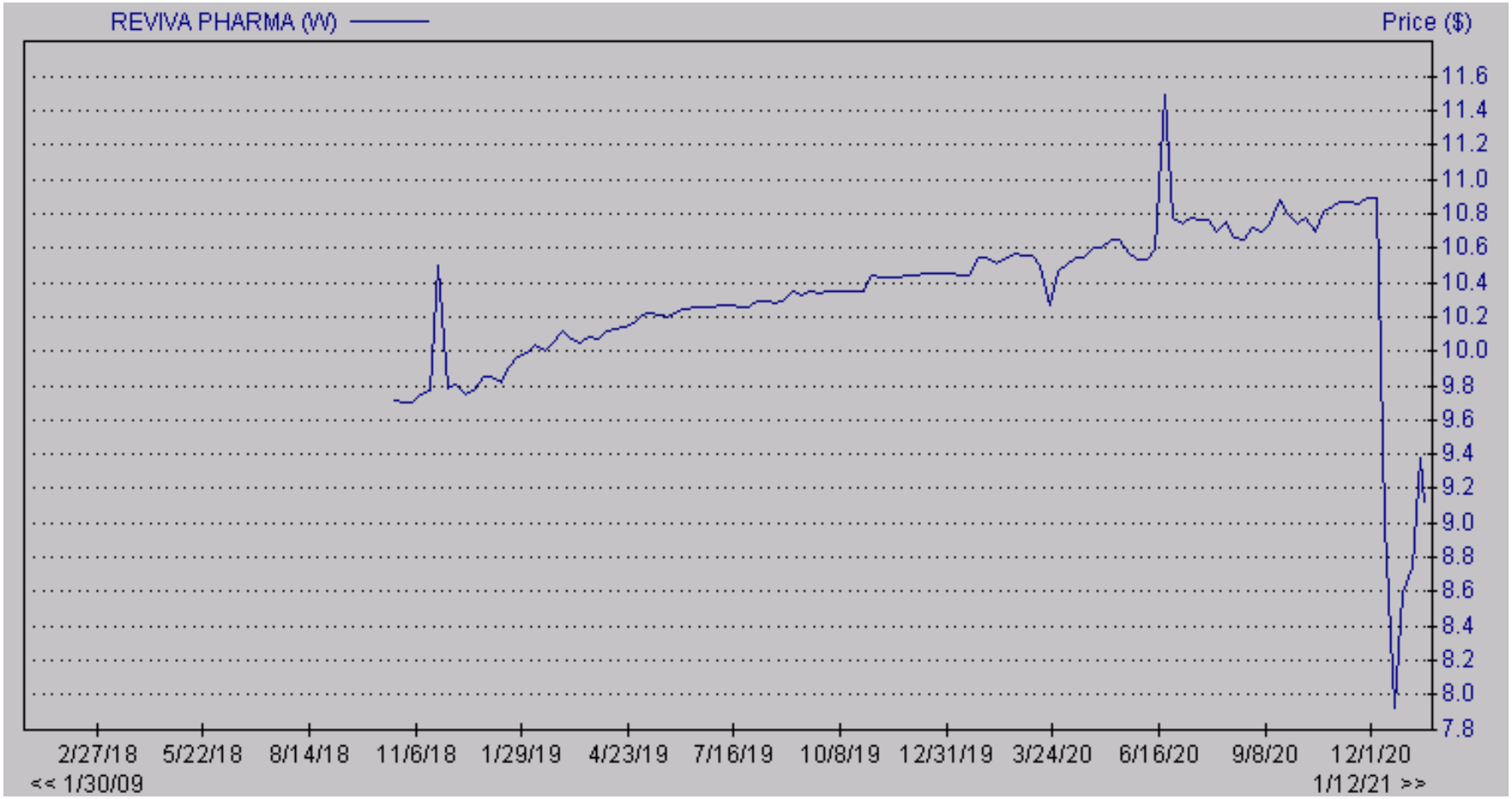
Reviva Pharmaceuticals	2019 A	Q1 A	Q2 A	Q3 A	Q4 E	2020 E	2021 E	2022 E
Total Revenues ($US)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth								
Research & Development	$196	$258	$36	$1	$1	$296	$17,500	$28,000
General & Administrative	$181	$361	$741	$511	$420	$2,033	$3,600	$4,202
Income from operations	($377)	($618)	($777)	($512)	($421)	($2,329)	($21,100)	($32,202)
Operating Margin						*# DIV/0!*	*# DIV/0!*	*# DIV/0!*
Other Income (Expense)	($469)	($130)	($74)	($146)	($120)	($470)	($405)	($422)
Pre-Tax Income	($846)	($748)	($851)	($659)	($541)	($2,799)	($21,505)	($32,624)
Provision for Income Tax	$1	$0	$0	$1	$0	$1	$0	$0
Tax Rate	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Net Income	**($847)**	**($748)**	**($851)**	**($659)**	**($541)**	**($2,800)**	**($21,505)**	**($32,624)**
Net Margin	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*	*# DIV/0!*
Reported EPS	**($0.05)**	**($0.04)**	**($0.05)**	**($0.04)**	**($0.06)**	**($0.17)**	**($1.11)**	**($1.63)**
YOY Growth	*1%*	*138.0%*	*211.6%*	*257.5%*	*1295.6%*	*275%*	*534%*	*47%*
Basic Shares Outstanding	18,181	18,181	18,181	18,198	9,500	16,015	19,415	20,000

Source: Company Filing // Zacks Investment Research, Inc. Estimates

[64] Historical financial statement information presents data as originally reported.
[65] Note that shares indicated in actual results reflects private shares for Reviva. Upon the completion of the combination with Tenzing, the new share balance is 9.2 million.

HISTORICAL STOCK PRICE

Reviva Pharmaceutical Holdings, Inc. – Share Price Chart[66][67]



[66] Source: Zacks Research System
[67] Note: Data prior to December 14, 2020 reflects share price for Tenzing Acquisition Corp.

DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

I, John Vandermosten, hereby certify that the view expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the recommendations or views expressed in this research report. I believe the information used for the creation of this report has been obtained from sources I considered to be reliable, but I can neither guarantee nor represent the completeness or accuracy of the information herewith. Such information and the opinions expressed are subject to change without notice.

INVESTMENT BANKING AND FEES FOR SERVICES

Zacks SCR does not provide investment banking services nor has it received compensation for investment banking services from the issuers of the securities covered in this report or article.

Zacks SCR has received compensation from the issuer directly or from an investor relations consulting firm engaged by the issuer for providing non-investment banking services to this issuer and expects to receive additional compensation for such non-investment banking services provided to this issuer. The non-investment banking services provided to the issuer includes the preparation of this report, investor relations services, investment software, financial database analysis, organization of non-deal road shows, and attendance fees for conferences sponsored or co-sponsored by Zacks SCR. The fees for these services vary on a per-client basis and are subject to the number and types of services contracted.

POLICY DISCLOSURES

This report provides an objective valuation of the issuer today and expected valuations of the issuer at various future dates based on applying standard investment valuation methodologies to the revenue and EPS forecasts made by the SCR Analyst of the issuer's business.
SCR Analysts are restricted from holding or trading securities in the issuers that they cover. ZIR and Zacks SCR do not make a market in any security followed by SCR nor do they act as dealers in these securities. Each Zacks SCR Analyst has full discretion over the valuation of the issuer included in this report based on his or her own due diligence. SCR Analysts are paid based on the number of companies they cover.
SCR Analyst compensation is not, was not, nor will be, directly or indirectly, related to the specific valuations or views expressed in any report or article.

ADDITIONAL INFORMATION

Additional information is available upon request. Zacks SCR reports and articles are based on data obtained from sources that it believes to be reliable, but are not guaranteed to be accurate nor do they purport to be complete. Because of individual financial or investment objectives and/or financial circumstances, this report or article should not be construed as advice designed to meet the particular investment needs of any investor. Investing involves risk. Any opinions expressed by Zacks SCR Analysts are subject to change without notice. Reports or articles or tweets are not to be construed as an offer or solicitation of an offer to buy or sell the securities herein mentioned.