Report on Reviva Pharmaceuticals' (RP5063) Phase 3 Clinical Trial Results and Future Outlook

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1 Introduction

Reviva Pharmaceuticals' Phase 3 clinical trial for RP5063, also known as brilaroxazine, aimed to assess the efficacy and safety of the drug in the treatment of schizophrenia. The trial employed a randomized, double-blind, placebo-controlled design for 28 days of treatment, followed by an open-label extension period of 52 weeks. This report analyzes the trial results, focusing on the primary endpoints, statistical significance, and the drug's potential market position relative to its competitors.

2 Clinical Trial Design

The trial was designed to have two main components:

- A 28-day double-blind, placebo-controlled treatment phase, assessing fixed doses of 15 mg or 50 mg of RP5063 once daily.
- A 52-week open-label extension phase, examining the long-term safety and tolerability of the drug at flexible doses (15, 30, or 50 mg once daily) in subjects with stable schizophrenia.

The total duration of the study was 56 weeks, including both the acute phase and the extension period. The main goal was to evaluate the efficacy of RP5063 in treating acute exacerbations of schizophrenia during the first 28 days, followed by a long-term assessment of its safety and tolerability.

3 Trial Results

The key findings from the trial are summarized in the following table, which includes the effect sizes (Cohen's d) and p-values for the primary endpoints:

Endpoint	Point Reduction/Improvement	Cohen's d Effect Size	P-value
PANSS Total Score	10.1	0.6	¡ 0.001
PANSS Positive Symptoms	2.8	0.5	¡ 0.001
PANSS Negative Symptoms	2.0	0.4	0.003
PANSS Negative Marder Factor	2.1	0.4	0.002
PANSS Social Cognition	1.6	0.5	¡ 0.001
PANSS Excitement/Agitation	2.1	0.5	¡ 0.001
Personal and Social Performance (PSP)	6.3	0.5	¡ 0.001
CGI-S	≥ 1	0.5	¡ 0.001

The results are statistically significant across all primary endpoints, with Cohen's d values ranging from 0.4 to 0.6, indicating moderate to large effect sizes. Notably, the PANSS Total Score, which reflects the severity of symptoms in schizophrenia, showed a substantial reduction, suggesting that RP5063 could be an effective treatment for schizophrenia.

4 Discussion

The trial results for RP5063 show promising efficacy in treating schizophrenia, with statistically significant improvements in both positive and negative symptoms. The Cohen's d values, ranging from 0.4 to 0.6, indicate moderate to large treatment effects, which are considered clinically significant. These results are comparable to other approved treatments for schizophrenia, such as aripiprazole, which also demonstrate moderate efficacy with manageable side effects.

However, despite these positive results, the stock price of Reviva Pharmaceuticals saw a significant drop following the announcement. This could be due to several factors, including investor expectations, concerns over long-term safety, or market competition. While the trial design was rigorous, involving both placebo-controlled and open-label phases, investors may have been expecting even more impressive short-term results, which did not materialize.

5 Comparison to Competitors

When comparing RP5063 to other similar drugs on the market, such as aripiprazole, risperidone, and olanzapine, it is important to note the similar trial design structures. Most of these drugs underwent randomized, double-blind, placebo-controlled trials with follow-up periods ranging from a few

weeks to several months. The use of effect size (Cohen's d) as an indicator of treatment magnitude is consistent across these trials, and RP5063's moderate effect size positions it similarly to these competitors in terms of efficacy.

6 Conclusion

Reviva Pharmaceuticals' RP5063 (brilaroxazine) has shown promising results in the treatment of schizophrenia, with statistically significant improvements in key endpoints and moderate to large effect sizes. Despite these positive outcomes, the company's stock price has dropped, potentially due to investor concerns or market dynamics. Going forward, the long-term safety data and the open-label extension phase will be critical in determining the drug's full potential. Further data, especially regarding the long-term use and its side effect profile, will be essential for RP5063's acceptance in the competitive schizophrenia treatment market.