ViewPoints: NeuroRx thinks feasibility study may have produced more than that

By *Michael Flanagan*
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NeuroRx is developing an agent for suicidal patients with bipolar depression, which is a group that has been long overlooked by drug developers precisely because of how difficult they are to treat, but results from a feasibility study of NRX-101 suggest the company is on the road to success.

The backstory

A pair of investigator-led Phase II studies looking at D-cycloserine showed that the NMDA antagonist – alone in major depressive disorder and with the D2-5HT2A antagonist lurasidone in bipolar depression – was safe and capable of achieving significant improvement in symptom scores. *(See Spotlight On: NeuroRx seeking a pharmacologic shock to the suicide prevention system* [1].*)*

CEO Jonathan Javitt told *FirstWord* that ketamine is an effective short-term means for treating acute suicidal ideation and behaviour (ASIB), but the drug is limited by hallucinations, dissociative side effects and carries a high risk of abuse liability. NeuroRx's plan is to follow a single stabilising dose of ketamine with NRX-101, a fixed-dose combination of D-cycloserine and lurasidone, to maintain the anti-depressive and prevent relapse of suicidal ideation.

What happened

This week, NeuroRx presented detailed data [2] from a company-sponsored Phase II trial that Javitt said represented a pair of important steps forward: it was an initial test of a proprietary tablet formulation of NRX-101 and the first time the compound had been tested in its target population of severe bipolar depression with ASIB.

The study enrolled a total of 20 patients who received a single intravenous infusion of ketamine followed by either NRX-101 or lurasidone for six weeks. Beyond demonstrating that the pharmacokinetics and pharmacodynamics of the tablet formulation works as intended, the study "unexpectedly" generated encouraging preliminary results on two efficacy metrics despite not being powered to do so.

Specifically, NRX-101 achieved a significant 11-point improvement on MADRS versus lurasidone at day 14 (p=0.03) and maintained the difference through six weeks (p=0.059). What's more, none of the 10 patients given NRX-101 relapsed compared to two of five in the placebo group.

The bigger picture

Javitt noted that this week's Phase II readout is especially encouraging because an ongoing pivotal Phase IIb/III trial, which is on the verge of dosing its first patient, is nearly identical in its design and being conducted under an SPA with the FDA.

"If the trends we are seeing in the early feasibility study play out the same way than the results should be very interesting," he remarked. The FDA apparently agreed with this assessment as the agency recently awarded NRX-101 with breakthrough therapy designation [3] (BTD) based on its interpretation of the data.

Final thoughts

NeuroRx has no intention of trying to launch NRX-101 itself and is instead eager to partner with a larger company that already has a commercial infrastructure in place

Down the road, Javitt suggested that the company may also look into the possibility of testing NRX-101 without the need for a rapid induction treatment with ketamine. A non-scheduled maintenance drug without abuse liability or hallucinogenic properties could be an attractive product.

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