Results of Phase 2b EAGLE trial; A double blind placebo control study evaluating the efficacy and safety of BL-1020, a GABA enhanced antipsychotic for the treatment of schizophrenia

Yona Geffen1, Ravi Anand2, Richard Keefe3, Michael Davidson4

1BioLineRx, Ltd, Jerusalem, Israel, Israel/2APC AG, St. Moritz, Switzerland, Switzerland/3Duke University and Neurocog, Durham, North Carolina, United States/4Tel Aviv University, Tel-Aviv, Israel, Israel

BACKGROUND:
BL-1020 is a new chemical entity that combines dopamine antagonism with GABAergic activity. PK studies demonstrate that BL-1020 enters the brain, increases dopamine release in the prefrontal cortex and hippocampus and has the ability to reverse cognitive impairment induced by PCP in animal’s behavioral models. Pre-clinical and clinical studies show that BL-1020 effectively reduces psychotic behavior with significantly fewer side effects.

METHODS:
The EAGLE (Effective Antipsychosis via GABA Level Enhancement) study was conducted under a U.S. FDA, IND application at 40 sites in U.S., Europe and India. In this 6-week study, 363 patients were randomized equally to treatment with low (10 mg/day) or high dose (20-30mg/day) of BL-1020, risperidone (2-8mg/day) or placebo. The study was designed to demonstrate statistically significant superiority of the BL-1020 high dose to placebo on the primary efficacy measure; the total score of the PANSS. Key secondary efficacy measures included the CGI-S, CGI-C, RDQ and an exploratory end point: Effect on cognition as measured by the Brief Assessment of Cognition in Schizophrenia (BACS). Risperidone at a dose of 2-8 mg was included as a positive control. Patients included were diagnosed with schizophrenia using the DSM-IV-TR experiencing an acute exacerbation of their psychosis, as evident from the following: PANSS total score ≥70; persistent positive symptoms; PANSS score ≥4 on conceptual disorganization, hallucinations, delusions, grandiosity, or suspiciousness; CGI-S rating of ≥4 (moderately ill); and duration of current episode less than one month.

RESULTS:
The results in the ITT population using the LOCF for the primary efficacy measure, the total PANSS scores, indicated that treatment with BL-1020 high dose (LS mean -23.6; 95% CI -28.4; -18.8), was statistically significant superior (p=0.002) to placebo; (LS mean -14.4; 95% CI -19.1; -9.7). Risperidone treatment also was associated with significant improvement (LS means-26.2; 95% CI -31.0; -21.3) to placebo. BL-1020 low dose did not separate from placebo. There were no statistically significant differences between BL-1020 high dose and risperidone (p=0.390). The BL-1020 high dose was also statistically significantly superior for PANSS positive symptoms (p<0.001) and general psychopathology (P= 0.003) and showed a trend for significance (P= 0.067) for negative symptoms compared to placebo. These positive results on the PANSS, supported by the findings on the CGI-S and CGI-C. BL-1020 high dose showed significant increase in the number of ‘responders’ compared to placebo.

The effect of BL-1020 on cognition provided evidence of a statistically significant and clinically relevant benefit. Analysis of the BACS composite score indicated significant superiority of the BL-1020 high dose group compared to placebo (p =0.027) and risperidone (p = 0.027) at the end of study, with an effect size of 0.5 compared to placebo.

The maximum change from baseline in the ESRS score was comparable to that of risperidone. BL-1020 increase in prolactin was significantly lower than that of risperidone (p<0.001). There were no statistically significant or clinically relevant changes in the measurements of the ECG, laboratory or vital signs (BP, HR. Temp). There were no statistically significant or clinically relevant AEs of body weight gain, glucose increases, and changes in lipids.

DISCUSSION:
These results are consistent with BL-1020 preclinical profile of an effective, safe and well tolerated, antipsychotic with GABA activity and a potential to improve cognition.

Submission Type: Independent Oral Presentation
Category: Neuropsychology
Travel Award: No
Accept Oral Presentation: Yes