LB-102 for Acute Schizophrenia in Adults: Efficacy and Safety From a Large Phase 2 Clinical Trial

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Poster S64

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Background

- Schizophrenia is a chronic, severe, complex, and debilitating psychiatric disorder characterized by disturbances in perception, thoughts, speech, drive, cognition, emotion, motivation, and/or motor activity.[1]
- Hallucinations and delusions (positive symptoms) are the most striking characteristic of schizophrenia.[2] Negative symptoms, including social withdrawal and lack of emotion, energy, and motivation, are also commonly present in people with schizophrenia,[3] as is cognitive impairment.[4]
- The course of schizophrenia is highly variable, with periods of psychosis and stabilization of varying duration and intensity. Sustained remission of both positive and negative symptoms occurs in a minority of patients even with prolonged antipsychotic therapy.[5]
- People with schizophrenia experience profoundly reduced quality of life, have a ~3.5 times higher rate of mortality compared to the general population, and are ~10 times more likely to commit suicide than the general population.[6]
- About half of the suicides among people with schizophrenia occur within the first 2 years of disease onset, pointing to the urgency for behavioral and pharmaceutical intervention.[7]
- Existing therapies fail to work for nearly 50% of people with schizophrenia due to poor efficacy and/or tolerability issues.[8]

LB-102

- LB-102 (*N*-methyl amisulpride) is a novel dopamine D_2/D_3/5-HT_7 receptor antagonist and potentially first-in-class benzamide antipsychotic currently under development for the treatment of schizophrenia.[9]
- Preclinical assays have shown equal, if not improved, receptor binding, pharmacokinetics, and behavioral modification properties for LB-102 compared to amisulpride.[9]
- In vivo studies have demonstrated that LB-102 has a favorable PK profile in rats and mice, similar to amisulpride, with as good as or better efficacy to amisulpride in animal schizophrenia models.[10]
- A phase 1, randomized, double-blind, placebo-controlled study demonstrated an acceptable safety profile of LB-102 in 64 healthy volunteers.[11]
- A phase 1, open-label PET study highlighted that LB-102 afforded dopamine receptor occupancy under steady-state conditions in the desired range of 60% to 80% required to treat schizophrenia in doses as low as 50 mg/day, and in a similar effect range as observed with amisulpride 400 mg.[12]

Methods

- NOVA[1] was a phase 2, multicenter, randomized, double-blind, placebo-controlled trial (ClinicalTrials.gov: NCT06179108) conducted in the United States (**Figure 1**).
- Study schedule included:
  - 7–14-day inpatient screening/washout period
  - 28-day inpatient treatment period
  - 5-day inpatient stabilization period
  - Outpatient safety follow-up visit ~2 weeks post-treatment
- Eligible participants were randomized (3:3:3:1) to oral once-daily placebo, LB-102 50 mg, LB-102 75 mg, or LB-102 100 mg, with the 100 mg dose considered exploratory.

Key Inclusion Criteria

- Adults 18–55 years diagnosed with schizophrenia and requiring hospitalization or continued hospitalization for a current acute exacerbation of psychotic symptoms
- Positive and Negative Syndrome Scale (PANSS) total score of 80–120
- PANSS positive subscale item scores of ≥4 on at least two key items
- Clinical Global Impression of Severity (CGI-S) score of ≥4

Key Exclusion Criteria

- Schizophrenia diagnosed ≤1 year ago
- History of treatment resistance
- Improvement of ≥20% from screening to baseline in PANSS total score

Outcomes and Analyses

- **Primary efficacy endpoint:** Change from baseline to week 4 in PANSS total score
- **Secondary efficacy endpoints:** Change from baseline in CGI-S score, changes from baseline in PANSS positive and negative subscale scores, and PANSS responder rates
- **Safety:** Adverse event reporting and other safety assessments
- 350 participants in the 3:3:3:1 randomization scheme were estimated to provide ≥85% power at a two-sided 5% significance level to detect a treatment difference on the primary endpoint between either LB-102 50 mg or 75 mg and placebo, with a Hochberg procedure applied to adjust for multiplicity.

Results

Disposition

- A total of 359 participants were randomized and were included in the safety and intent-to-treat populations.
  - 293 participants (82%) completed the Week 4 treatment visit, and 261 participants (73%) completed the trial.
- Demographics and baseline characteristics were similar across treatment arms and reflective of an inpatient schizophrenia population (**Table 1**).
- The most commonly co-occurring medical conditions were insomnia (n=266, 74.1%), anxiety (n=211, 58.8%), headache (n=144, 40.1%), depression (n=118, 32.9%), and agitation (n=108, 30.1%).

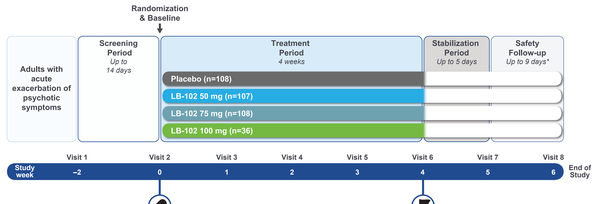
Efficacy

- LB-102 met the primary endpoint, with both 50 mg and 75 mg arms statistically superior to placebo (**Figure 2**).
- Least-squares mean changes from baseline to Week 4 in PANSS total score were:
  - Placebo, −9.3
  - LB-102 50 mg, −14.3 (p=0.0009 vs placebo; effect size=0.61)
  - LB-102 75 mg, −14.0 (p=0.0022 vs placebo; effect size=0.41)
  - LB-102 100 mg, −16.1 (nominal p=0.0017 vs placebo; effect size=0.83)
- The treatment effect of LB-102 on PANSS total score was observed with all doses as early as Day 8, and maintained throughout the 4-week study period.
- Analysis of change from baseline to Week 4 on the CGI-S score identified a statistically significant improvement for all LB-102 doses compared to placebo (**Figure 3**).

Safety and Tolerability

- Treatment-emergent adverse events (TEAEs) were reported in 56% (placebo), 69% (50 mg), 57% (75 mg), and 75% (100 mg) of participants (**Table 2**).
  - 10 participants (2.8%) experienced a TEAE that led to treatment withdrawal (**Table 2**).
  - 5 participants (1.4%) experienced a serious TEAE (**Table 2**).
- Insomnia was the most commonly reported TEAE across treatment arms, followed by headache, anxiety, and agitation (**Table 3**).
- A total of 25 participants treated with LB-102 experienced hyperprolactinemia or increased blood prolactin (**Table 3**), 3 experienced galactorrhea (50 mg, n=2; 75 mg, n=1), 1 experienced breast enlargement (100 mg), and 1 experienced erectile dysfunction (100 mg).
- There was an increase in weight across all treatment arms by the end of Week 4 (placebo, 2.1 kg; 50 mg, 4.6 kg; 75 mg, 3.5 kg; 100 mg, 3.6 kg). Increases in weight and BMI were not directly associated with any change in cardiovascular or metabolic markers.
- There was no change in suicidal ideation or behavior at the end of Week 4, as measured by the Columbia–Suicide Severity Rating Scale.

Figure 1. Trial Design



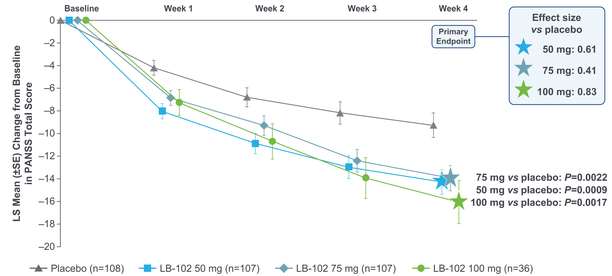
*The safety follow-up visit occurred ~2 weeks after the end of the treatment period.

Table 1. Demographics and Baseline Characteristics

		Placebo (n=108)	50 mg (n=107)	75 mg (n=108)	100 mg (n=36)	Overall (N=359)
Age at informed consent, mean (SD)		39.1 (9.1)	39.0 (9.6)	39.2 (9.2)	39.1 (9.2)	39.1 (9.3)
Sex, n (%)	Male	85 (79%)	87 (81%)	90 (83%)	28 (78%)	290 (81%)
	Female	23 (21%)	20 (19%)	18 (17%)	8 (22%)	69 (19%)
Ethnicity, n (%)	Latino	17 (16%)	12 (11%)	8 (7%)	6 (17%)	43 (12%)
Race, n (%)	White	24 (22%)	17 (16%)	18 (17%)	9 (25%)	68 (19%)
	Black	80 (74%)	87 (81%)	83 (77%)	25 (69%)	275 (77%)
	Asian	1 (1%)	0	2 (2%)	0	3 (1%)
	Native American	0	0	2 (2%)	0	2 (1%)
Weight at baseline (kg), mean (SD)		85.6 (17.2)	84.0 (19.5)	88.4 (18.5)	85.9 (18.0)	86.0 (18.4)
BMI at baseline (kg/m^2), mean (SD)		28.2 (5.2)	27.4 (6.0)	28.8 (5.6)	28.0 (6.0)	28.1 (5.6)
Baseline PANSS total score at baseline, mean (SD)		93.8 (8.2)	93.9 (7.5)	93.6 (7.8)	93.9 (9.0)	–
Years since diagnosis, mean (range)		16.4 (2–41)	15.2 (2–38)	16.2 (2–39)	13.5 (2–36)	15.8 (2–41)

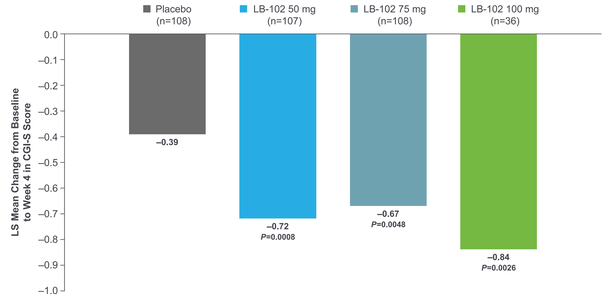
BMI, body mass index; PANSS, Positive And Negative Syndrome Scale; SD, standard deviation.

Figure 2. Change from Baseline in PANSS Total Score Over Time through Week 4



Analyzed using a mixed model for repeated measures (MMRM) that included treatment, visit, treatment-by-visit interaction, and study site as categorical effects, and baseline PANSS total score as continuous covariate.
LS, least squares; PANSS, Positive And Negative Syndrome Scale; SE, standard error.

Figure 3. Mean Change From Baseline in CGI-S Score at Week 4



Analyzed using a mixed model for repeated measures (MMRM) that included treatment, visit, treatment-by-visit interaction, and study site as categorical effects, and baseline CGI-S score as continuous covariate.
CGI-S, Clinical Global Impressions–Severity of illness; LS, least squares.

Table 2. Summary of Treatment-Emergent Adverse Events (TEAEs)

Participants, n (%)	Placebo (n=108)	50 mg (n=107)	75 mg (n=108)	100 mg (n=36)	Overall (N=359)
Any adverse event	67 (62%)	77 (72%)	68 (63%)	28 (78%)	240 (67%)
Any TEAE	60 (56%)	74 (69%)	62 (57%)	27 (75%)	223 (62%)
Any treatment-related TEAE	23 (21%)	49 (46%)	34 (31%)	17 (47%)	123 (34%)
Any TEAE leading to early withdrawal	2 (1.9%)	2 (1.9%)	3 (2.8%)	3 (8.3%)	10 (2.8%)
Any severe TEAE	3 (2.8%)	0	1 (0.9%)	1 (2.8%)	5 (1.4%)
Any serious TEAE	2 (1.9%)	1 (0.9%)	1 (0.9%)	1 (2.8%)	5 (1.4%)
Any serious treatment-related TEAE	0	1 (0.9%)	1 (0.9%)	0	2 (0.6%)
Any TEAE leading to death	1 (0.9%)	0	0	0	1 (0.3%)

Table 3. Treatment-Emergent Adverse Events Reported ≥5% in Any Treatment Arm

Participants, n (%)	Placebo (n=108)	50 mg (n=107)	75 mg (n=108)	100 mg (n=36)
Insomnia	24 (22.2%)	27 (25.2%)	23 (21.3%)	14 (38.9%)
Headache	10 (9.3%)	12 (11.2%)	9 (8.3%)	2 (5.6%)
Anxiety	9 (8.3%)	10 (9.3%)	9 (8.3%)	4 (11.1%)
Agitation	10 (9.3%)	11 (10.3%)	6 (5.6%)	4 (11.1%)
Weight increased	4 (3.7%)	13 (12.1%)	8 (7.4%)	3 (8.3%)
Hyperprolactinemia[†]	0	11 (10.3%)	8 (7.4%)	6 (16.7%)
Blood creatine phosphokinase increased	3 (2.8%)	4 (3.7%)	1 (0.9%)	2 (5.6%)
Alanine aminotransferase increased	1 (0.9%)	3 (2.8%)	1 (0.9%)	2 (5.6%)
Somnolence	0	1 (0.9%)	4 (3.7%)	2 (5.6%)
Constipation	0	4 (3.7%)	1 (0.9%)	2 (5.6%)

[†]Combined adverse event preferred terms for "hyperprolactinemia" and "blood prolactin increased".

CONCLUSION

- LB-102, a novel potentially first-in-class benzamide D_2/D_3/5-HT_7 receptor antagonist, was effective and generally safe and well-tolerated in participants with acute schizophrenia.

DISCUSSION

- This phase 2 clinical trial provided rigorous evidence demonstrating the efficacy and safety of LB-102 for the treatment of adults with acute schizophrenia, supporting continued clinical development of LB-102 for schizophrenia treatment.

References

1. McCutcheon RA, et al. *JAMA Psychiatry*. 2020;77(2):201-210.
2. Mourgues-Codern C, et al. *Biol Psychiatry*. 2025 Feb 26:S0006-3223(25)00990-4.
3. Cohen AS, et al. *Schizophr Bull*. 2021;47(1):44-53.
4. Correll CU, et al. *J Clin Psychiatry*. 2024;85(3):24r15316.
5. Carpiniello B, et al. *Schizophr Res*. 2022;239:34-41.
6. Correll CU, et al. *World Psychiatry*. 2022;21(2):248-271.
7. Tandon R, Jibson MD. *Curr Opin Psychiatry*. 2003;16(2):193-197.
8. Huhn M, et al. *Lancet*. 2019;394(10202):939-951.
9. Grattan V, et al. *ACS Omega*. 2019;4(9):14151-14154.
10. Neill JC, et al. *Eur Neuropsychopharmacol*. 2017;27(S4):S922-S923.
11. Biernat L, et al. *Psychopharmacology (Berl)*. 2022;239(9):3009-3018.
12. Wong DF, et al. *Neuropsychopharmacology*. 2024;50(2):372-377.

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AE, LC, BL, and **AV** are full time employees and shareholders of LB Pharmaceuticals. **NB** serves as a consultant to LB Pharmaceuticals. **ZP** is a co-founder and former Chief Executive Officer of LB Pharmaceuticals; he currently serves as a consultant to LB Pharmaceuticals. **JK** has served as a consultant to, received honoraria, received travel support, and/or participated in speakers' bureaus for AbbVie, Alkermes, Allergan, Boehringer-Ingelheim, Bristol Meyer-Squibb, Cerevel, Dainippon Sumitomo, HealthRhythms, HLS Therapeutics, Indivior, Intracellular Therapies, Janssen Pharmaceutical, Johnson & Johnson, LB Pharmaceuticals, Lundbeck, Mapi, Maplight, Merck, Minerva, Neurocrine, Newron, Novartis, NW PharmaTech, Otsuka, Roche, Saladax, Sunovion, and Teva; has participated on advisory boards for AbbVie, Alkermes, Boehringer-Ingelheim, Cerevel, Click Therapeutics, BMS, Lundbeck, Merck, Newron, Novartis, Otsuka, Sumitomo, Terran, and Teva; has received grant support from Lundbeck, Janssen, Otsuka, and Sunovion; holds stock or stock options in HealthRhythms, LB Pharmaceuticals, Medincell, North Shore Therapeutics, NW Pharmatech, Reviva, Saladax, Terran, and Vanguard Research Group; and receives royalties from Up to Date.