PS02-1273

LB-102 for acute schizophrenia in adults: Efficacy and safety from a large phase 2 clinical trial

Anna Eramo,[1] Leslie Callahan,[1] Niccolo Bassani,[2] Baker P. Lee,[1] Zachary Prensky,[1] Andrew R. Vaino,[1] John M. Kane[3]

[1]LB Pharmaceuticals Inc, New York, NY, USA; [2]Worldwide Clinical Trials, Nottingham, UK; [3]The Donald and Barbara Zucker School of Medicine, Hempstead, NY, USA

Scan the QR code to access a PDF copy of this poster

Background

- LB-102 is a novel $D_2/D_3/5\text{-}HT_7$ antagonist in development for schizophrenia and other neuropsychiatric disorders.
- Preclinical assays showed similar receptor binding, pharmacokinetics, and behavioral modification properties between LB-102 and amisulpride.[1]
- A phase 1, open-label PET study showed LB-102 50 mg exhibited similar receptor occupancy under steady-state to amisulpride 400 mg.[2]
- A phase 1, double-blind, placebo-controlled trial in 64 healthy volunteers demonstrated LB-102 was generally safe and well tolerated in doses up to 150 mg/day.[3]

Objective

- To report the efficacy and safety of LB-102 vs placebo for the treatment of adults with acute schizophrenia, with a focus on positive symptoms.

Methods

Study design and selection criteria

- NOVA[1] was a phase 2, multicenter, randomized, double-blind, placebo-controlled trial in adults with schizophrenia conducted in the US (ClinicalTrials.gov: NCT06179108) (**Figure 1**).
- Eligible adults (18–55 years) were diagnosed with schizophrenia, required hospitalization or continued hospitalization for a current acute exacerbation of psychotic symptoms, and had:
  - Positive and Negative Syndrome Scale (PANSS) total score of 80–120,
  - PANSS positive subscale item score of ≥4 on ≥2 key items, and
  - Clinical Global Impressions–Severity (CGI-S) score of ≥4
- People diagnosed with schizophrenia ≤1 year before screening, who had a history of schizophrenia treatment resistance, or who had an improvement of ≥20% from screening to baseline in PANSS total score were excluded.
- 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.

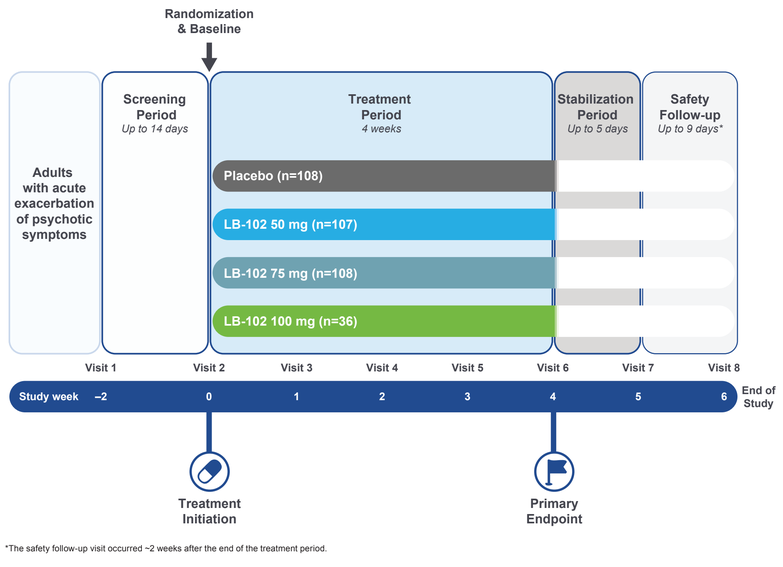
Outcomes and analyses

- **Primary efficacy endpoint:** Change from baseline to week 4 in PANSS total score
- **Secondary endpoints analyzed here:** Change from baseline to week 4 in CGI-S score, PANSS Positive Symptoms subscale score, and PANSS Marder Positive Symptoms factor score
- **Safety:** Treatment-emergent adverse events (TEAEs; MedDRA Version 26.1) and other safety assessments
- **Extrapyramidal symptoms (EPS):** TEAEs as well as the Simpson-Angus Scale (SAS), Barnes Akathisia Rating Scale (BARS), and Abnormal Involuntary Movement Scale (AIMS)

Results

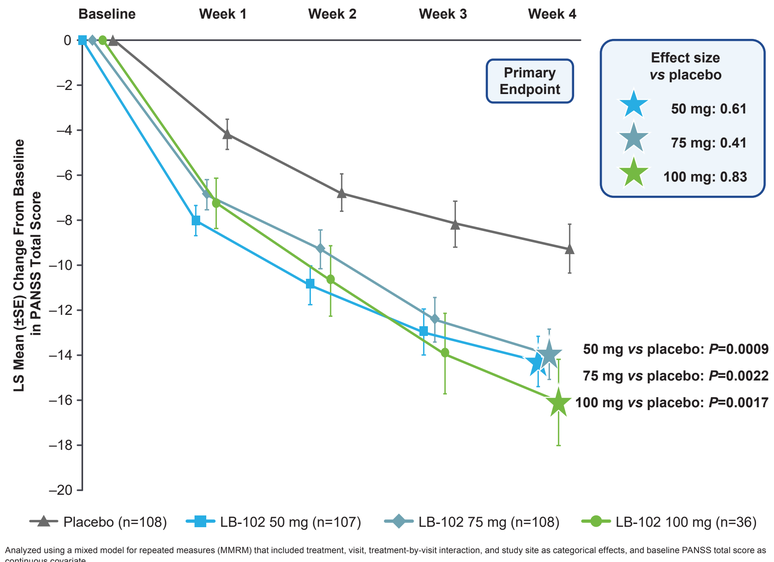
- 359 participants were randomized with similar characteristics and demographics across treatment arms (**Table 1**).
  - 293 participants (82%) completed week 4.
  - 261 participants (73%) completed the trial.
- Ongoing psychiatric and neurological medical conditions at baseline, occurring in ≥5% of the total population, included insomnia (74.1%), anxiety (58.8%), headache (40.1%), depression (32.9%), and agitation (30.1%) (**Table 2**).
- LB-102 met the primary endpoint, with 50 mg and 75 mg statistically superior to placebo (Hochberg multiplicity correction) (**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 (all doses) on PANSS total score was observed as early as week 1 and maintained throughout the 4-week treatment period (**Figure 2**).
- A similar dose-related effect was observed for LB-102 (all doses) on the PANSS Positive Symptoms subscale (**Figure 3**) and PANSS Marder Positive Symptoms factor scores (**Figure 4**).
- Least-squares mean change from baseline to week 4 in CGI-S scores were:
  - Placebo, –0.39
  - LB-102 50 mg, –0.72 (*P*=0.0008 vs placebo)
  - LB-102 75 mg, –0.67 (*P*=0.0048 vs placebo)
  - LB-102 100 mg, –0.84 (*P*=0.0026 vs placebo)
- TEAEs were reported in 56% (placebo), 69% (50 mg), 57% (75 mg), and 75% (100 mg) of participants (**Table 3**).
  - 10 participants (2.8%) experienced a TEAE that led to treatment withdrawal.
  - 5 participants (1.4%) experienced a serious TEAE.
- TEAEs in ≥5% of any arm included: insomnia, headache, anxiety, agitation, weight increase, hyperprolactinemia, blood prolactin increase, blood creatine phosphokinase increase, alanine aminotransferase increase, somnolence, and constipation (**Table 4**).
  - Several common baseline comorbidities, including insomnia, anxiety, headache, and agitation, were amongst the most frequently reported TEAEs.
- Elevated prolactin levels at day 28 compared to baseline were reported across all treatment arms (placebo, +1.3 ng/ml; 50 mg, +59.1 ng/ml; 75 mg, +50.3 ng/ml; 100 mg, +51.3 ng/ml).
  - Clinical adverse events related to prolactin increase were reported in 5 participants, including galactorrhea (50 mg, n=2; 75 mg, n=1), breast enlargement (100 mg, n=1), and erectile dysfunction (100 mg, n=1).
- EPS adverse events were minimal (placebo, n=4; 50 mg, n=1; 75 mg, n=6; 100 mg, n=2), with no change from baseline to week 4 in SAS, AIMS, and BARS (**Table 5**).

Figure 1. NOVA[1] Trial Design



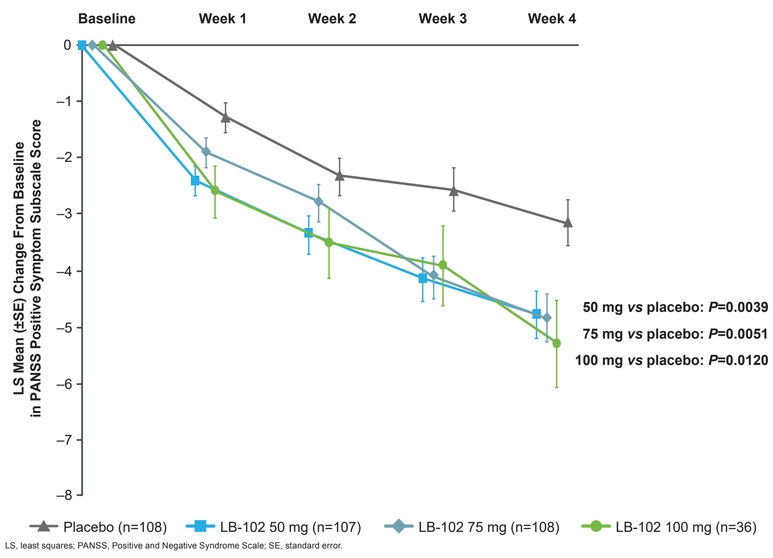
*The safety follow-up visit occurred ~2 weeks after the end of the treatment period.

Figure 2. Change in PANSS Total Score



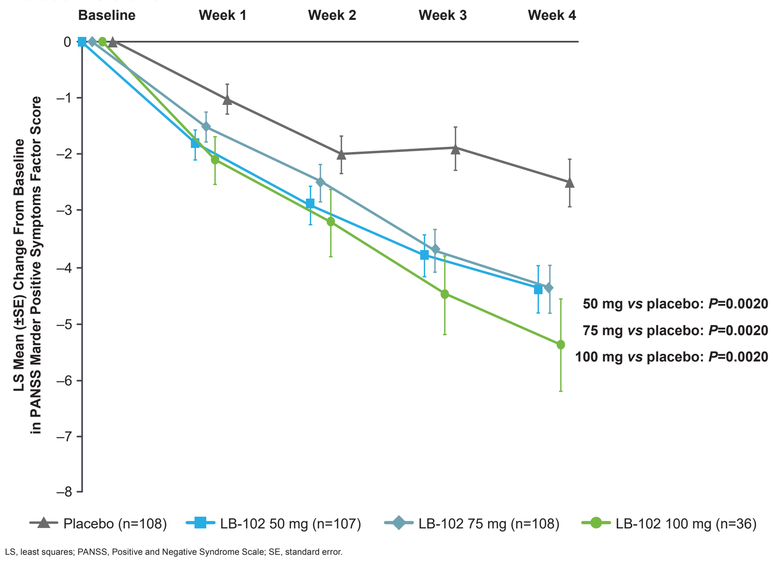
Analyzed using a mixed model for repeated measures (MMRM) that included treatment, visit, treatment-by-visit interaction, and study site as categorical effects, and baseline PANSS total score as continuous covariate.
LS, least squares; PANSS, Positive and Negative Syndrome Scale; SE, standard error.

Figure 3. Change in PANSS Positive Symptoms Subscale Score



LS, least squares; PANSS, Positive and Negative Syndrome Scale; SE, standard error.

Figure 4. Change in PANSS Marder Positive Symptoms Factor Score



LS, least squares; PANSS, Positive and Negative Syndrome Scale; SE, standard error.

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/m²), 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.

Table 2. Ongoing Psychiatric & Neurological Medical History in ≥5% of the Total Population

	Placebo (n=108)	50 mg (n=107)	75 mg (n=108)	100 mg (n=36)	Overall (N=359)
Psychiatric disorders	**108 (100%)**	**107 (100%)**	**108 (100%)**	**36 (100%)**	**359 (100%)**
Schizophrenia	108 (100%)	107 (100%)	108 (100%)	36 (100%)	359 (100%)
Insomnia	79 (73.1%)	83 (77.6%)	75 (69.4%)	29 (80.6%)	266 (74.1%)
Anxiety	59 (54.6%)	68 (63.6%)	63 (58.3%)	21 (58.3%)	211 (58.8%)
Depression	36 (33.3%)	43 (40.2%)	34 (31.5%)	5 (13.9%)	118 (32.9%)
Agitation	32 (29.6%)	41 (38.3%)	26 (24.1%)	9 (25.0%)	108 (30.1%)
Nervous system disorders	**48 (44.4%)**	**53 (49.5%)**	**46 (42.6%)**	**18 (50.0%)**	**165 (46.0%)**
Headache	41 (38.0%)	49 (45.8%)	37 (34.3%)	17 (47.2%)	144 (40.1%)

Table 3. 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 4. TEAEs 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[1]	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%)

[1]Sum of the preferred terms "hyperprolactinemia" and "blood prolactin increased."

Table 5. Summary of TEAEs Related to Extrapyramidal Symptoms (EPS)

Participants, n (%)	Placebo (n=108)	50 mg (n=107)	75 mg (n=108)	100 mg (n=36)
Dystonia	1 (0.9%)	0	3 (2.8%)	1 (2.8%)
Akathisia	1 (0.9%)	1 (0.9%)	2 (1.9%)	0
Extrapyramidal disorder	2 (1.9%)	0	1 (0.9%)	1 (2.8%)
Total related to EPS	4 (3.7%)	1 (0.9%)	6 (5.6%)	2 (5.6%)

CONCLUSION

- **LB-102, a novel and potentially first-in-class benzamide $D_2/D_3/5\text{-}HT_7$ receptor antagonist, demonstrated statistically significant efficacy on PANSS scores—showing greater improvements in overall symptoms and positive symptoms compared with placebo—and was generally safe and well-tolerated in the NOVA[1] acute schizophrenia population.**

DISCUSSION

- **This phase 2 clinical trial provided robust evidence demonstrating the efficacy and safety of LB-102 for the treatment of adults with acute schizophrenia, which will inform the continued clinical development of LB-102 for schizophrenia treatment.**
- **A phase 3 clinical development program in schizophrenia is currently being planned.**

References

1. Grattan V, et al. *ACS Omega.* 2019;4(9):14151-14154.
2. Wong DF, et al. *Neuropsychopharmacology.* 2024;50(2):372-377.
3. Biernat L, et al. *Psychopharmacology (Berl).* 2022;239(9):3009-3018.

Acknowledgements

Medical writing and poster development support were provided by The Medicine Group, LLC (New Hope, PA, USA) in accordance with Good Publication Practice guidelines.

Funding

This study and poster development support was sponsored by LB Pharmaceuticals Inc, New York, NY, USA.

Disclosures

AE, **LC**, and **BPL** are full-time employees and shareholders of LB Pharmaceuticals. **NB** serves as a consultant to LB Pharmaceuticals. **ARV** is a co-founder and former Chief Science Officer of LB Pharmaceuticals; he currently 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. **JMK** has served as a consultant to, received honoraria, received travel support, and/or participated in speakers' bureaus for AbbVie, Alkermes, Allergan, Boehringer-Ingelheim, Bristol Myers 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, Bristol Myers Squibb, Boehringer-Ingelheim, Cerevel, Click Therapeutics, 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 UpToDate.

Presented at the 38th European College of Neuropsychopharmacology (ECNP) Congress | October 11–14, 2025 | Amsterdam, The Netherlands