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LB-102 for acute schizophrenia in adults: Results from the phase 2 clinical trial (NOVA¹) with a focus on negative symptoms

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Background

- Schizophrenia is a prevalent and heterogeneous disorder comprising positive, negative, and cognitive symptom domains, yet most approved antipsychotics were designed primarily to address positive symptoms.^{1,2}
- Negative symptoms—including affective flattening, alogia, anhedonia, asociality, and avolition—often emerge early, persist throughout the illness course, and are the strongest predictors of functional disability and economic burden.³⁻⁸
- Even with treatment, many patients experience residual or treatment resistant positive symptoms in addition to substantial metabolic, neurologic, and endocrine adverse effects.^{9,10}
- There are currently no approved treatment options for primary negative symptoms in patients with schizophrenia, underscoring the need for agents that engage novel mechanisms and treat multiple symptom domains.¹¹⁻¹⁴
- LB-102 is a novel D₂/D₃/5-HT₇ antagonist currently in development for schizophrenia and other neuropsychiatric disorders.
- Preclinical assays highlighted receptor binding, pharmacokinetics, and behavioral modification properties for LB-102 that are similar to amisulpride.¹⁵
- A phase 1, open-label PET study showed that LB-102 50 mg daily exhibited similar receptor occupancy under steady-state conditions to amisulpride 400 mg daily.¹⁶
- A phase 1, double-blind, placebo-controlled trial in 64 healthy volunteers demonstrated LB-102 was generally safe and well-tolerated.¹⁷
- Primary analysis of the phase 2 NOVA¹ trial of LB-102 in adults with acute schizophrenia (NCT06179108) highlighted a clinically significant treatment effect on the Positive and Negative Syndrome Scale (PANSS) total score and Clinical Global Impressions–Severity of illness (CGI-S) score after 4 weeks of treatment (see ECNP 2025 presentation: **PS02-1273**).

Objective

- To investigate the treatment effect of LB-102 on negative symptoms in the total population and in the subgroup with negative symptoms, defined as a PANSS Negative Symptoms subscale score of ≥24 at baseline.

Methods

- The phase 2 NOVA¹ clinical trial was a multicenter, randomized, double-blind, placebo-controlled trial in adults (18–55 years) diagnosed with schizophrenia who required hospitalization or continued hospitalization for a current acute exacerbation of psychotic symptoms (**Figure 1**).
- Key inclusion criteria were:
 - PANSS total score of 80–120, PANSS Positive Symptoms subscale score of ≥4 on ≥2 key items, and CGI-S score ≥4.
- 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 (exploratory).
- Primary endpoint:** Change from baseline to week 4 in PANSS total score.
- Secondary endpoints analyzed here:** Change from baseline to week 4 in PANSS Negative Symptoms subscale score.
- Safety:** Treatment-emergent adverse events (TEAEs; MedDRA Version 26.1) and other safety assessments.

Results

- 359 participants were randomized and included in the safety and intent-to-treat populations.
 - 293 participants (82%) completed week 4.
 - 261 participants (73%) completed the trial.
- 171 participants (47.6% of the total population) had a PANSS Negative Symptoms subscale score ≥24 at baseline.
 - Demographics and clinical characteristics were similar across treatment arms (**Table 1**) and consistent with the total population.
- 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 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 least-squares mean changes from baseline to week 4 in PANSS Negative Symptoms subscale score in the total population were (**Figure 3**):
 - Placebo, −1.1
 - LB-102 50 mg, −2.2 (Δ −1.08, *p*=0.0116 vs placebo)
 - LB-102 75 mg, −1.7 (Δ −0.61, *p*=0.1633 vs placebo)
 - LB-102 100 mg, −1.8 (Δ −0.70, *p*=0.2632 vs placebo)
- The least-squares mean changes from baseline to week 4 in PANSS Negative Symptoms subscale score in participants with PANSS Negative Symptoms subscale score ≥24 at baseline (**Figure 4**) were:
 - Placebo, −1.6
 - LB-102 50 mg, −3.4 (Δ −1.70, *p*=0.0045 vs placebo; effect size=0.67)
 - LB-102 75 mg, −2.6 (Δ −1.00, *p*=0.1501 vs placebo, effect size=0.34)
 - LB-102 100 mg, −3.3 (Δ −1.70, *p*=0.0658 vs placebo, effect size=0.60)
- Across all analyses, the treatment effect was seen as early as week 1, which continued through week 4.
- 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.
 - Several common baseline comorbidities, including insomnia, anxiety, headache, and agitation, were amongst the most frequently reported TEAEs.
- No clinically meaningful difference was observed on QTcF (**Table 3**), with stopping criteria not met for any dose.
- 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).

Figure 1. NOVA¹ Trial Design

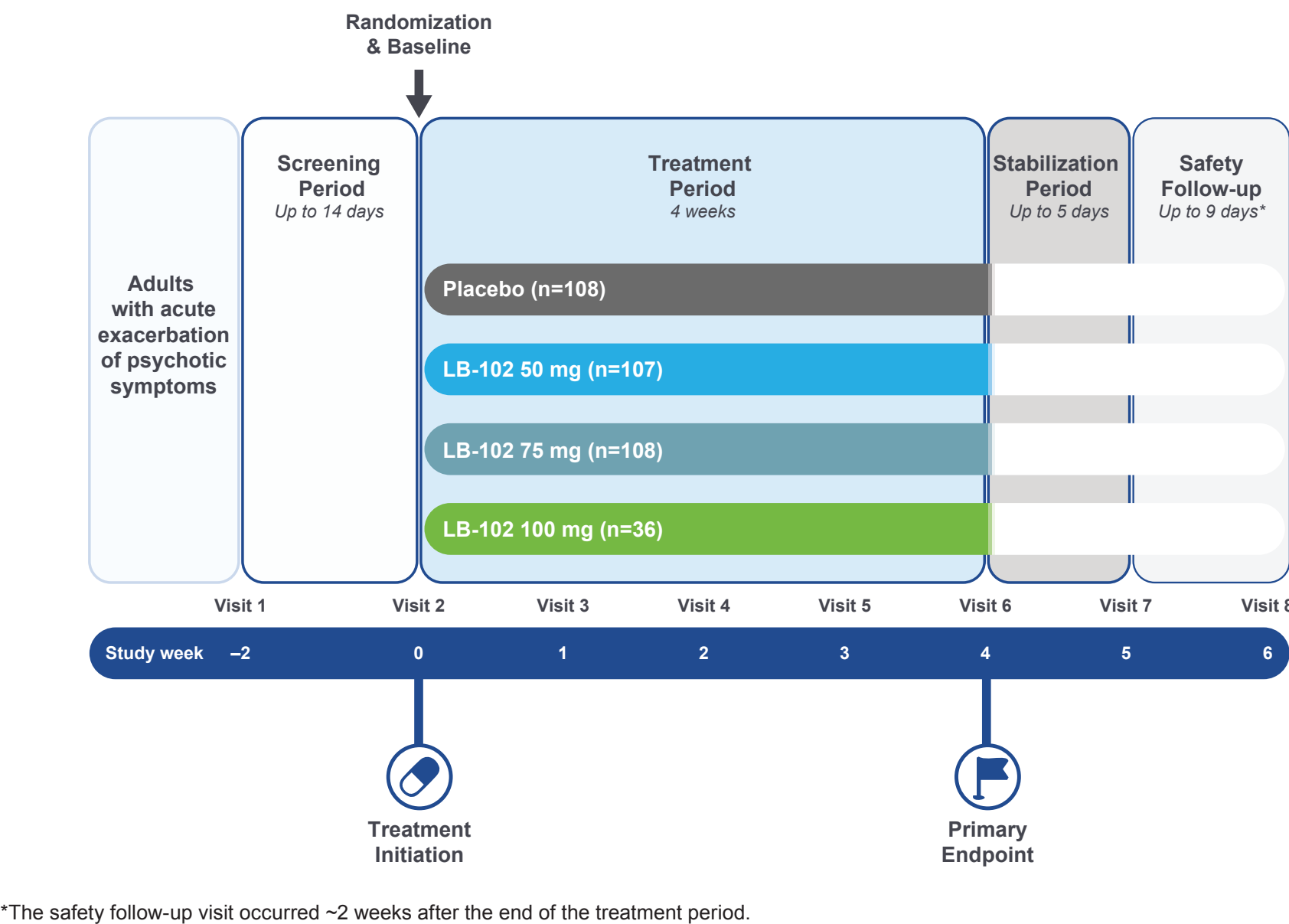


Figure 2. Change in PANSS Total Score in the Total Population

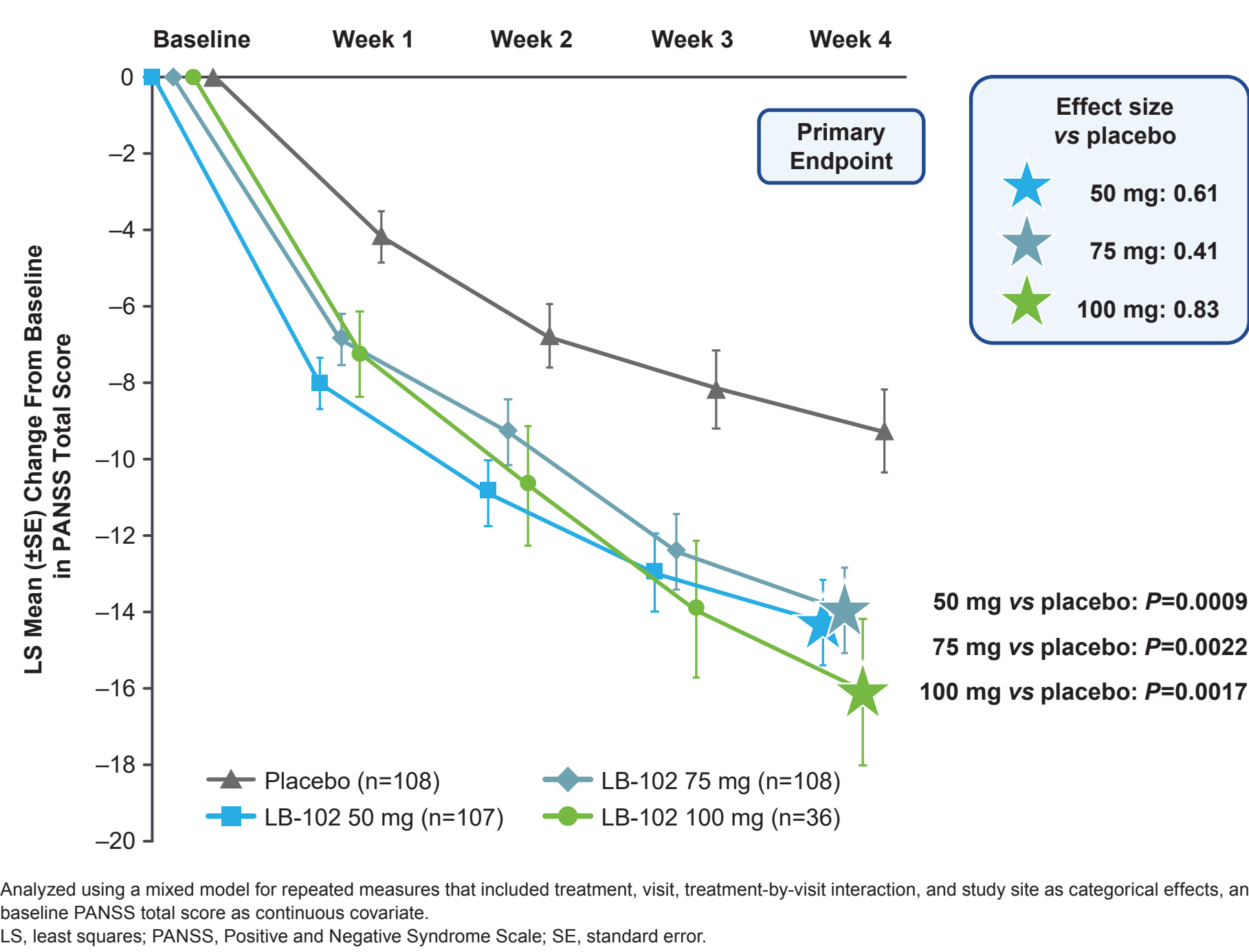


Figure 3. Change in PANSS Negative Symptoms Subscale Score in the Total Population

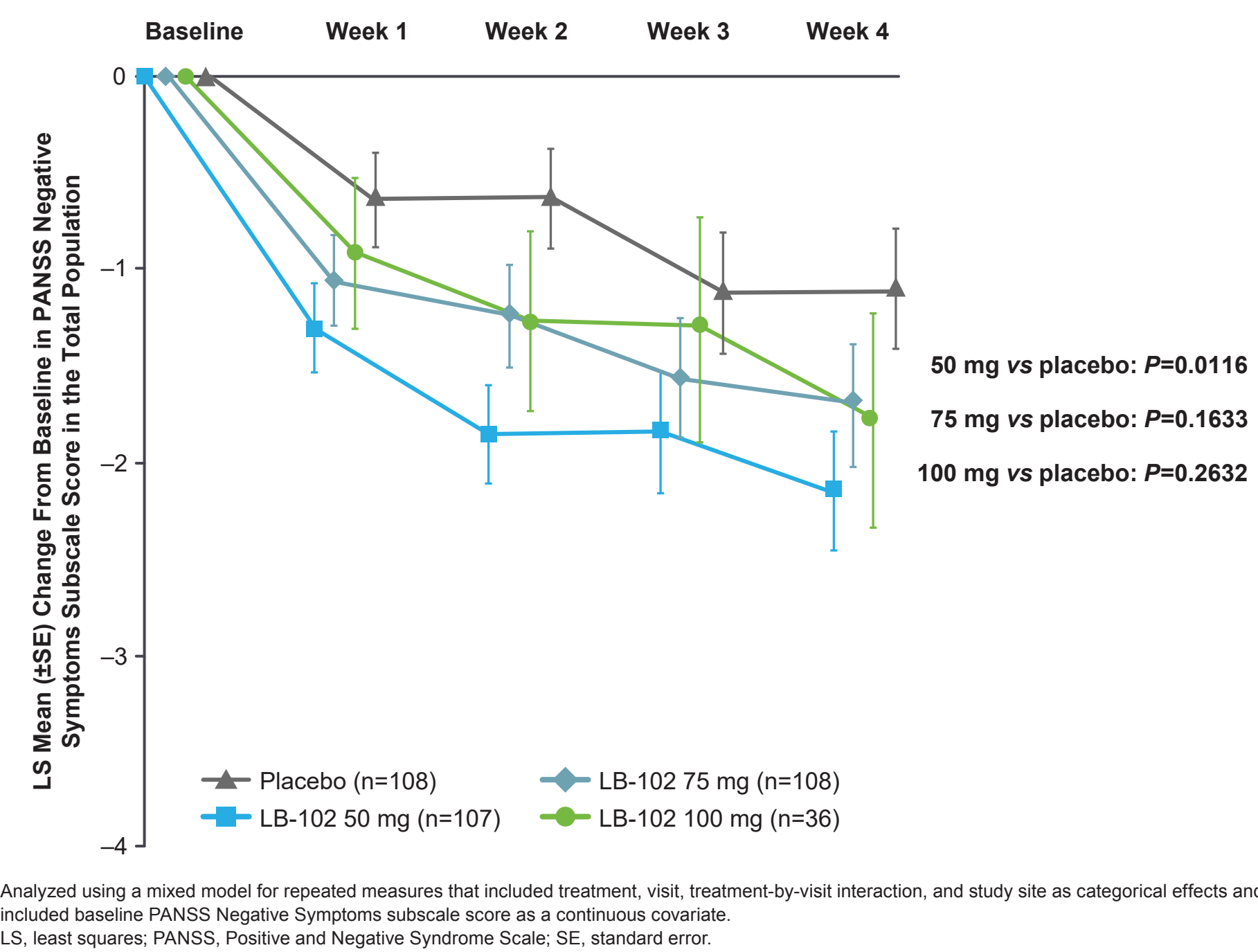


Figure 4. Change in PANSS Negative Symptoms Subscale Score in Participants With PANSS Negative Symptoms Subscale Score ≥24 at Baseline

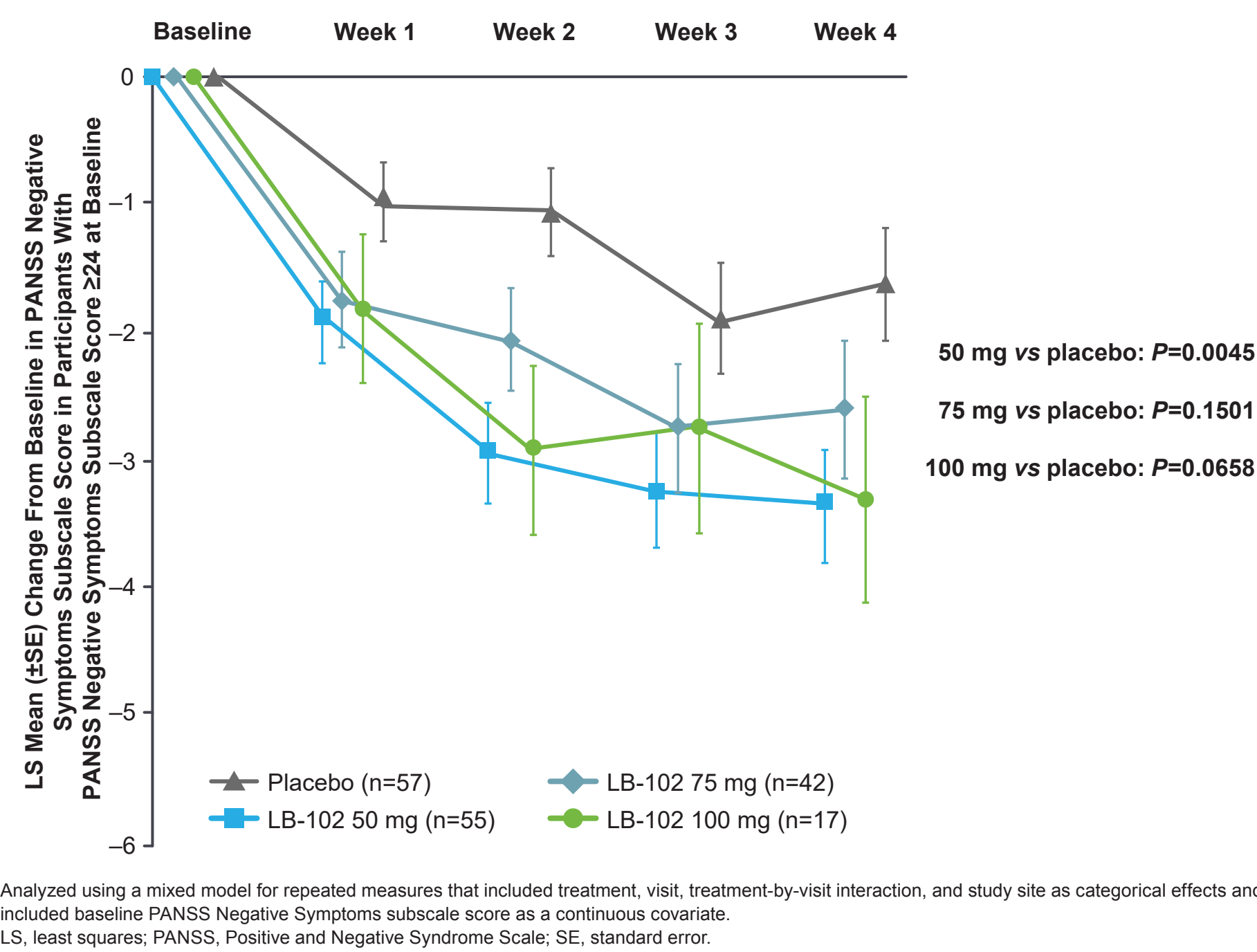


Table 1. Demographics and Baseline Characteristics of Participants With PANSS Negative Symptoms Subscale Score ≥24 at Baseline

	Placebo (n=57)	LB-102 50 mg (n=55)	LB-102 75 mg (n=42)	LB-102 100 mg (n=17)	Overall (N=171)
Age at IC (years), mean (SD)	37.9 (8.4)	38.7 (9.7)	40.5 (9.8)	37.5 (8.7)	38.7 (9.2)
Sex, n (%)					
Male	45 (78.9)	44 (80.0)	33 (78.6)	13 (76.5)	135 (78.9)
Ethnicity, n (%)					
Hispanic or Latino	11 (19.3)	5 (9.1)	4 (9.5)	3 (17.6)	23 (13.5)
Not Hispanic or Latino	46 (80.7)	50 (90.9)	38 (90.5)	14 (82.4)	148 (86.5)
Race, n (%)					
White	12 (21.1)	6 (10.9)	6 (14.3)	4 (23.5)	28 (16.4)
Black or African American	42 (73.7)	47 (85.5)	30 (71.4)	12 (70.6)	131 (76.6)
Asian	0	0	2 (4.8)	0	2 (1.2)
American Indian or Alaska Native	0	0	1 (2.4)	0	1 (0.6)
Other	3 (5.3)	2 (3.6)	3 (7.2)	1 (5.9)	9 (5.3)
Weight at baseline (kg), mean (SD)	87.0 (17.5)	85.7 (21.5)	85.0 (17.5)	85.1 (16.8)	85.9 (18.7)
BMI at baseline (kg/m ²), mean (SD)	28.8 (5.4)	28.0 (6.2)	28.1 (5.3)	27.1 (5.8)	28.2 (5.7)

IC, informed consent; 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 TEAEs in the Total Population

	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%)
QTcF results					
Baseline QTcF (ms), mean	393.4	393.4	394.7	390	–
Change from baseline to Day 28 (ms), mean	1.7	4.9	4.3	5.4	–
QTcF >500 ms*	0	0	0	0	–

Values are the n (%) participants unless indicated otherwise. *At any point during the trial. TEAE, treatment-emergent adverse event.

CONCLUSION

- LB-102, a novel and potentially first-in-class benzamide D₂/D₃/5-HT₇ receptor antagonist, demonstrated a significant improvement in participants with schizophrenia after 4 weeks of treatment, including a clinical improvement in those participants with negative symptoms at baseline.
- LB-102 was generally safe and well-tolerated.

DISCUSSION

- This phase 2 clinical trial provided robust evidence demonstrating the efficacy and safety of LB-102 for adults with acute schizophrenia, including participants with negative symptoms at baseline, informing the ongoing clinical development of LB-102.
- A phase 3 clinical development program for LB-102 in schizophrenia is planned.

References

1. Li P, et al. *Curr Top Med Chem*. 2016;16(29):3385–403.
2. Howes OD, et al. *Curr Pharm Des*. 2009;15(22):2550–9.
3. Salazar de Pablo G, et al. *Br J Psychiatry*. 2023;223(1):282–94.
4. Galderisi S, et al. *Lancet Psychiatry*. 2018;5(8):664–77.
5. Galderisi S, et al. *World Psychiatry*. 2020;19(1):81–91.
6. Sicras-Mainar A, et al. *BMC Psychiatry*. 2014;14:225.
7. Bobes J, et al. *J Clin Psychiatry*. 2010;71(3):280–6.
8. Hegarty JD, et al. *Am J Psychiatry*. 1994;151(10):1409–16.
9. Stroup TS, Gray N. *World Psychiatry*. 2018;17(3):341–56.

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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, Mapl, Maglight, Merck, Minerva, Neurocrine, Newron, Novartis, NW PharmaTech, Otsuka, Roche, Salada, Sunovion, and Teva; has participated on advisory boards for AbbVie, Alkermes, BMS, 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, Salada, Terran, and Vanguard Research Group; and receives royalties from UpToDate.