LB-102 for Acute Schizophrenia in Adults

Results From the Phase 2 NOVA[1] Clinical Trial, With a Focus on PANSS Marder Factor Scores

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Disclosure information

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Potential Conflict of Interest	Organization
Consultant, honoraria, travel support, and/or speakers' bureaus	**LB Pharmaceuticals**
Stock / stock options	**LB Pharmaceuticals**
Grant support	None
Advisory board participation	None
Royalties	None

Disclosure: LB-102 is an investigational compound under development by LB Pharmaceuticals Inc.

Funding: This study and medical writing support was funded by LB Pharmaceuticals Inc.

Acknowledgments: Medical writing support was provided by The Medicine Group, LLC (New Hope, PA) in accordance with Good Publication Practice guidelines.

Background

LB-102: A Novel Benzamide for the Treatment of Neuropsychiatric Disorders

Preclinical

Receptor binding similar to amisulpride[1]

PK/PD

Dose-proportional pharmacokinetics, once-daily dosing with predictable exposure

Phase 1

Generally safe and well tolerated in 64 healthy volunteers[2]

PET

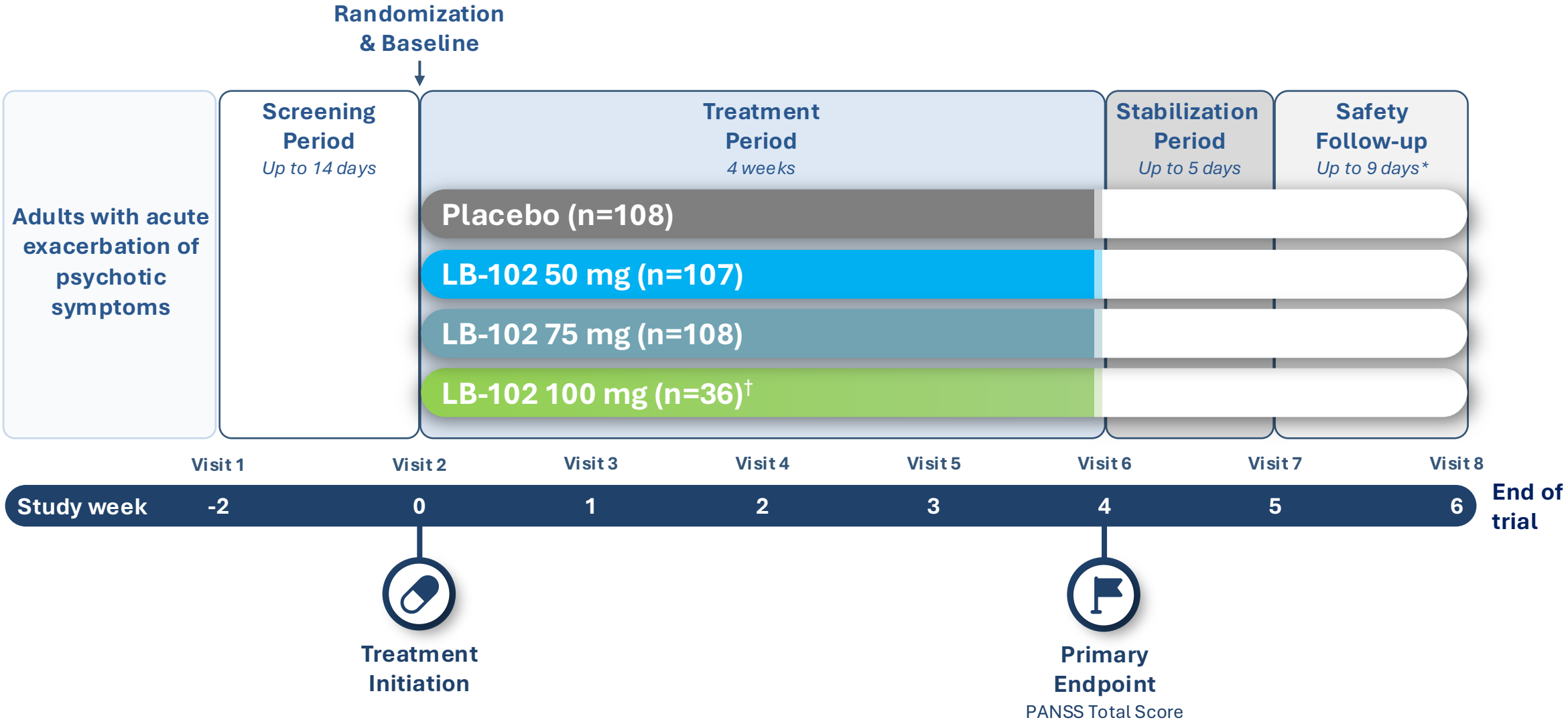
Dopamine receptor occupancy is between ~70% and ~80% for LB-102 50 mg and 100 mg when at steady-state[3]

LB-102 (*N*-methyl amisulpride) is a novel $D_2/D_3/5\text{-}HT_7$ antagonist with minimal off-target activity[1]

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

NOVA[1] Trial

Efficacy, Safety, and Tolerability of LB-102 in Adults With Schizophrenia



ClinicalTrials.gov identifier: NCT06179108. *The safety follow-up visit occurred ~2 weeks after the end of the treatment period. † LB-102 100mg arm considered exploratory.

NOVA[1] Trial

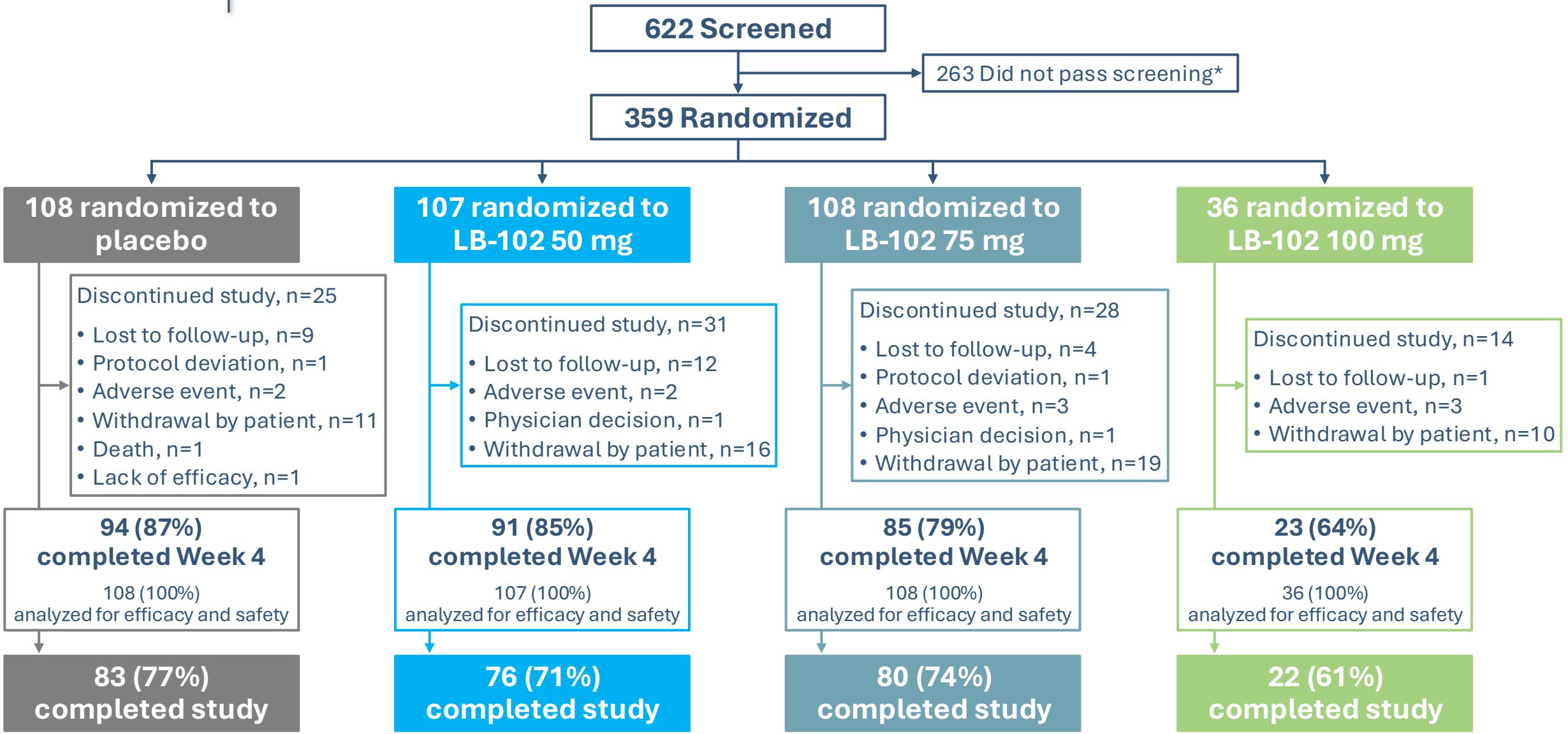
Demographics and Baseline Characteristics

		Placebo (n=108)	LB-102 50 mg (n=107)	LB-102 75 mg (n=108)	LB-102 100 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 (%)	Hispanic or Latino	17 (16%)	12 (11%)	8 (7%)	6 (17%)	43 (12%)
	Not Hispanic or Latino	91 (84%)	95 (89%)	100 (93%)	30 (83%)	316 (88%)
Race, n (%)	Black	80 (74%)	87 (81%)	83 (77%)	25 (69%)	275 (77%)
	White	24 (22%)	17 (16%)	18 (17%)	9 (25%)	68 (19%)
	Asian	1 (1%)	0	2 (2%)	0	3 (1%)
	Native American	0	0	2 (2%)	0	2 (1%)
	Multiple	0	2 (2%)	1 (1%)	1 (3%)	4 (1%)
	Other	3 (3%)	1 (1%)	2 (2%)	1 (3%)	7 (2%)
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, 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.

NOVA[1] Trial

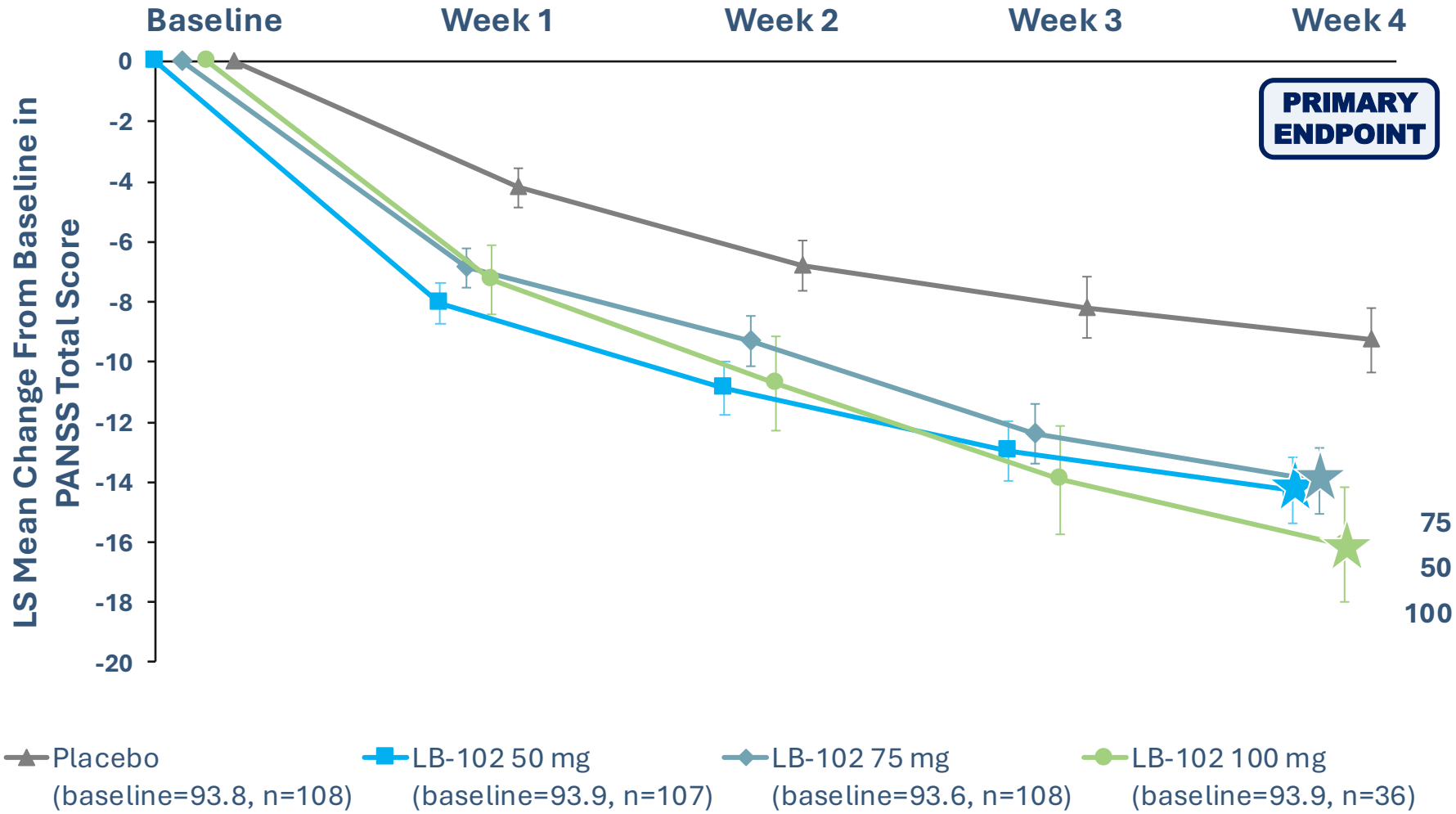
Participant Disposition



*Initially, 270 participants did not pass screening; however, after re-screening 13 participants, 7 were found to be eligible and were randomized.

NOVA[1] Trial

Change From Baseline Through Week 4 in PANSS Total Score



Effect size *vs* placebo

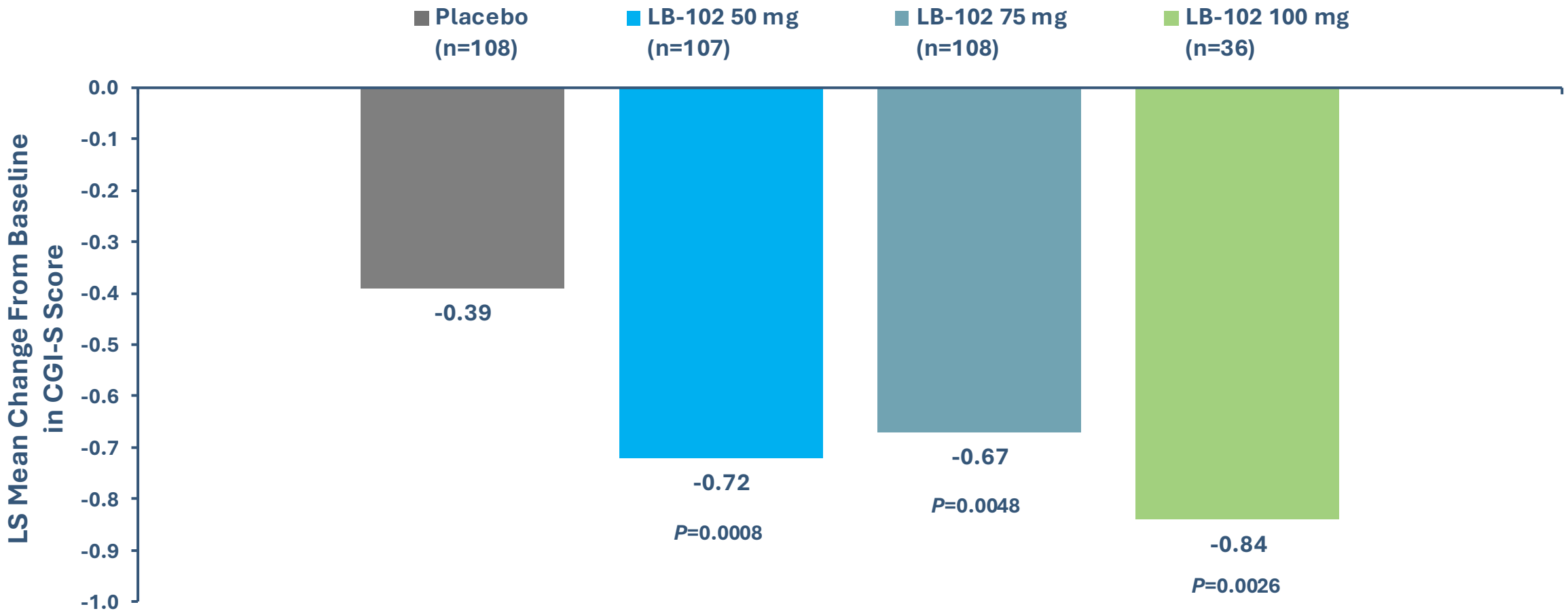
- 50 mg: 0.61
- 75 mg: 0.41
- 100 mg: 0.83*

75 mg *vs* placebo: *P*=0.0022
50 mg *vs* placebo: *P*=0.0009
100 mg *vs* placebo: *P*=0.0017

Error bars represent standard error. LS, least squares; PANSS, Positive And Negative Syndrome Scale.
Calculation of effect size based on completer population. *LB-102 100mg arm considered exploratory, with nominal p-value.

NOVA[1] Trial

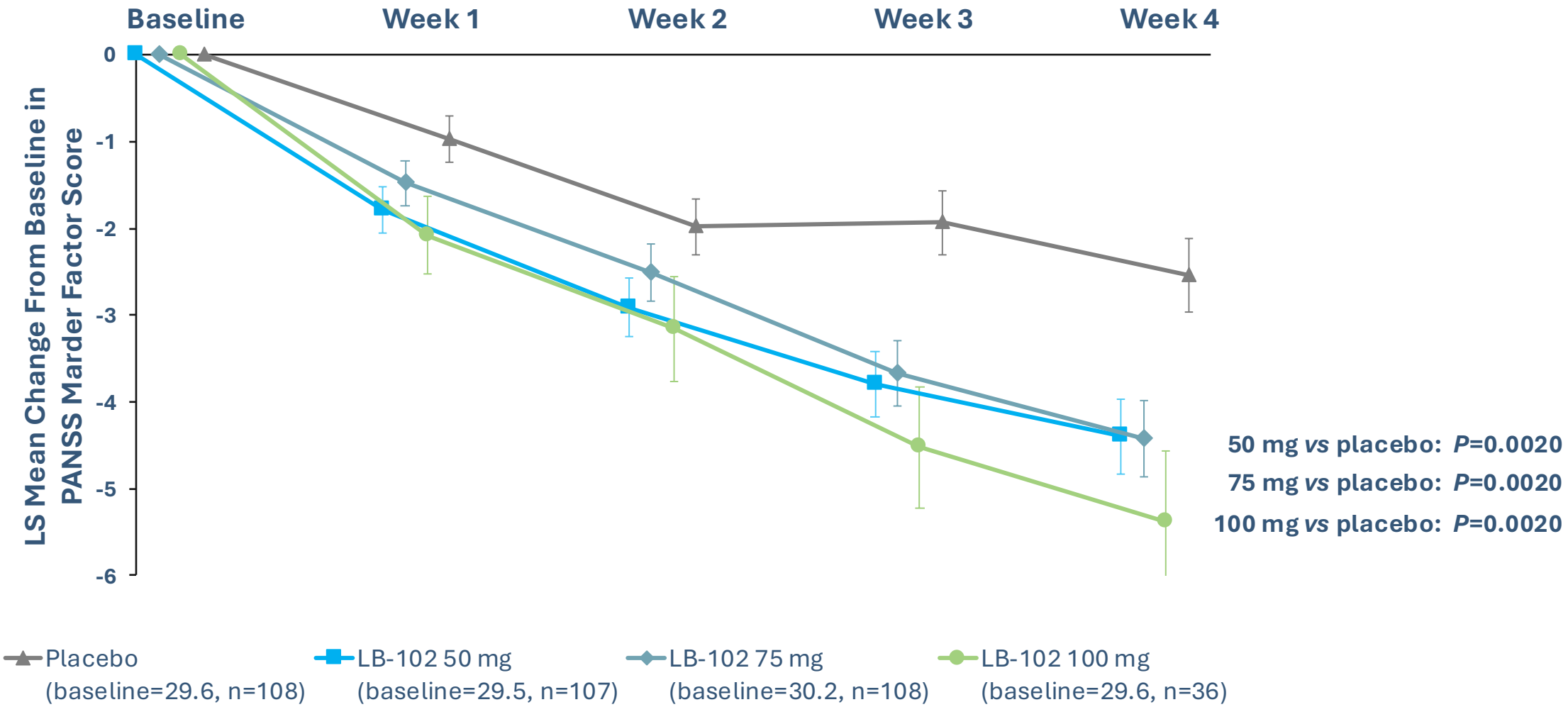
Change From Baseline in CGI-S Score After 4 Weeks of Treatment



LS, least squares; PANSS, Positive And Negative Syndrome Scale.

NOVA[1] Trial

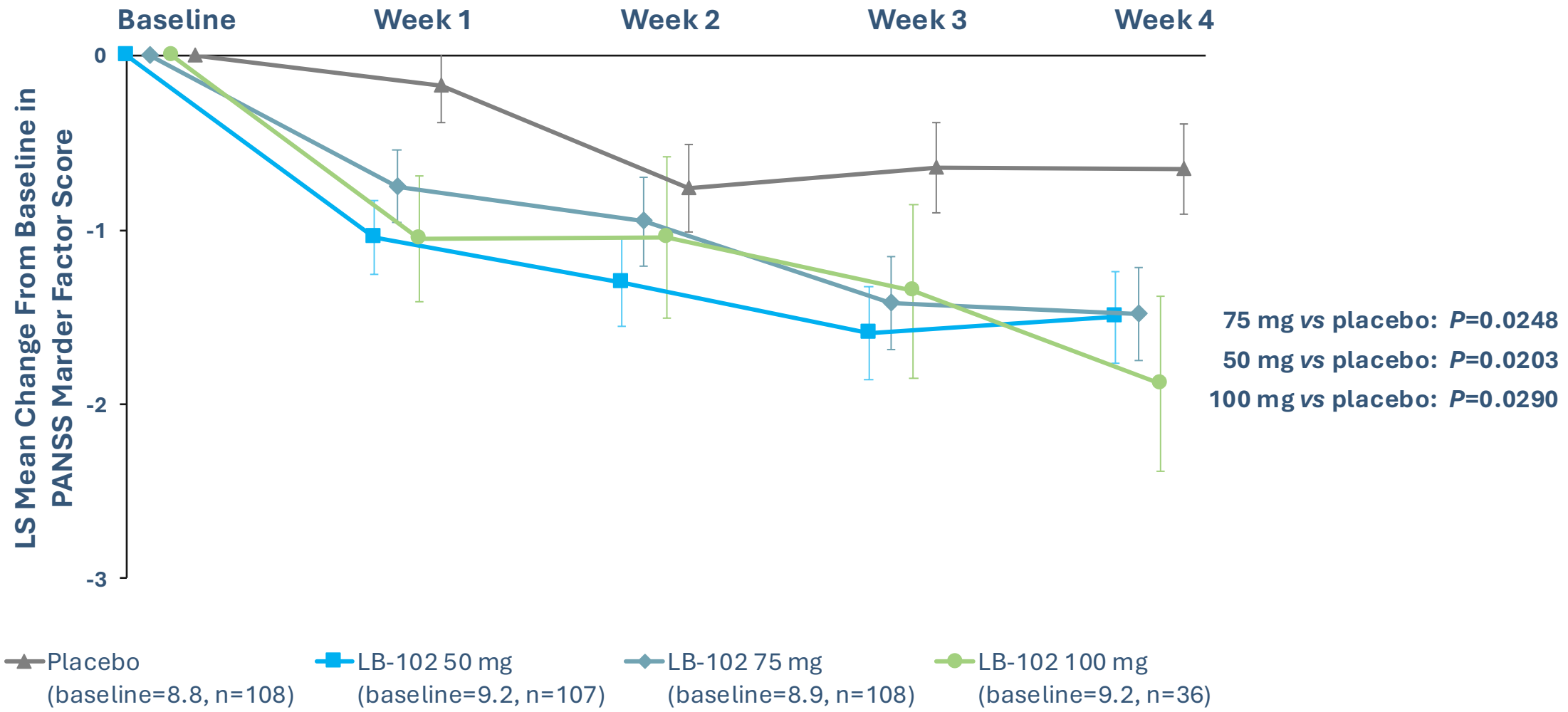
Change From Baseline Through Week 4 in PANSS Marder Positive Symptoms



Error bars represent standard error. LS, least squares; PANSS, Positive And Negative Syndrome Scale. Marder SR, et al. *J Clin Psychiatry*. 1997;58(12):538-546.

NOVA[1] Trial

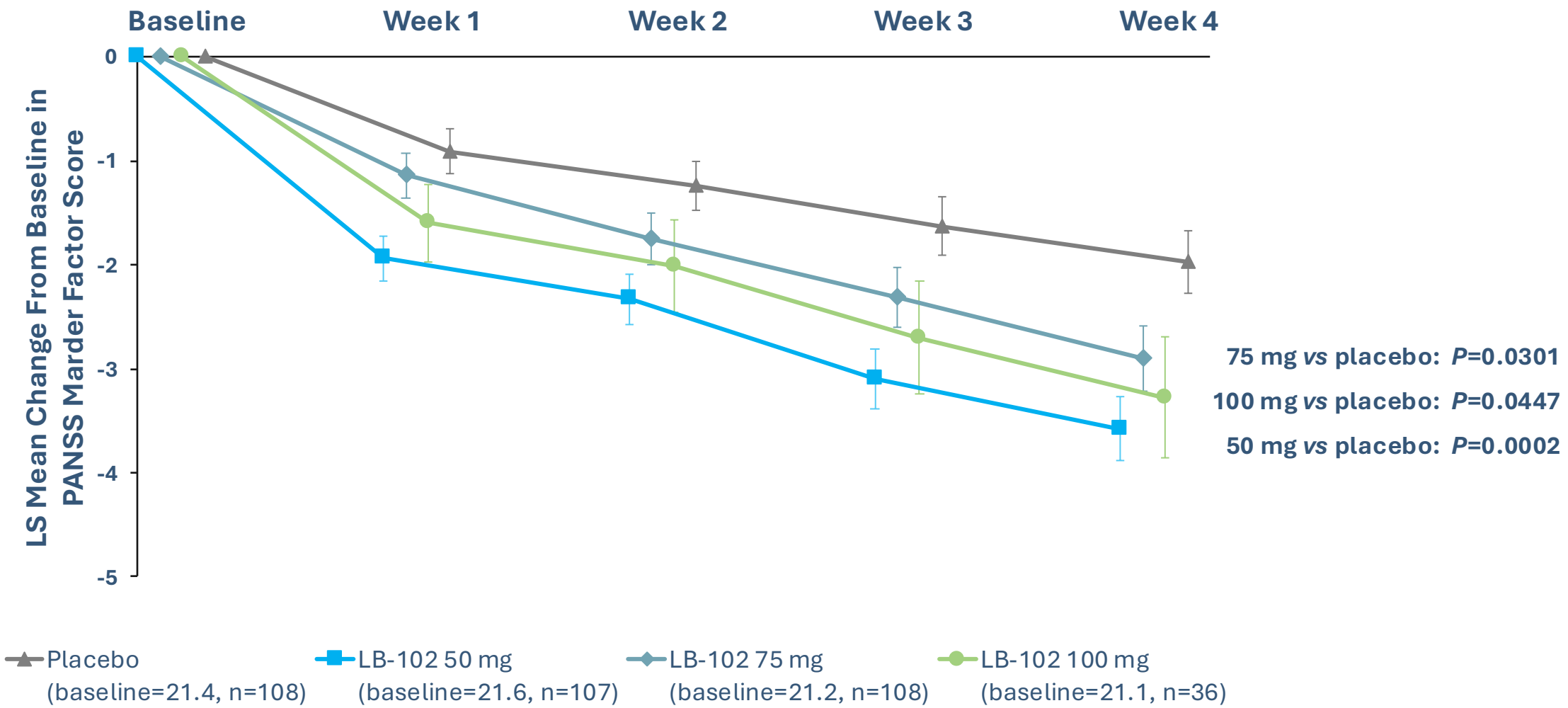
Change From Baseline Through Week 4 in PANSS Marder Uncontrolled Hostility/Excitement



Error bars represent standard error. LS, least squares; PANSS, Positive And Negative Syndrome Scale. Marder SR, et al. *J Clin Psychiatry*. 1997;58(12):538-546.

NOVA[1] Trial

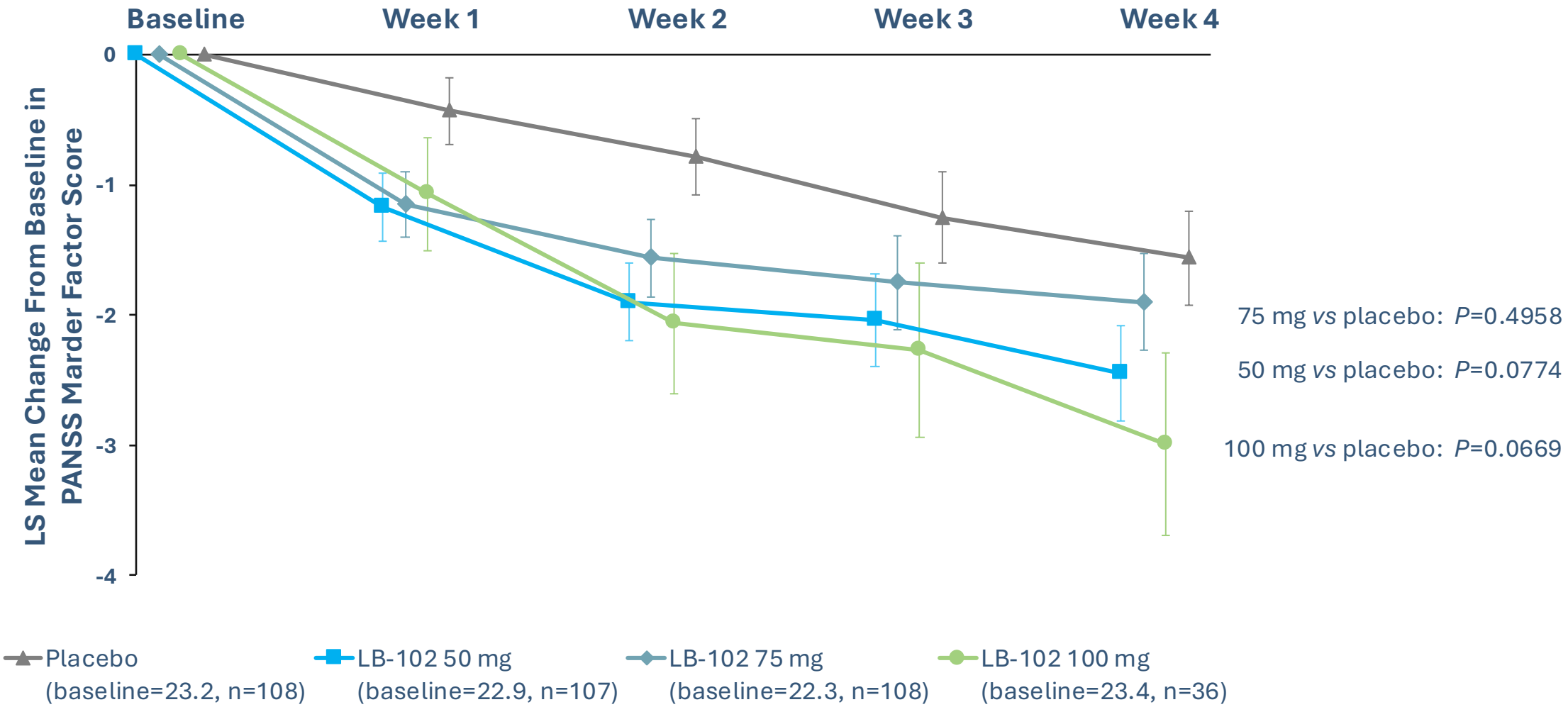
Change From Baseline Through Week 4 in PANSS Marder Disorganized Thought



Error bars represent standard error. LS, least squares; PANSS, Positive And Negative Syndrome Scale. Marder SR, et al. *J Clin Psychiatry*. 1997;58(12):538-546.

NOVA[1] Trial

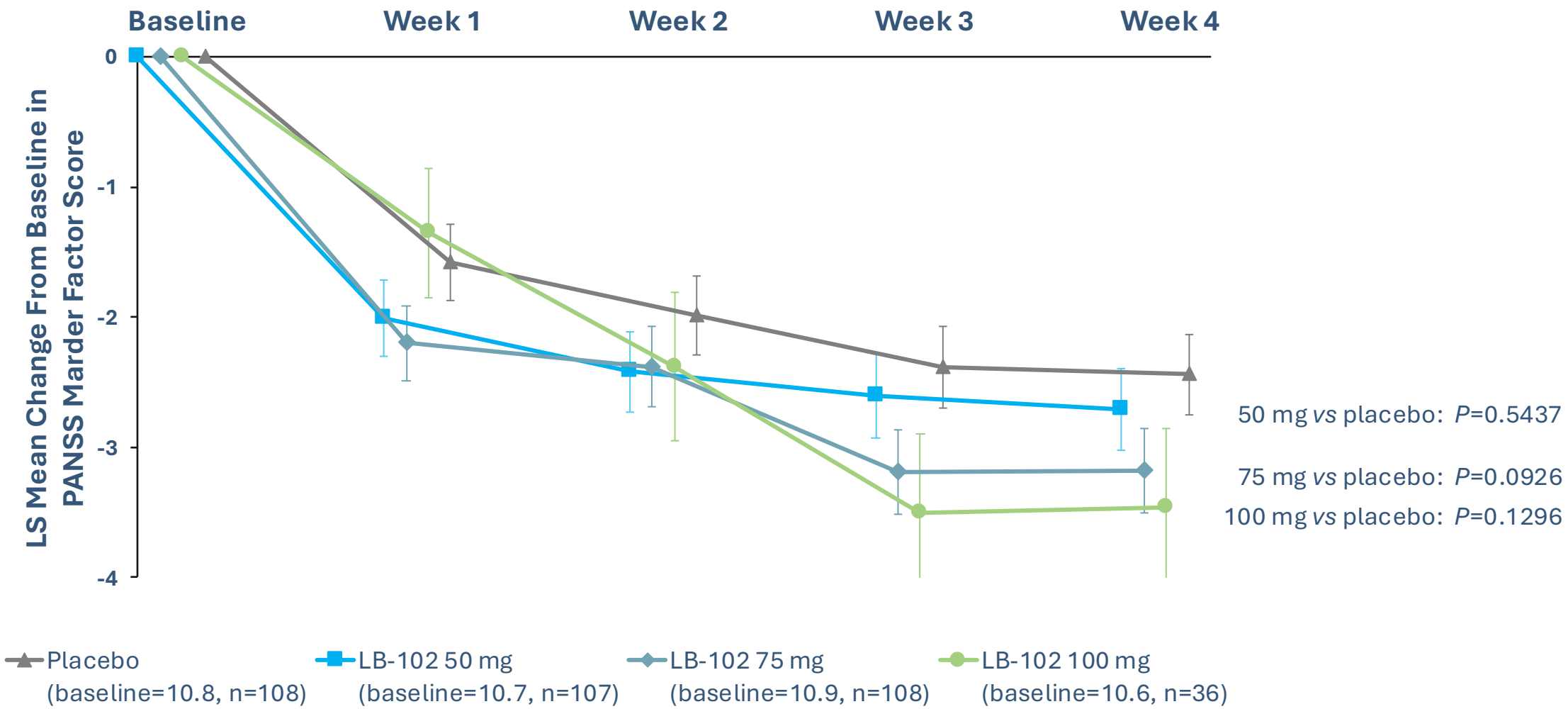
Change From Baseline Through Week 4 in PANSS Marder Negative Symptoms



Error bars represent standard error. LS, least squares; PANSS, Positive And Negative Syndrome Scale. Marder SR, et al. *J Clin Psychiatry*. 1997;58(12):538-546.

NOVA[1] Trial

Change From Baseline Through Week 4 in PANSS Marder Anxiety/Depression



Error bars represent standard error. LS, least squares; PANSS, Positive And Negative Syndrome Scale. Marder SR, et al. *J Clin Psychiatry*. 1997;58(12):538-546.

NOVA[1] Trial

Overview of Adverse Events Through Week 4

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%)

TEAE, treatment-emergent adverse event.

NOVA[1] Trial

Most Common Treatment-Emergent Adverse Events

(≥5% of 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%)

At screening, participants self-reported a high incidence of insomnia (74.1%), anxiety (58.8%), headache (40.1%), and agitation (30.1%)

*Sum of the preferred terms “hyperprolactinemia” and “blood prolactin increased.”

NOVA[1] Trial

TEAEs of Special Interest

	Participants, n (%)	Placebo (n=108)	50 mg (n=107)	75 mg (n=108)	100 mg (n=36)
Related to Extrapyramidal Symptoms (EPS)	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%)**
Related to Prolactin Increase	Galactorrhea	0	2 (1.9%)	1 (0.9%)	0
	Breast enlargement	0	0	0	1 (2.8%)
	Erectile dysfunction	0	0	0	1 (2.8%)
	Total related to prolactin	**0**	**2 (1.9%)**	**1 (0.9%)**	**2 (5.6%)**
QTcF Prolongation	Baseline QTcF (ms)	393.5	393.3	394.8	390.0
	Change at Day 28 (ms)	**1.2**	**4.9**	**4.3**	**5.4**
Sedation		0	0	1 (0.9%)	0

EPS, extrapyramidal symptoms; ms, millisecond; QTcF, QT corrected for heart rate by Fridericia's cube root formula; TEAE, treatment-emergent adverse event

NOVA[1] Trial

LB-102: A Novel Benzamide for the Treatment of Schizophrenia

Robust, clinically significant treatment effect

– Reduction in PANSS observed as early as Week 1

Clinical treatment effect across Marder Factor Scores

– Highlights a potentially broad, multifactorial antipsychotic effect

Dose-related efficacy profile over 4 weeks of treatment

– Dose-response suggests improved benefits with 100 mg

Generally safe and well-tolerated, with negligible sedation

– Low rates of EPS-related adverse events, including akathisia

CGI-S, Clinical Global Impressions–Severity of illness; EPS, extrapyramidal symptoms; PANSS, Positive And Negative Syndrome Scale.