# Treatment Effects of Paliperidone Palmitate 6-Month Formulation on Negative Symptoms in Patients With Schizophrenia: Post-Hoc Analysis Over 3 Years

AUTHORS: Jordy Mehawej,<sup>1\*</sup> José Antunes,<sup>2</sup> Camilo Obando,<sup>1</sup> Ibrahim Turkoz,<sup>1</sup> Liping Sun,<sup>3</sup> Leslie Killion,<sup>4</sup> R. Karl Knight<sup>1</sup>

AFFILIATIONS: <sup>1</sup>Johnson & Johnson, Titusville, NJ, USA; <sup>2</sup>Johnson & Johnson, Porto Salvo, Portugal; <sup>3</sup>Cytel, Cambridge, MA, USA; <sup>4</sup>Johnson & Johnson, Horsham, PA, USA

\*Presenting Author

# Introduction

- Schizophrenia is a complex and often debilitating neuropsychiatric disorder, in which negative symptoms, cognitive impairments, and functional deficits are major contributors to disability.<sup>1,2</sup>
- Negative symptoms can persist over extended periods, with their remission recognized as essential for functional recovery in patients with Schizophrenia.<sup>1,2</sup>
- Paliperidone palmitate 6-month formulation (PP6M) has demonstrated efficacy in patients with schizophrenia in preventing relapse in a 12-month phase 3 noninferiority double-blind (DB) study (NCT03345342)<sup>3</sup> and in 24-month single-arm, open-label extension (OLE; NCT04072575)<sup>4</sup> of this DB study.

# Objective

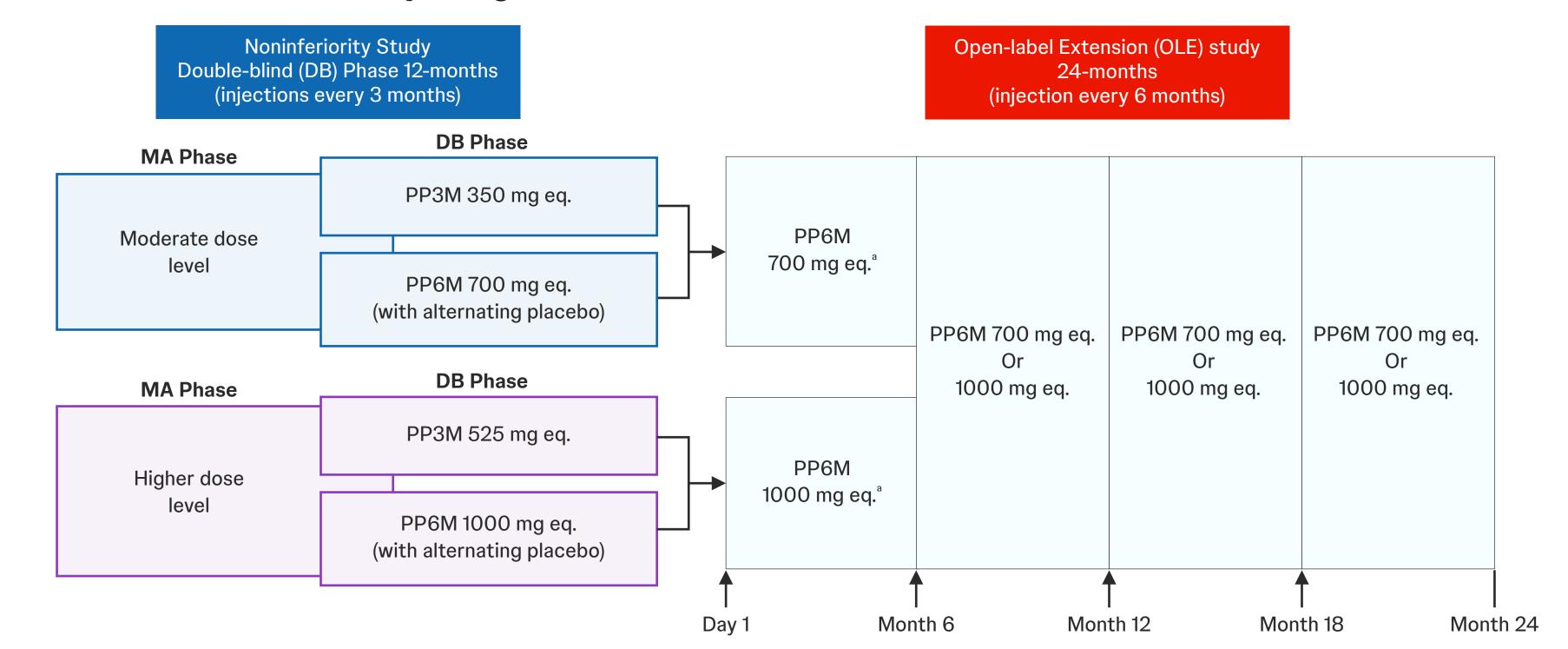
This post-hoc analysis assessed the effect of PP6M on negative symptoms over 3 years.

# Methods

# Study design

- Adult patients with schizophrenia previously stabilized on paliperidone palmitate 1-month/paliperidone palmitate 3-month (PP1M/PP3M) completing 12-month DB phase of noninferiority study (NCT03345342) of PP6M/PP3M without relapse, continued on PP6M in 24-month, OLE (NCT04072575) (**Figure 1**).
- A subset of patients with prominent negative symptoms (≥2 negative symptoms items [from N1-N5, N7]) rated ≥4 (moderate) and Positive and Negative Syndrome Scale (PANSS) negative subscale (N1-N5, N7) sum score ≥15, from these studies were included in this post-hoc analysis.

#### FIGURE 1. Overview of Study design



<sup>a</sup>The initial dose of PP6M in this study was determined based on the dose level ("moderate" or "higher") that the participant was receiving during the double-blind Phase of noninferiority study. The PP6M dose level was to be adjusted (to 700 or 1000 mg eq.) later in the study, based on clinical judgment. However, the long-acting nature of PP6M was to be taken into consideration. Any dose change might have taken many months to become apparent. ↑=PP6M injection, EOS=End of Study; MA=Maintenance; PP3M=paliperidone palmitate 3-month formulation.

#### Assessments

- Improvements in following over 36-months were assessed:
- PANSS Negative Subscale Score
- PANSS Factor Score for Negative Symptoms
- Secondary negative symptoms factor scores for Disorganized Thoughts, Uncontrolled Hostility or Excitement, Anxiety or Depression
- Functional improvements in Personal and Social Performance Scale (PSP) total score

#### Statistical analysis

- PANSS Total, Factor, and Symptom scores, and PSP Total score were analyzed descriptively.
- No adjustments were made for multiplicity.

# Results

# Baseline demographic and clinical characteristics of subset of patients with negative symptoms

- A total of 130 patients who presented with prominent negative symptoms, completed DB phase; mean standard deviation [SD] age: 42.8 (12.09) years; 71.5% male (**Table 1**).
- Demographics and baseline characteristics were similar between the PP6M and PP3M groups in the DB phase.
- Of 130 patients, 113 completed the DB phase without relapse, and 31 patients continued PP6M in the OLE (PP6M/PP6M=23; PP3M/PP6M=8).

#### TABLE 1. Baseline demographic and clinical characteristics of subset of patients with negative symptoms

	PP3M (N=34)	PP6M (N=96)	Total (N=130)
Age, mean (SD), years	41.4 (11.55)	43.3 (12.30)	42.8 (12.09)
Sex, Male, n (%)	23 (67.6%)	70 (72.9%)	93 (71.5%)
Race, n (%)			
Asian	2 (5.9%)	10 (10.4%)	12 (9.2%)
Black or African American	6 (17.6%)	15 (15.6%)	21 (16.2%)
Native Hawaiian or Other Pacific Islander	O	1 (1.0%)	1 (0.8%)
White	24 (70.6%)	69 (71.9%)	93 (71.5%)
Multiple	2 (5.9%)	O	2 (1.5%)
Not reported	O	1 (1.0%)	1 (0.8%)
Baseline (OL) weight, mean (SD), kg	84.7 (16.68)	83.5 (20.17)	83.8 (19.27)
Baseline (OL) BMI, mean (SD), kg/m²	29.3 (5.46)	28.3 (5.85)	28.6 (5.75)
Duration of psy hosp prior to study entry, mean (SD), days <sup>a</sup>	55.9 (70.81)	101.3 (98.78)	90.9 (94.18)
Baseline (MA) PANSS, mean (SD)	61.0 (5.17)	59.6 (5.12)	60.0 (5.15)
Baseline (DB) PANSS, mean (SD)	58.6 (7.18)	57.6 (6.09)	57.8 (6.38)
Baseline (MA) PSP, mean (SD)	52.9 (9.54)	55.4 (9.39)	54.7 (9.46)
Baseline (DB) PSP, mean (SD)	55.2 (10.26)	56.5 (10.23)	56.2 (10.21)

# Improvements in PANSS Negative Subscale Score

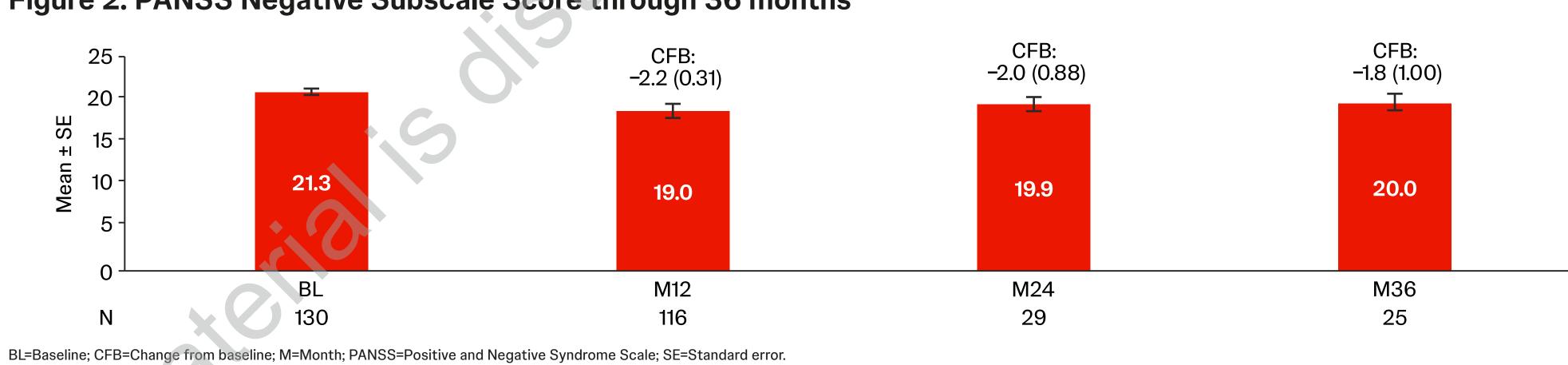
 Mean (standard error [SE]) noninferiority study baseline PANSS Negative Subscale Score was 21.3 (0.21) indicating moderate to severe level of negative impairment in enrolled patients.

oitalization for psychosis any time prior to study start (not restricted to 24 months prior to study start). BMI=Body mass index; DB=Double-blind; MA=Maintenance; OL=Open-label phase of DB study;

- The PANSS Negative Subscale Score showed improvements throughout the 12-months DB phase of the noninferiority study (Figure 2).
- The improvement was maintained through 36 months in OLE study (mean [SE]=20.0 [0.95]).

PANSS=Positive and Negative Syndrome Scale; PP3M=Paliperidone palmitate 3-month formulation; PP6M=Paliperidone palmitate 6-month formulation; SD=Standard deviation

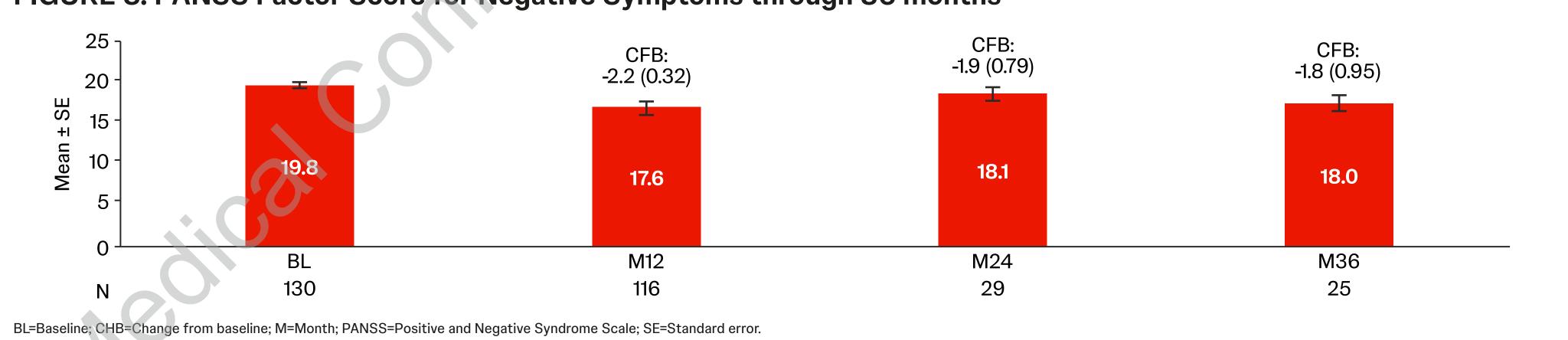
# Figure 2. PANSS Negative Subscale Score through 36 months



# Improvements in PANSS Factor Score for Negative Symptoms

- Mean (SE) noninferiority study baseline PANSS Factor Score for Negative Symptoms was 19.8 (0.26).
- The PANSS Factor Score for Negative Symptoms showed improvements throughout the 12 months DB phase of the noninferiority study (**Figure 3**).
- The improvements were maintained through 36-months in OLE study (mean [SE]: 18.0 [0.86]).

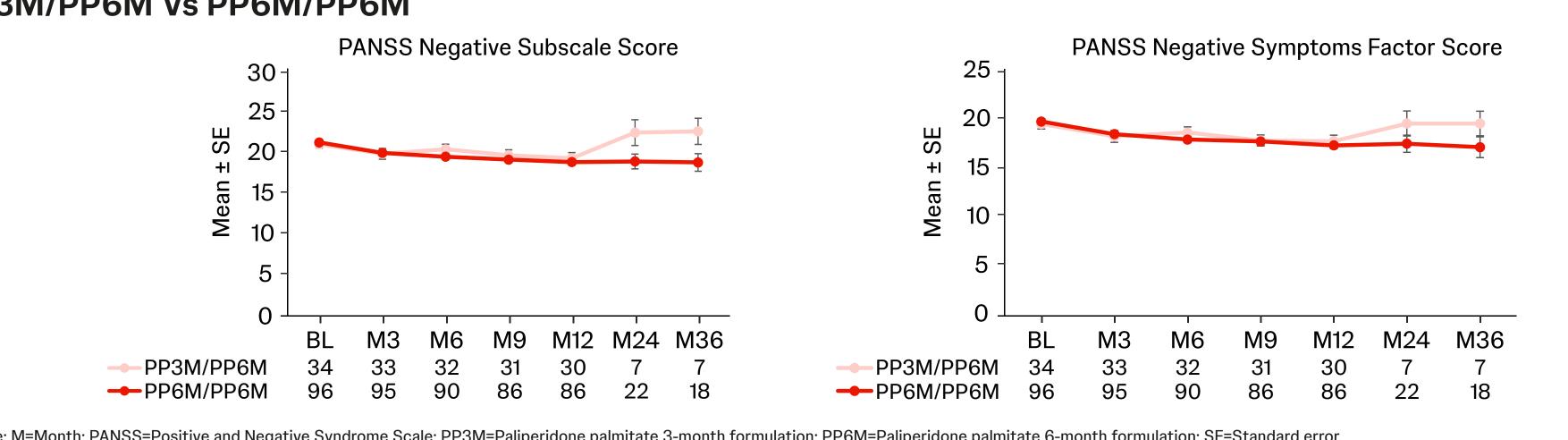
# FIGURE 3. PANSS Factor Score for Negative Symptoms through 36 months



# Improvements in PANSS Negative Subscale Score and Negative Symptoms Factor Score through 36-months in PP3M/PP6M Vs PP6M/PP6M

The Negative Subscale Score and Negative Factor Symptoms Score showed a more consistent gradual decline in PP6M/PP6M patients compared to PP3M/PP6M patients (Figure 4).

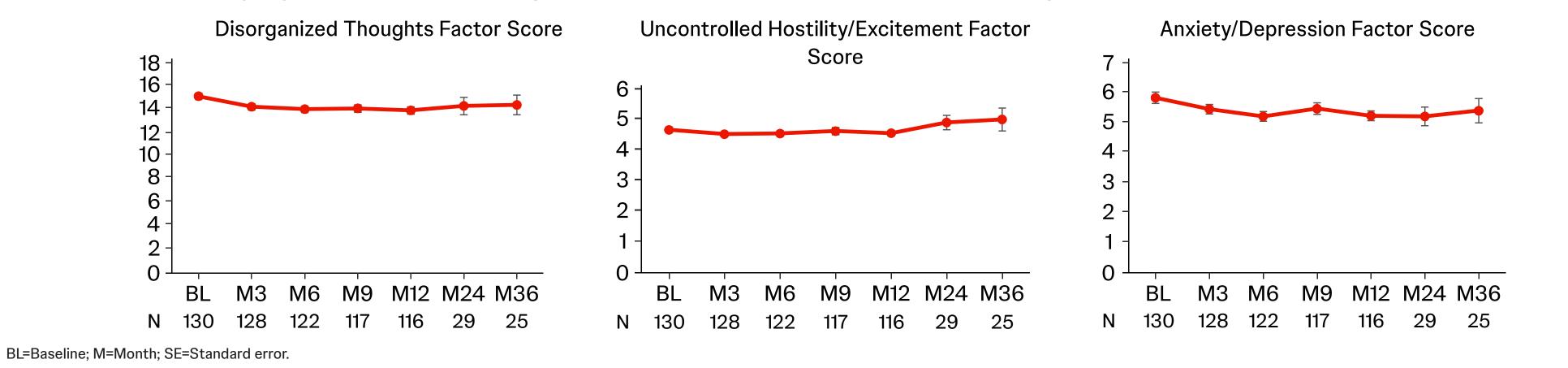
FIGURE 4. Mean (SE) of PANSS Negative Subscale Score and Negative Symptoms Factor Score through 36 months in PP3M/PP6M Vs PP6M/PP6M



### Secondary negative symptoms factor scores

• Through 36 months, secondary negative symptoms factor scores for Disorganized Thoughts, Uncontrolled Hostility/ Excitement, and Anxiety/Depression remained stable relative to the noninferiority study baseline (**Figure 5**).

## FIGURE 5. Mean (SE) of Secondary negative symptoms factor scores through 36 months



# Functional improvements

- Mean (SE) noninferiority study baseline PSP total score was 54.7 (0.83).
- The PSP total score showed improvements throughout the 36-months of the study:
  Mean (SE) at 12-months: 58.4 (1.06); mean (SE) change from noninferiority study baseline (CFB): 3.9 (0.69)
- The functional improvements were observed through 36-months in both PP3M/PP6M and PP6M/PP6M groups. **Safety**

Mean (SE) at 36-months: 66.2 (2.87); mean (SE) change from noninferiority study baseline (CFB): 7.5 (2.10)

• The subset of patients with negative symptoms had similar safety profile as that of total study populations.

# Conclusions



Patients with schizophrenia displaying prominent negative symptoms, treated long-term (over 3-years) with PP6M

- Maintained improved negative symptoms levels
- Maintained functional improvements
- Did not develop secondary negative symptoms

#### Limitations

- The lack of a comparator in the 2 year extension and post hoc nature of this analysis of negative symptoms of schizophrenia may limit broader interpretation of the results.
- Limited number of patients met the criteria for low positive symptoms at baseline.

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# Disclosures

**Jordy Mehawej, José Antunes, Camilo Obando, Ibrahim Turkoz, Leslie Killion,** and **R. Karl Knight** are employees of Johnson & Johnson and may hold stocks/stock options in Johnson & Johnson. **Liping Sun** is an employee of Cytel on assignment at Johnson & Johnson.

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