A Placebo-Controlled, Single Blind Extension Study (OA-07) Evaluating the Safety and Efficacy of Lorecivivint in Subjects with Severe Osteoarthritis of the Knee: Radiographic and Pain Outcomes at 24 and 36 months

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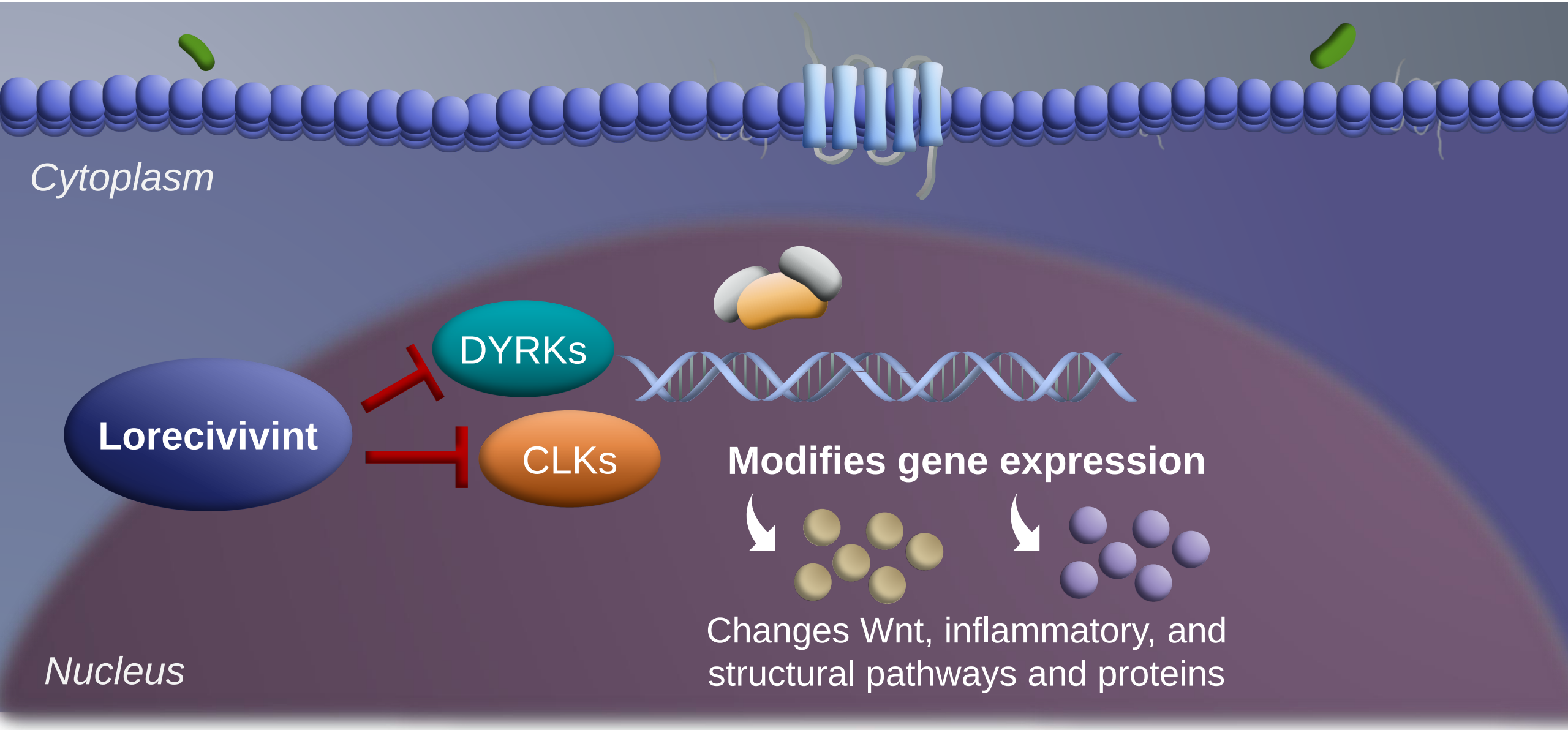
Disclosures

- T. McAlindon:
  - Consultant and Investigator, Biosplice Therapeutics,
  - Consultant: Kolon TissueGene, Organogenesis, Remedium-Bio, Medipost, ChemoCentryx, Xalud
  - Business: Ambulomics Inc

- Y. Yazici, C.J. Swearingen, H. Ghandehari, J. Britt, I. Simsek, M. Fineman, S. Kennedy, J. Tambiah
  - Current or former employees of Biosplice Therapeutics, Inc.

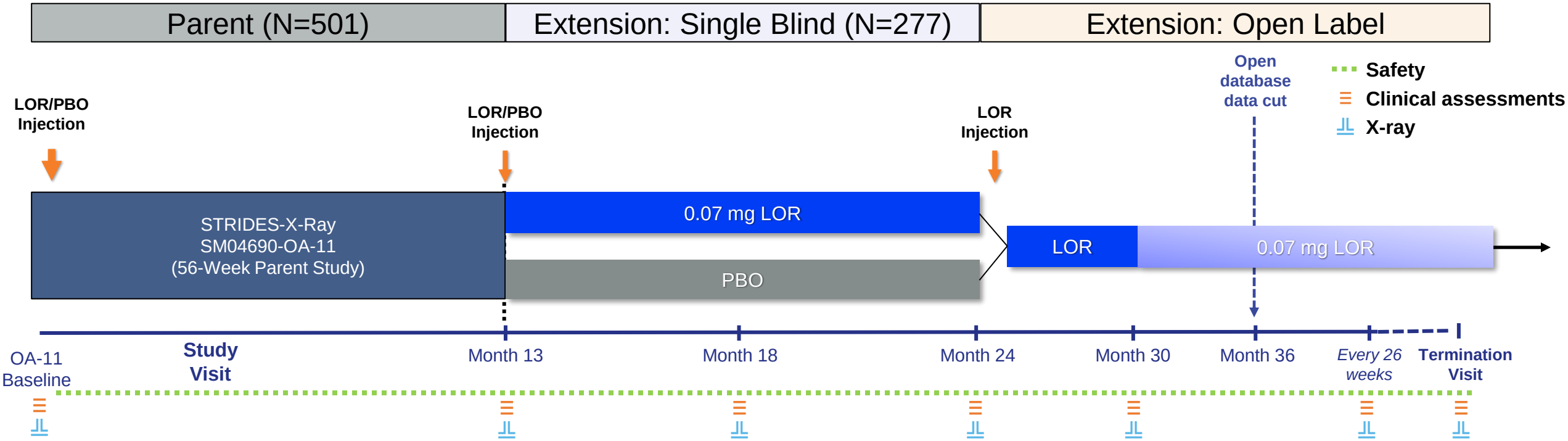
- LOR is an investigational compound currently in clinical trials; LOR has not been approved by the FDA or any other pharmaceutical regulatory authority, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidate. The complete mechanism of action (MOA) for LOR is unknown, and further investigation is being conducted.
- This presentation is intended as a scientific exchange of medical information, is provided for educational purposes only, and is not intended for any promotional purpose or to offer medical advice.

LOR, a CLK/DYRK inhibitor, may modify Wnt and inflammatory pathways



CLK: CDC-like kinase, DYRK: Dual-specificity tyrosine phosphorylation-regulated kinase

STRIDES X-Ray Extension: Study Design



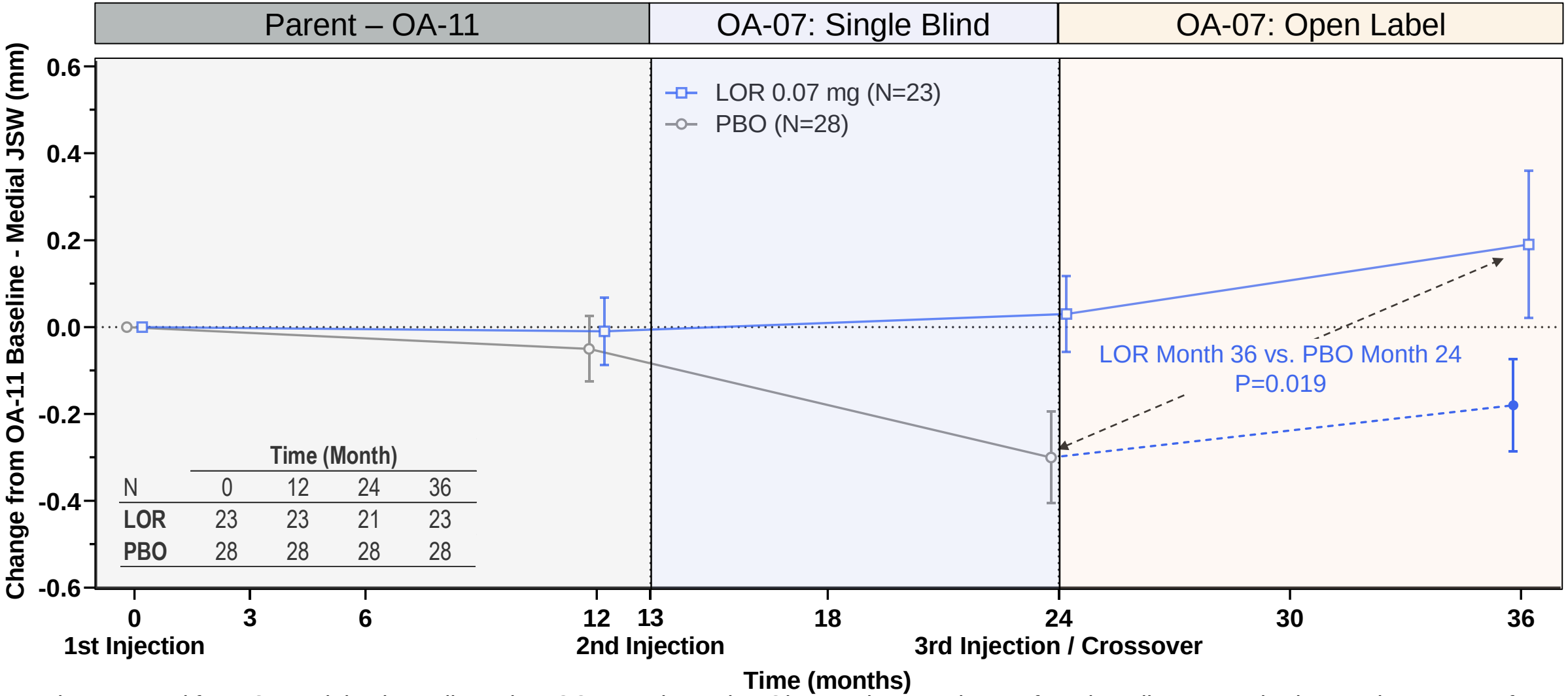
- ~50% of participants from the parent study enrolled in the extension study
- **Participants and investigators remained blind to initial treatment throughout**

STRIDES-X-Ray Extension (OA-07) Demographics

	LOR 0.07 mg	PBO
N	139	138
Age (years)*	60.5 (7.7)	61.6 (8.6)
Female [N (%)]	91 (65.5%)	83 (60.1%)
Race [N (%)]		
White	101 (72.7%)	96 (69.6%)
Black	36 (25.9%)	35 (25.4%)
Other	2 (1.4%)	7 (5.0%)
Hispanic / Latino [N (%)]	22 (15.8%)	30 (21.7%)
KL Grade 2 [N (%)]	74 (53.2%)	77 (55.8%)
Unilateral Symptomatic OA [N (%)]	51 (36.7%)	40 (29.0%)
BMI (kg/m^2)*	31.85 (4.92)	31.79 (4.80)
Baseline medial JSW	2.62 (0.75)	2.64 (0.63)

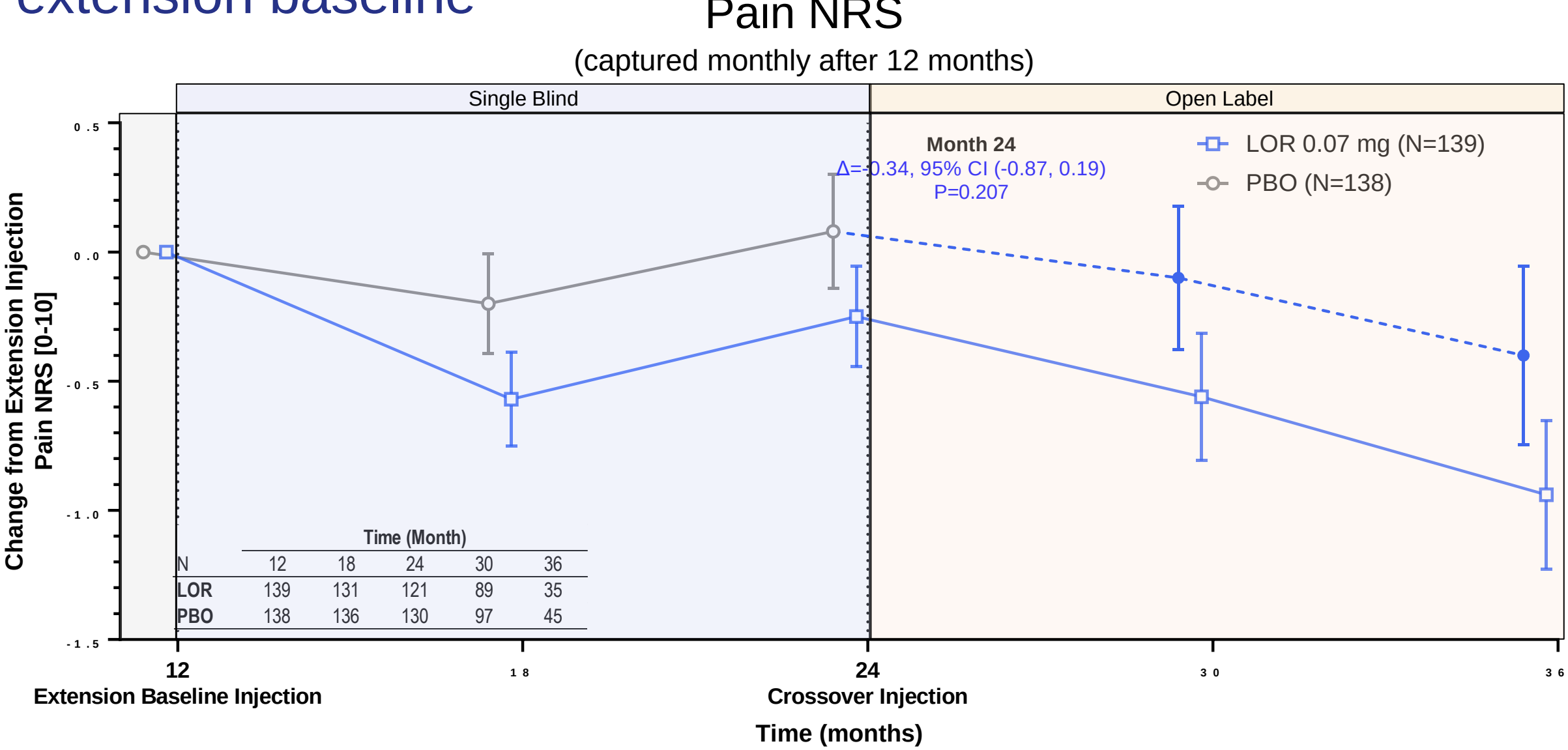
*Mean (SD) reported. Otherwise, N (%) reported..

Potential benefit of 0.07 mg LOR compared to PBO in medial JSW was observed



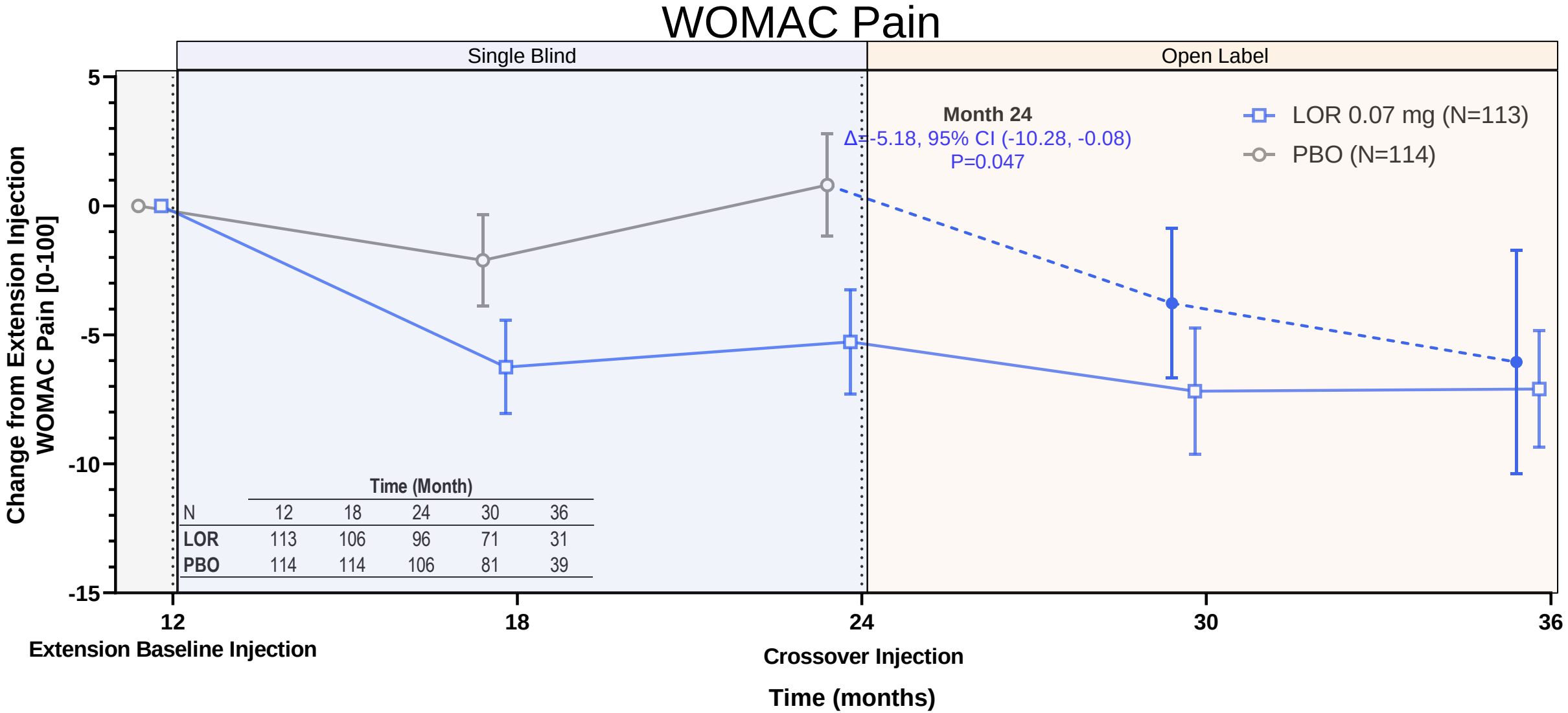
P-value reported from OA-11 injection-adjusted ANCOVA at timepoint. Observed mean change from baseline ± standard error shown. Data from open database. **36-month completer analysis**; LOR: Lorecivivint; PBO: Placebo; JSW: Joint Space Width

LOR improvements in Pain NRS were seen in change from extension baseline



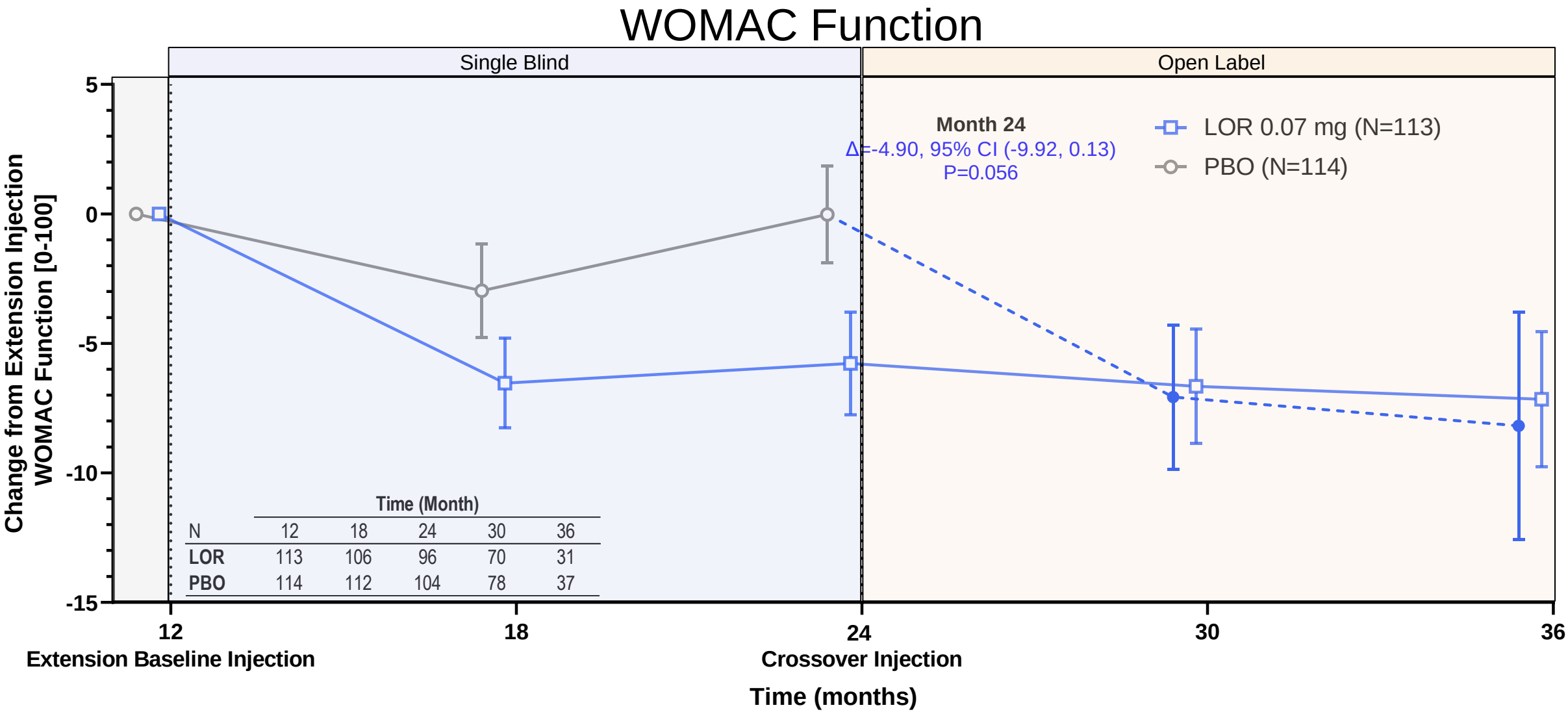
P-value reported from OA-07 injection-adjusted ANCOVA at timepoint. Observed mean change from baseline ± standard error shown.
Data from open database. Completer Analysis from Full Analysis Set; LOR: Lorecivivint; PBO: Placebo

LOR improvements in WOMAC Pain were seen in change from extension baseline



P-value reported from OA-07 injection-adjusted ANCOVA at timepoint. Observed mean change from baseline ± standard error shown.
Data from open database. Full Analysis Set; LOR: Lorecivivint; PBO: Placebo

LOR improvements in WOMAC Function were seen in change from extension baseline



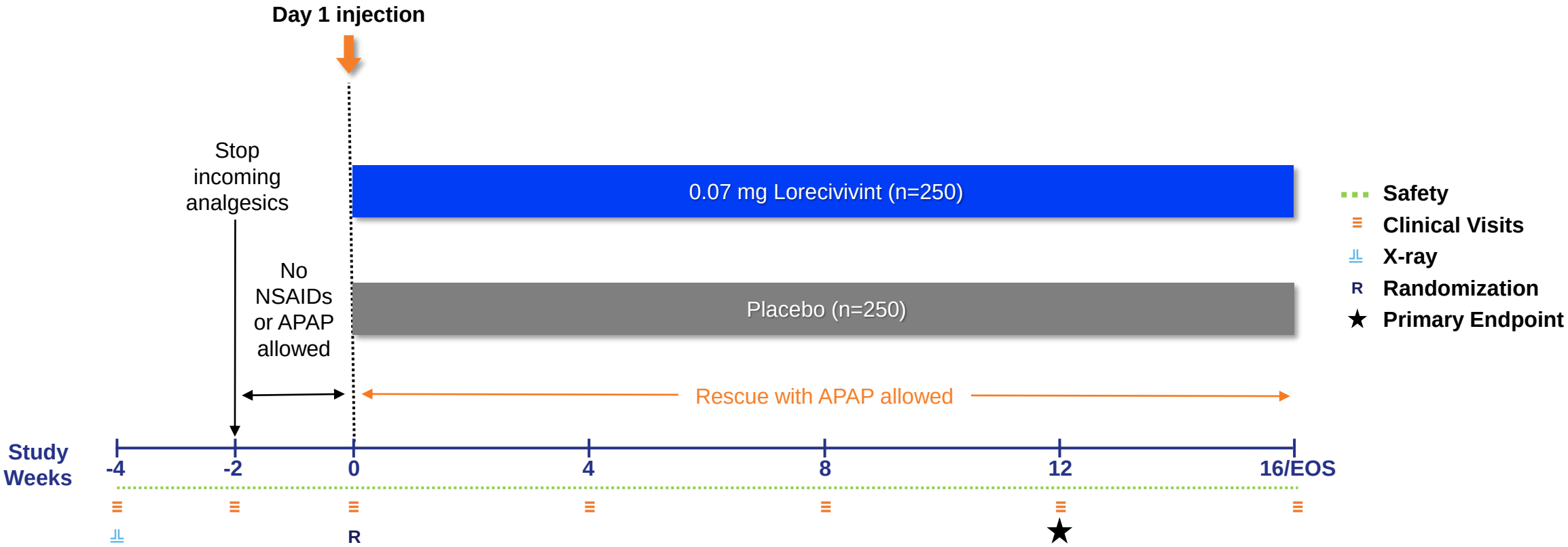
P-value reported from OA-07 injection-adjusted ANCOVA at timepoint. Observed mean change from baseline ± standard error shown.
Data from open database. Full Analysis Set; LOR: Lorecivivint; PBO: Placebo

STRIDES-X-Ray extension (OA-07) conclusions:

Within this structurally advanced knee OA cohort

- LOR 0.07 mg continues to appear safe and well tolerated
- Medial JSW: Potential benefit of LOR vs PBO after second injection observed @24 months, with additional benefit following third injection seen @ 36 months
- PROs: Potential LOR benefit compared to blinded PBO also observed
- Following crossover from PBO to LOR @ 24 months, participants showed medial JSW and PRO improvements @ 36 months, reinforcing potential treatment effects
- This study is ongoing.

OA-21 Trial Design



Population: BMI <35, targeting 70% KL2 and 30% KL3. For KL3, OARSI JSN [0-1]
N: ~500
Primary Endpoint: Pain NRS at Week 12
Secondary Endpoints: WOMAC Function and Patient Global Assessment at Week 12

Thank you

Biosplice thanks the investigators and participants for their time and effort necessary for this trial.