CR845-CLIN2002

June 29, 2017

Study Results

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Forward Looking Statement

Statements contained in this presentation regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Examples of these forward-looking statements include statements concerning Oral CR845's potential to treat chronic pain patients and expand the potential clinical utility of CR845 beyond acute pain, the establishment of the clinical utility of Oral CR845 and the future clinical development of Oral CR845, including the expected timing and design of any additional clinical trial(s). Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks are described more fully in Cara Therapeutics' filings with the Securities and Exchange Commission, including the "Risk Factors" section of the Company's Annual Report on Form 10-K for the year ended December 31, 2016, and its other documents subsequently filed with or furnished to the Securities and Exchange Commission.

All forward-looking statements contained in this presentation speak only as of the date on which they were made. Cara Therapeutics undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Ongoing Osteoarthritis Phase 2b Trial CLIN2002 Protocol Overview

Main Study Objective

- Efficacy of oral CR845 in patients with osteoarthritis (OA) of the hip or knee
- Safety and tolerability over 8 week period in patients

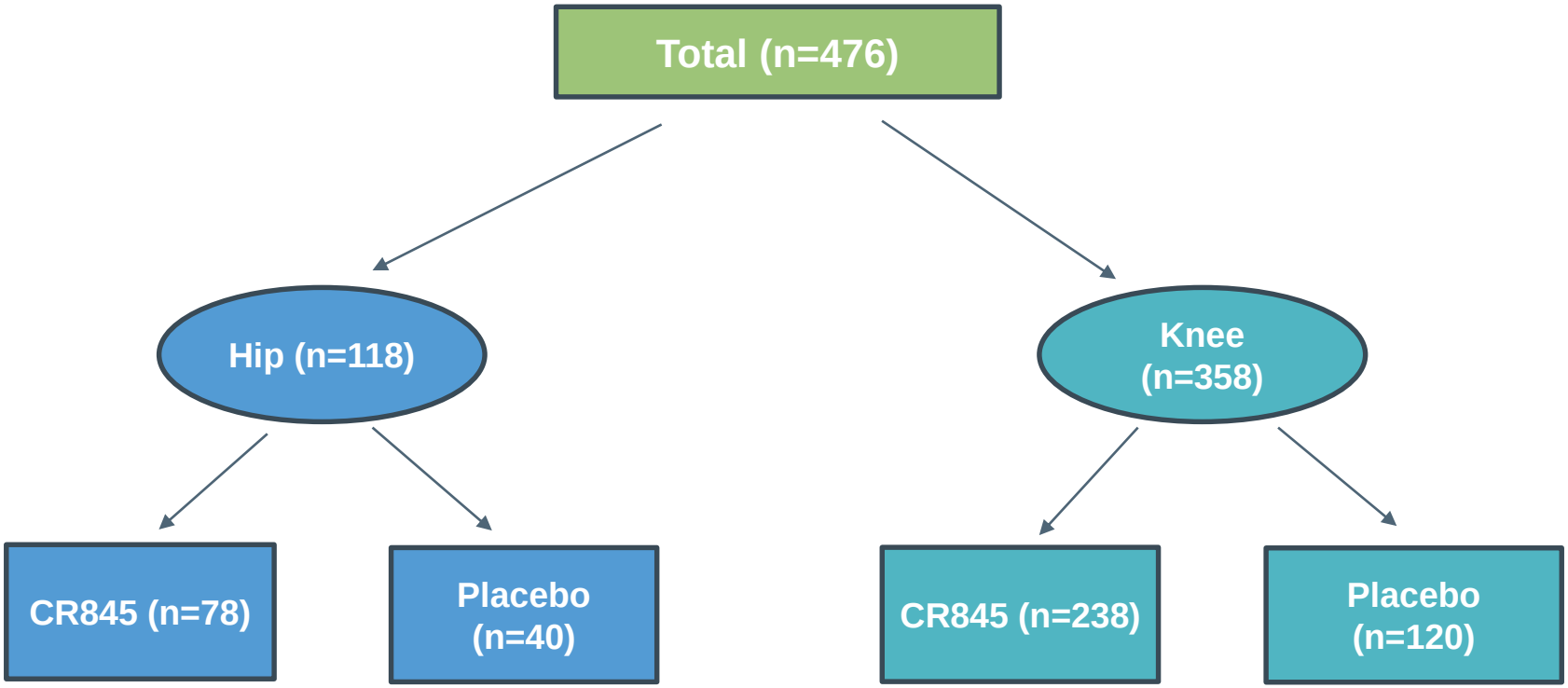
Study Design

- Double-blind, placebo-controlled study with twice daily (b.i.d.) doses of oral CR845 over an eight week treatment period in patients with moderate-to-severe pain (≥ 5) associated with OA.
  - Four week titration period for a response (tablet strengths 1mg, 2.5mg & 5mg).
  - Four week maintenance period on dose with response.

Patients

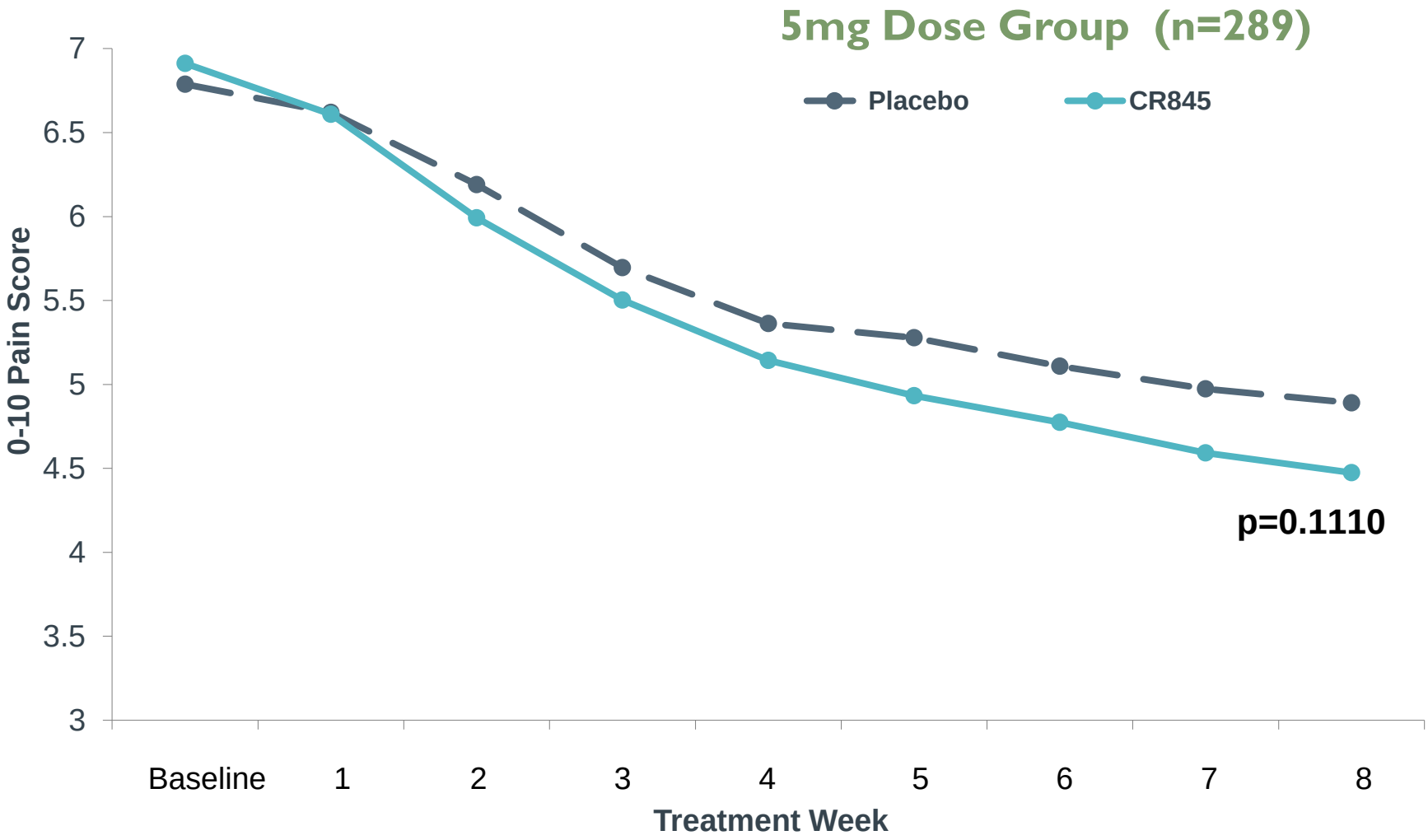
- 476 male and female patients – 33 U.S. sites

CLIN2002 Patient Disposition (Safety Population)



- Similar completion rates between treatments in patients with hip OA
- Higher completion rates in Placebo in patients with knee OA

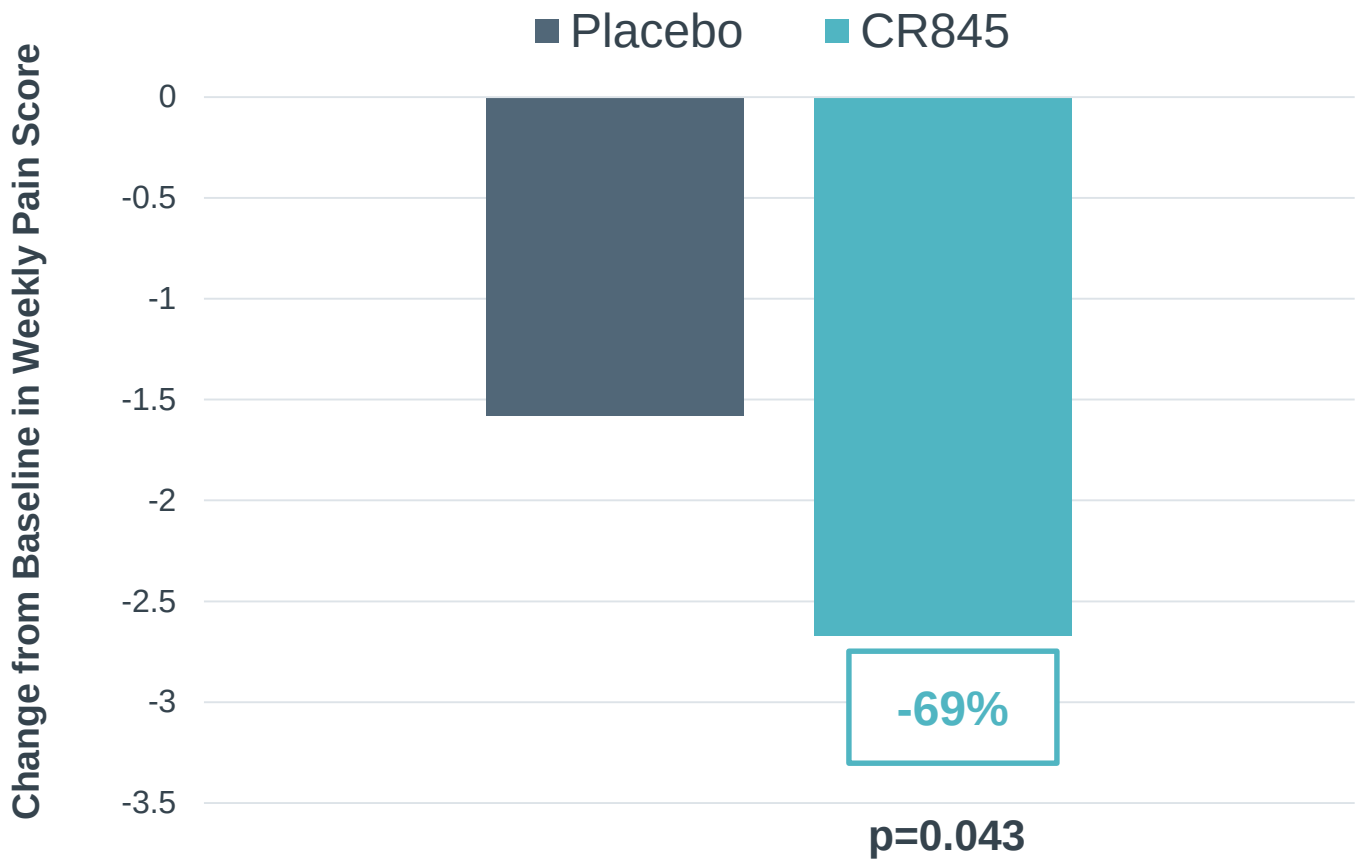
CLIN2002 Mean Weekly NRS Pain Score



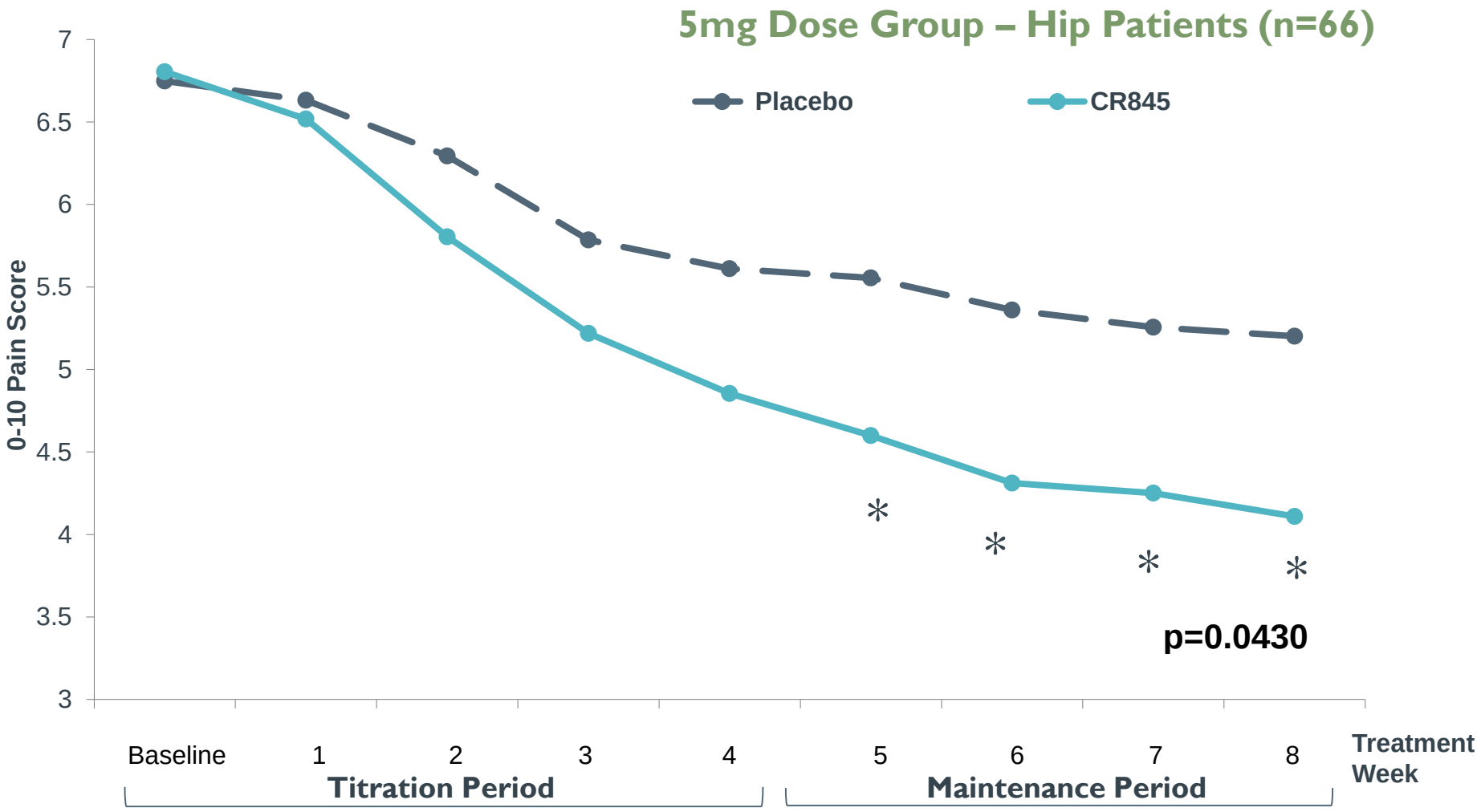
LS Means from MMRM with treatment, week, treatment by week interaction as terms in the model, baseline pain and strata as covariates, and subject as a random effect

CLIN2002 Change from Baseline at Week 8

5mg Dose Group – Hip Patients (n=66)

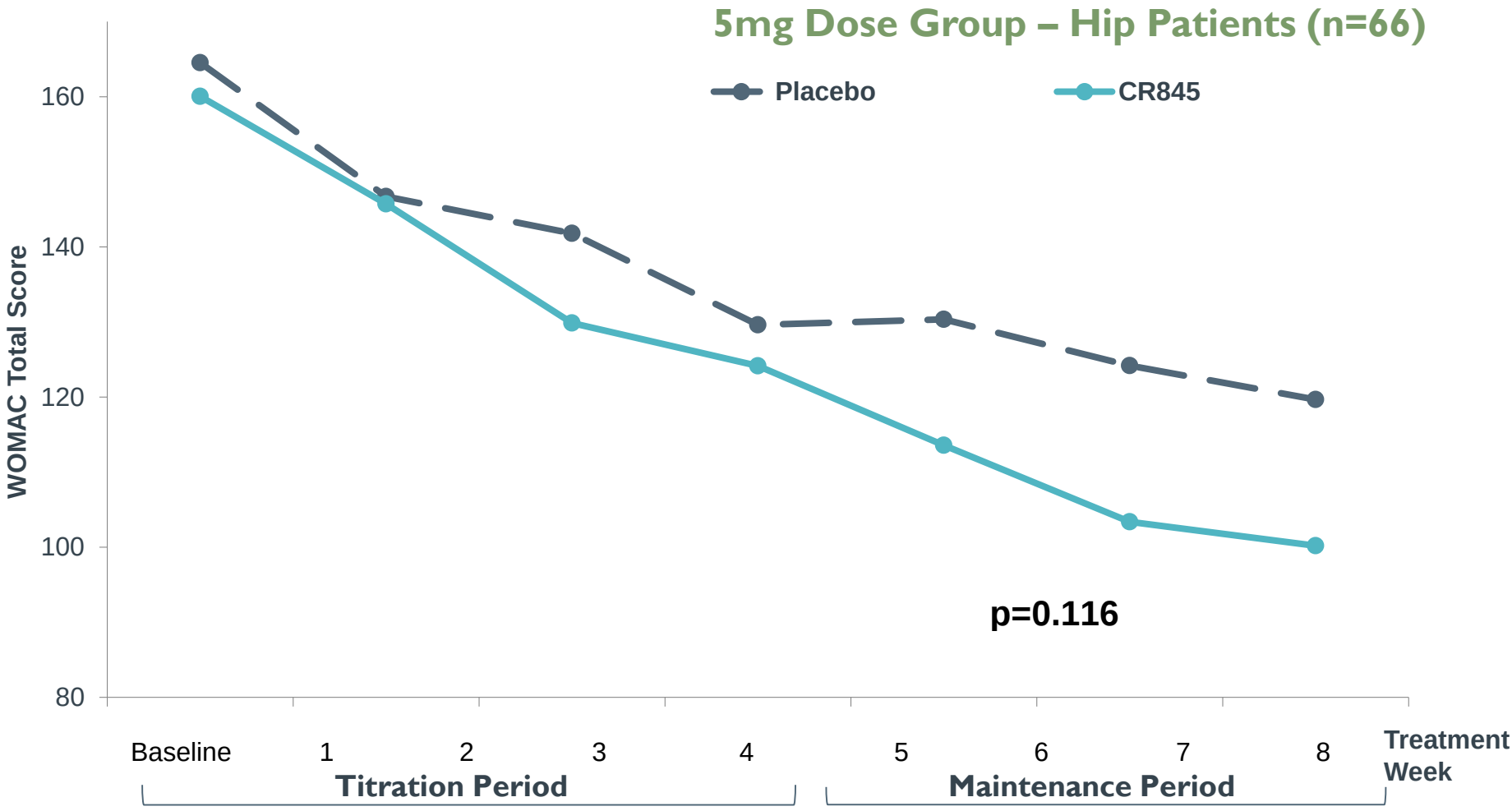


CLIN2002 Mean Weekly NRS Score



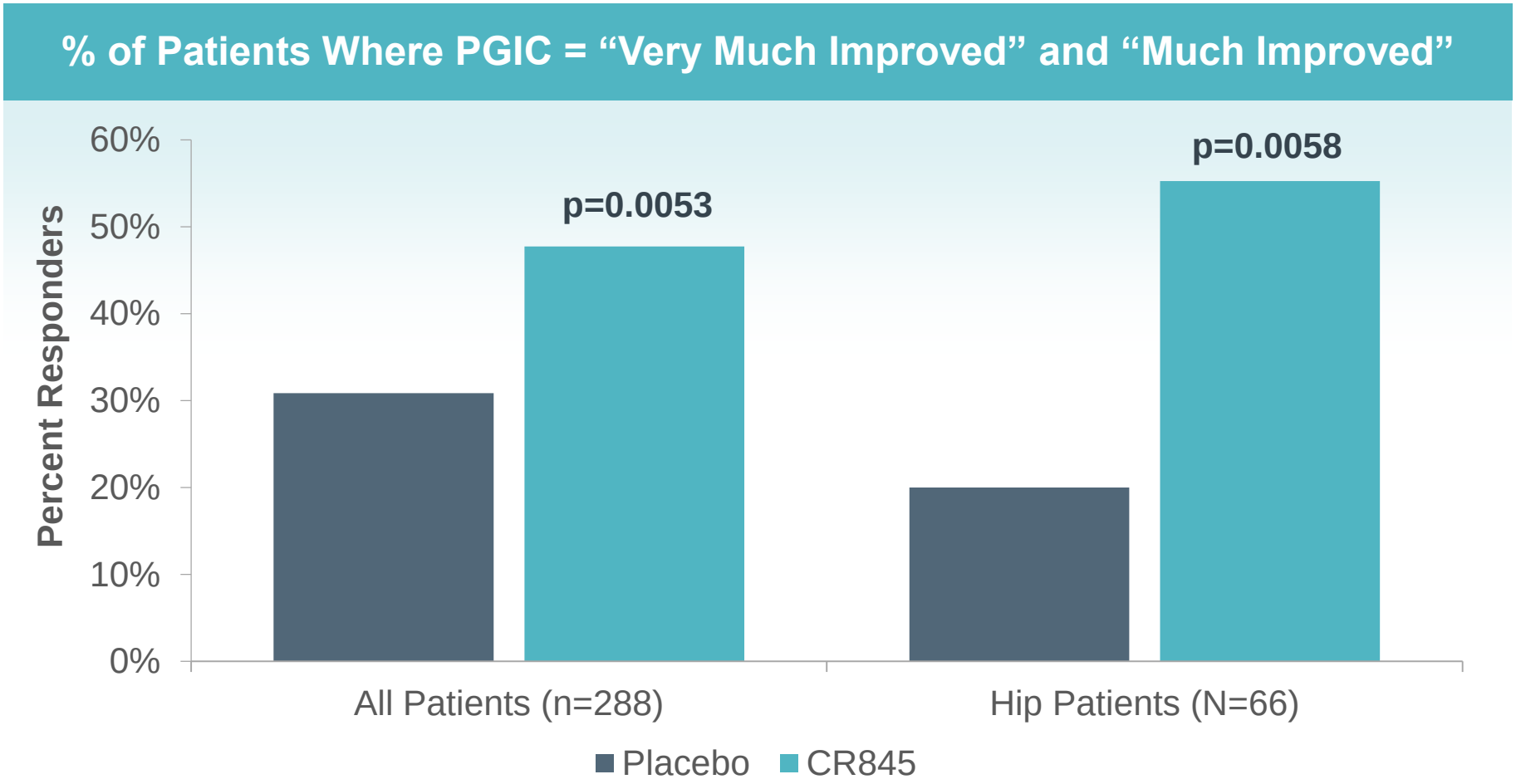
LS Means from MMRM with treatment, week, treatment by week interaction as terms in the model, baseline pain as a covariate, and subject as a random effect

CLIN2002 WOMAC Total Score



LS Means from MMRM with treatment, week, treatment by week interaction as terms in the model, baseline pain as a covariate, and subject as a random effect

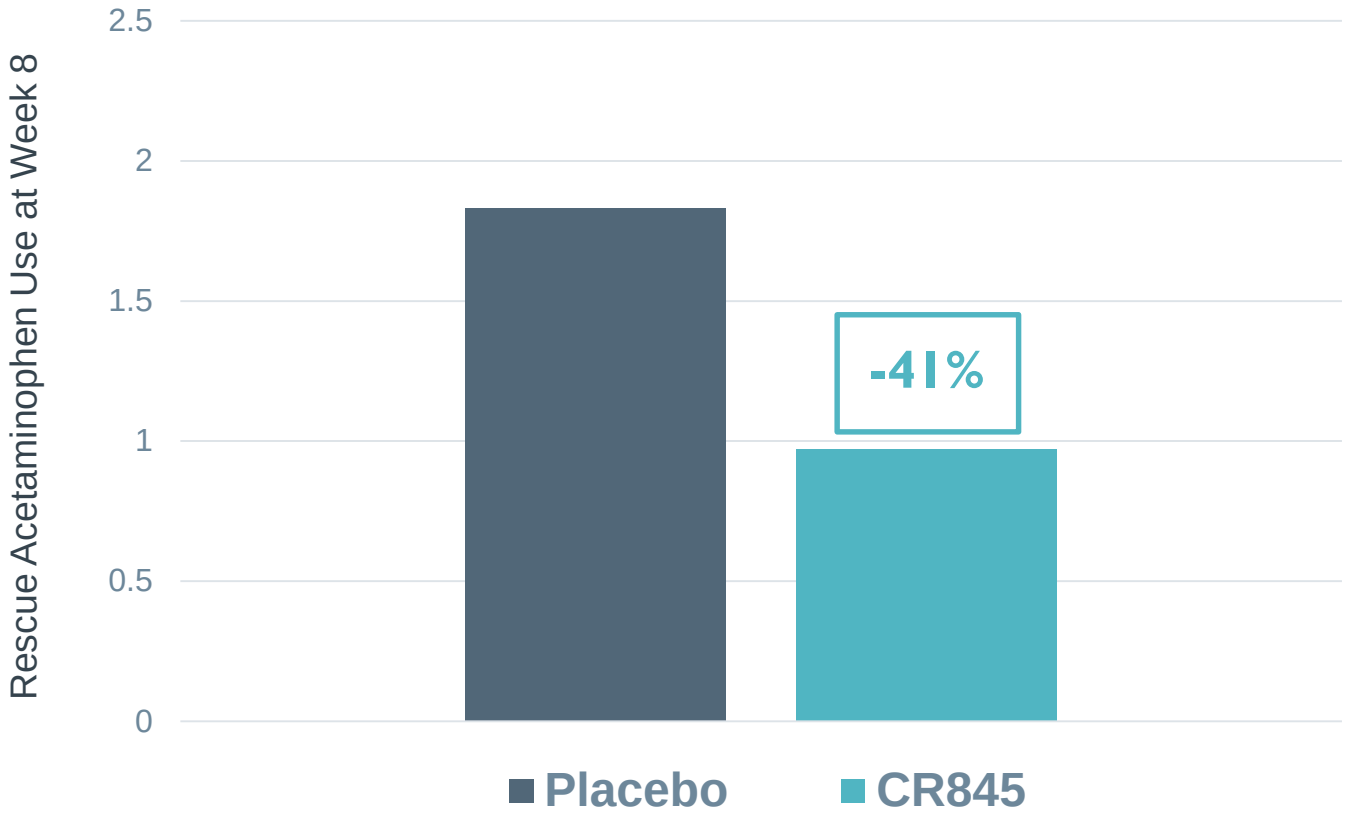
CLIN2002 PGIC Responders – 5mg Dose Group



(Cochran-Mantel-Haenszel test, 2-sided).

CLIN2002 Acetaminophen Use at Week 8

5mg Dose Group – Hip Patients (n=66)



67% of CR845 vs 43% of Placebo Patients Did Not Require Any Rescue Medication, Week 8

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CLIN2002 Adverse Events ≥5% for CR845 All Doses vs. 5mg

Adverse Event	Placebo n=160 (%)	CR845 5 mg n=181 (%)	CR845 All Doses n=316 (%)
Dizziness	3 (1.9%)	5 (2.8%)	26 (8.2%)
Dry mouth	3 (1.9%)	11 (6.1%)	18 (5.7%)
Constipation	3 (1.9%)	21(11.6%)	42 (13.3%)

- 86% of AEs occur within the first 4 weeks of titration
- Majority of AEs were transient and resolved spontaneously without treatment or intervention

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CLIN2002 Comparison of Adverse Events ≥ 5%

Adverse Event	Placebo	CR845	[a]OxyContin- IR	[b]Duloxetine
Constipation	1.9%	13.3%	23-26%	10%
Dizziness	1.9%	8.2%	13-16%	9%
Dry mouth	1.9%	5.7%	6-7%	11%

a. https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/020553s059lbl.pdf
b. http://pi.lilly.com/us/cymbalta-pi.pdf

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Comparative Efficacy in NRS Pain in OA Studies

Drug	Time	Change from BL	% Change from BL
Naproxen[1]	2 weeks	-2.5	35%
Celecoxib[1]	2 weeks	-2.5	35%
Duloxetine[2] (30mg/day)	2 weeks	-1.6	26%
Oxycodone CR[3]	12 weeks	-1.7	26%
CR845 (5mg)	2 weeks	-2.1	34%
CR845 (5mg) - Hip	8 weeks	-2.7	39%

[1] Benson, et. al. Treatment of Osteoarthritis with Celecoxib, a Cyclooxygenase-2 Inhibitor: a Randomized Controlled Trial. *Mayo Clin Proc. 1999;74:1095-1105.*

[2] Chappell et. Al., Duloxetine, a centrally acting analgesic, in the treatment of patients with osteoarthritis knee pain: A 13-week, randomized, placebo-controlled trial. *PAIN.* Volume 146, Issue 3, 5 December 2009, Pages 253–260.

[3] Markenson, et. al., Treatment of Persistent Pain Associated With Osteoarthritis With Controlled-Release Oxycodone Tablets in a Randomized Controlled Clinical Trial. *Clin J Pain* Volume 21, Number 6, November/December 2005.

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Next Steps:

- Complete full analysis of CLIN2002 Trial
- Initiation of Phase 2 adaptive trial:
  - Increased tablet strength: 5mg-10mg
  - Increased hip OA patient exposure
- Request FDA Type C meeting to outline path forward