

# **KORSUVA™ Injection**

## **KALM-I Phase 3 Pivotal Topline Results**

**A Multicenter, Randomized, 12-Week Double-Blind, Placebo-Controlled U.S. Study to Evaluate the Safety and Efficacy of Intravenous Dose of CR845 (KORSUVA™ Injection, 0.5 mcg/kg) In Patients Undergoing Hemodialysis With Moderate-to-Severe Pruritus**



# Forward-Looking Statements

This presentation contains certain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward-looking statements by the words “anticipate,” “believe,” “continue,” “estimate,” “expect,” “objective,” “ongoing,” “plan,” “propose,” “potential,” “projected”, or “up-coming” and/or the negative of these terms, or other comparable terminology intended to identify statements about the future. Examples of these forward-looking statements in this presentation include, among other things, statements concerning plans, strategies and expectations for the future, including statements regarding the expected timing of our planned clinical trials and the potential results of ongoing and planned clinical trials.

These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Factors that may cause actual results to differ materially from any future results expressed or implied by any forward-looking statements include the risks described in the “Risk Factors” section of the Company’s Annual Report on Form 10-K for the year ended December 31, 2018, as well as those set forth from time to time in the Company’s other SEC filings, available at <http://www.sec.gov>. Any forward-looking statements speak only as of the date of this presentation.

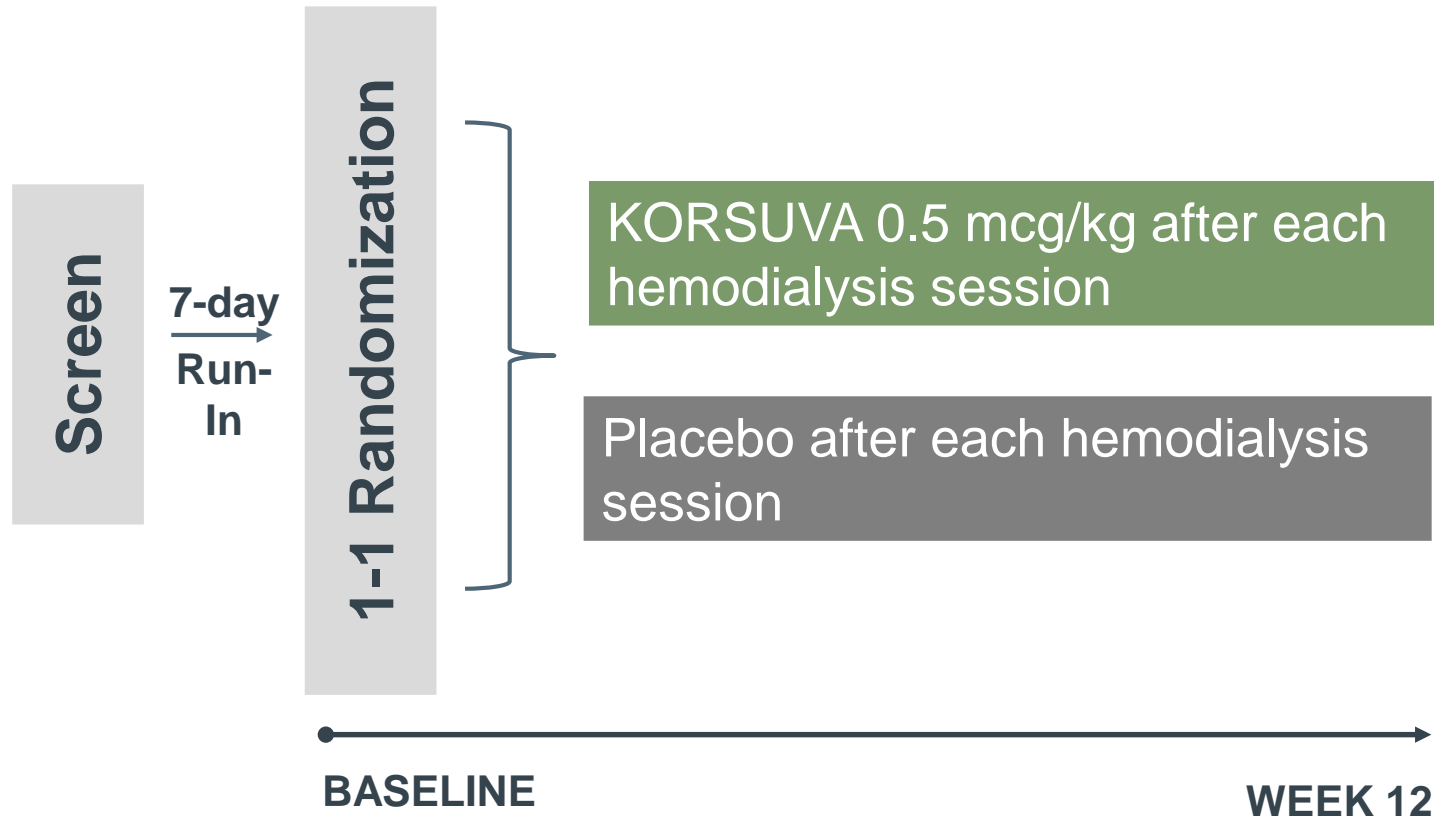
The Company undertakes no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise except as required by law.

# Executive Summary

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- ▶ KALM-1 Phase 3 pivotal study of KORSUVA™ Injection met primary and all secondary endpoints for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in subjects undergoing hemodialysis
- ▶ KORSUVA™ Injection was generally well tolerated with the safety profile consistent with prior studies at the 0.5 mcg/kg dose
- ▶ Breakthrough designation in the US for this indication

# KALM-1 Phase 3 Pivotal Study Design



*52 Week Open-Label Extension Ongoing*

## Endpoints: Week 12

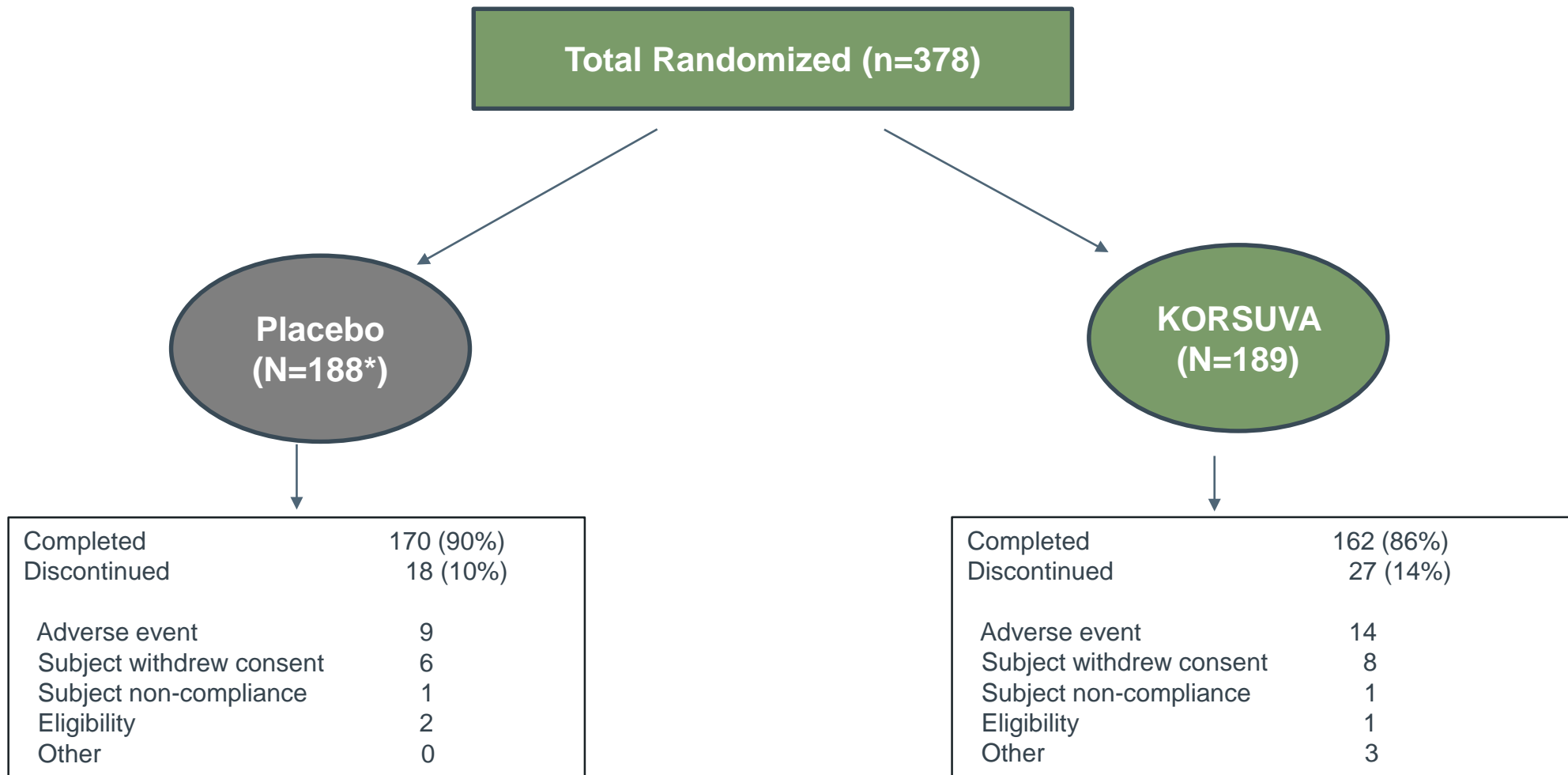
### Primary

- Proportion of subjects achieving  $\geq 3$  point improvement from baseline in weekly mean of daily worst itching intensity NRS (WI-NRS)

### Secondary

- Proportion of subjects achieving  $\geq 4$  point improvement from baseline in weekly mean of daily WI-NRS
- Change from baseline in itch-related Quality of Life as measured by 5-D Itch and Skindex-10 questionnaires

# KALM-I: Disposition in Double-blind Treatment Period



\*1 subject was randomized to Placebo but did not receive study drug

# KALM-I: Key Baseline Disease Characteristics

Baseline Characteristic Mean (SD) or %	Placebo N = 188	KORSUVA N = 189
Years Undergoing Hemodialysis,	4.7 (4.22)	4.4 (3.98)
Years of Pruritus	3.5 (3.37)	3.2 (3.24)
Use of Anti-Itch Medication	41.5 %	38.1 %
Baseline Worst Itching Intensity NRS	7.3 (1.61)	7.1 (1.44)
Baseline 5-D Itch Total Score	17.9 (3.47)	16.9 (3.47)
Baseline Skindex-10 Total Score	38.3 (15.40)	36.2 (14.36)

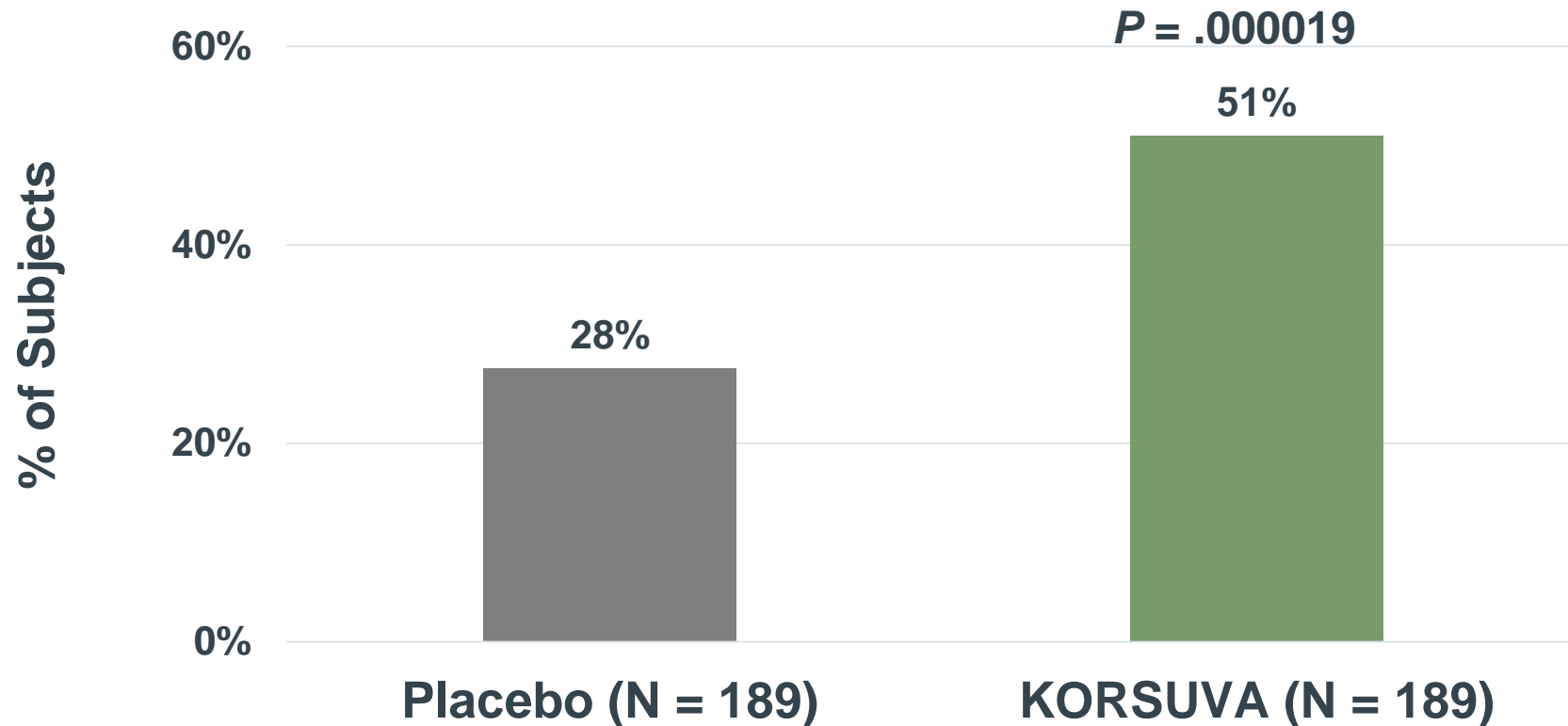
*NRS: Numeric Rating Scale (0 to 10) where 0 = no itch and 10 = worst itching imaginable*

*5-D Itch score ranges from 0 to 25 (lower scores indicate better QoL and reduced itch symptoms)*

*Skindex-10 scale ranges from 0 to 60 (lower scores indicate better QoL)*

# Primary Endpoint: $\geq 3$ point improvement WI-NRS (Wk 12)

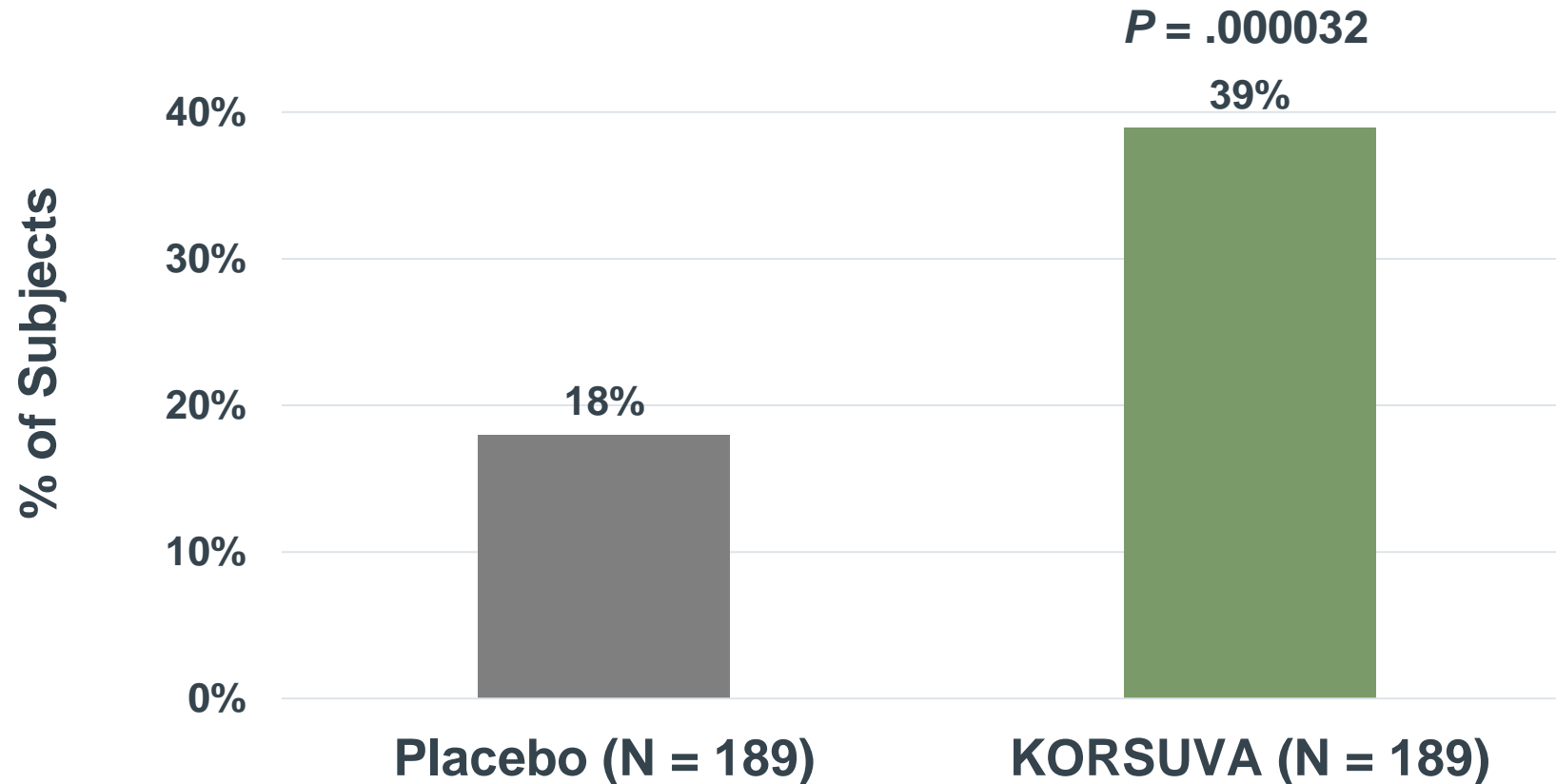
**KORSUVA subjects >2.5 times more likely to experience  $\geq 3$  point improvement**



Estimated percentage & P-value based on a logistic regression model with terms for treatment group, baseline WI-NRS score, and strata  
Missing data imputed using multiple imputation (MI) under missing at random (MAR) assumption

## Secondary: $\geq 4$ point improvement WI-NRS (Wk 12)

KORSUVA subjects ~3 times more likely to experience  $\geq 4$  point improvement

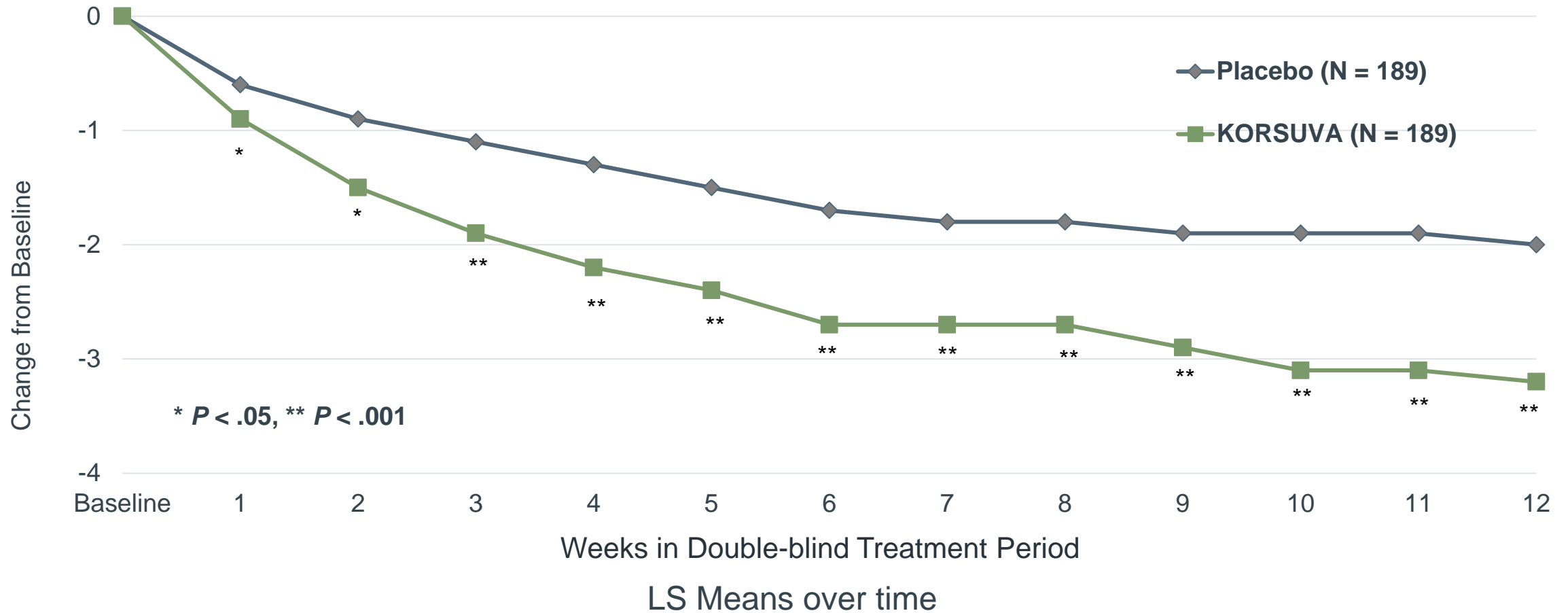


Estimated percentage & P-value based on a logistic regression model with terms for treatment group, baseline WI-NRS score, and strata  
Missing data imputed using multiple imputation MI) under missing at random (MAR) assumption  
Odds Ratio: 2.9



# KALM-I Change in Worst Itching Intensity NRS Over Time

Significant differences in WI-NRS Change between KORSUVA and Placebo Starting at Week 1



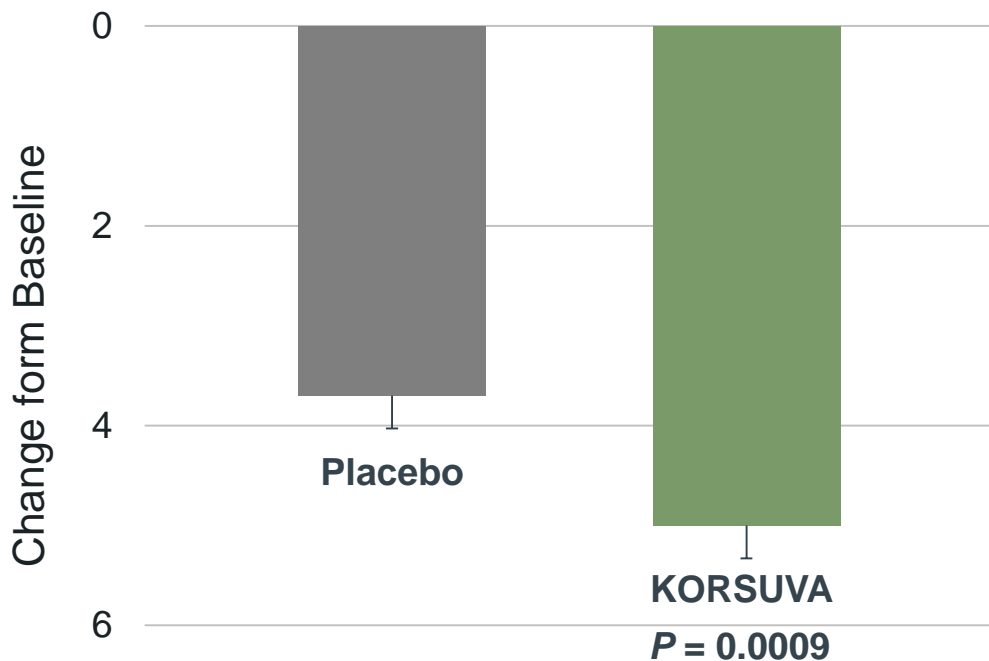
LS Means from MMRM with terms for treatment group, week, week by treatment interaction, baseline score and strata  
Missing data imputed using multiple imputation (MI) under missing at random (MAR) assumption

# Secondary Endpoints: 5D-Itch and Skindex-10 at Week 12

Demonstrated significant improvements in itch-related QoL measures

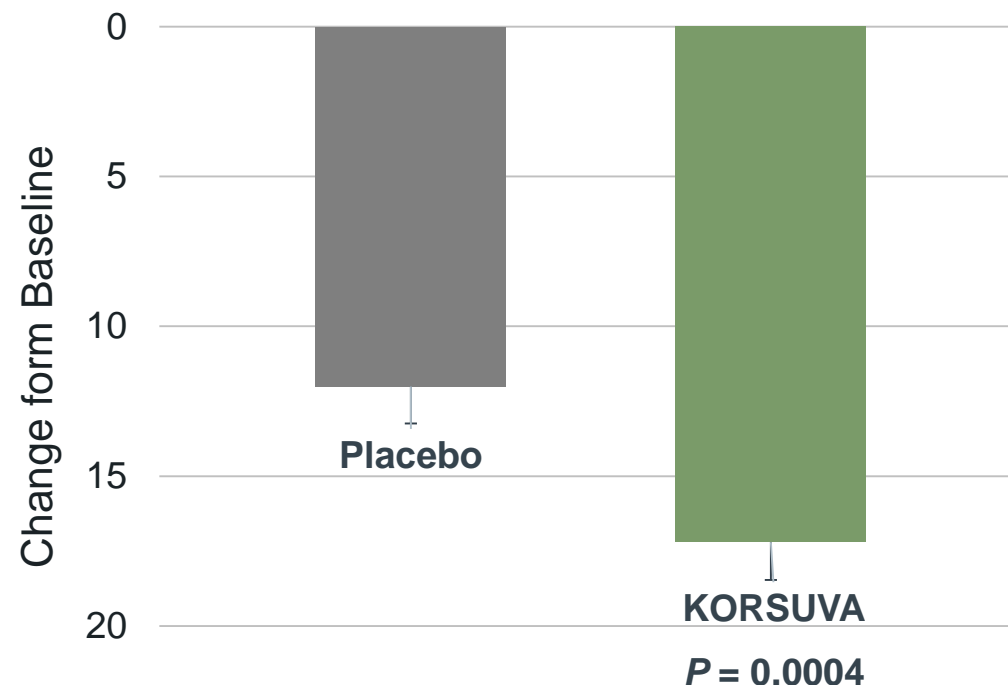
## 5-D

35% improvement over placebo



## Skindex-10

43% improvement over placebo



LS Mean, standard error & P-value based on ANCOVA with terms for treatment group, baseline score, and strata  
Missing values imputed using multiple imputation (MI) under MAR assumption

# KALM-I Phase 3 Pivotal Results Summary

Study met primary and all secondary endpoints

Endpoints at Week 12 KORSUVA 0.5 mcg/kg vs placebo	P Value
<b><u>Primary</u></b> <ul style="list-style-type: none"><li>○ Proportion subjects with <math>\geq 3</math> point improvement in weekly mean of daily WI-NRS</li></ul>	0.000019
<b><u>Secondary</u></b> <ol style="list-style-type: none"><li>1) Proportion subjects <math>\geq 4</math> point improvement in weekly mean of daily WI-NRS</li><li>2) Change from baseline in 5-D Itch score</li><li>3) Change from baseline in total Skindex-10 score</li></ol>	0.000032 0.0009 0.0004

# KALM-I Summary of Safety

Treatment-emergent Adverse Events	Placebo N = 188 n (%)	KORSUVA N = 189 n (%)
Subjects with at least one treatment-emergent adverse event	117 (62)	130 (69)
Subjects with at least one serious treatment-emergent adverse event	41 (22)	49 (26)
Deaths	2 (1)	2 (1)
Non-fatal SAEs	39 (21)	47 (25)
Treatment-emergent adverse events resulting in discontinuation	9 (4.8)	14 (7.4)

# KALM-I Most Commonly Reported TEAEs

Treatment-emergent Adverse Events at $\geq 5\%$ frequency	Placebo N = 188 n (%)	KORSUVA N = 189 n (%)
Diarrhea	7 (3.7)	18 (9.5)
Dizziness	2 (1.1)	13 (6.9)
Vomiting	6 (3.2)	10 (5.3)
Nasopharyngitis	10 (5.3)	6 (3.2)

# Conclusions

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- ▶ KALM-1 Phase 3 pivotal study KALM-1 with KORSUVA™ Injection met primary and all secondary endpoints, demonstrating statistically robust improvements in itch intensity and itch-related quality of life measures
- ▶ KORSUVA™ Injection was generally well tolerated with a safety profile consistent with prior studies in this patient population
- ▶ Second pivotal Phase 3 study (KALM-2) continues to enroll with top line data expected in 2H 2019 based on current enrolment expectations