Targeting Pruritus with Novel Peripherally-Restricted Kappa Agonist Therapeutics

November 2019

CARA THERAPEUTICS

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 regulatory submissions; the potential results of ongoing and planned clinical trials; future regulatory and development milestones for the Company's product candidates; the potential of Korsuva to be a therapeutic option for pruritus; the size of the potential markets that are potentially addressable for the Company’s product candidates, including the pruritus market and the potential commercialization of Korsuva™.

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.

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Development Pipeline: Chronic Pruritus

Program	Indication	STAGE OF DEVELOPMENT				Commercial Rights (ex-Japan and S. Korea)^
		Preclinical	Phase 1	Phase 2	Phase 3	
KORSUVA™ Injection	Pruritus CKD-HD**					US- Cara EU/Other- VFMCRP#
Oral KORSUVA™	Pruritus CKD (III-V)					Cara
Oral KORSUVA™	Pruritus CLD					Cara
Oral KORSUVA™	Pruritus Atopic Dermatitis					Cara

The FDA has conditionally accepted KORSUVA™ as the trade name for CR845 / difelikefalin for pruritic indications. CR845 / difelikefalin is an investigational drug product, and its safety and efficacy have not been fully evaluated by any regulatory authority.

^ Commercialization rights to CR845 in defined indications - Japan: Maruishi Pharma; South Korea: CKD Pharma
** Breakthrough Designation for IV CR845 for Pruritus CKD-HD
# VFMCRP and Cara have rights to promote in Fresenius Medical Care dialysis clinics in the US under a profit share agreement

CKD-HD: Chronic Kidney Disease- Hemodialysis; **CLD**: Chronic Liver Disease

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US Market Opportunity for KORSUVA™ Injection in Dialysis Patients

60%
of ESRD patients have pruritus[2,3]

>500K
patients on dialysis

~40%
have moderate to severe pruritus

Per NKF, >500K patients undergoing dialysis in the US[1]

- ~60% have some form of pruritus[2,3]
- Itching severity associated with worsening Quality of Life (QoL) Sleep disturbance, depressed mood/anxiety, socialization
- Increased mortality risk

KORSUVA™ granted Breakthrough Therapy Designation for CKD-aP

- Significant unmet need
- No FDA approved therapies

Per Nov. 2018 CMS rule:

within the ESRD Prospective Payment System all new dialysis drugs eligible for reimbursement at ASP for 2 yrs under TDAPA, effective Jan. 1, 2020[4]

1. National Kidney Foundation
2. Pisoni RL, Wikstrom B, Elder SJ, et al. Nephrol Dial Transplant. 2006;21:3495-3505.
3. Ramakrishnan et al. International Journal of Nephrology and Renovascular Disease. 2014:7 1–12
4. https://www.govinfo.gov/content/pkg/FR-2018-11-14/pdf/2018-24238.pdf

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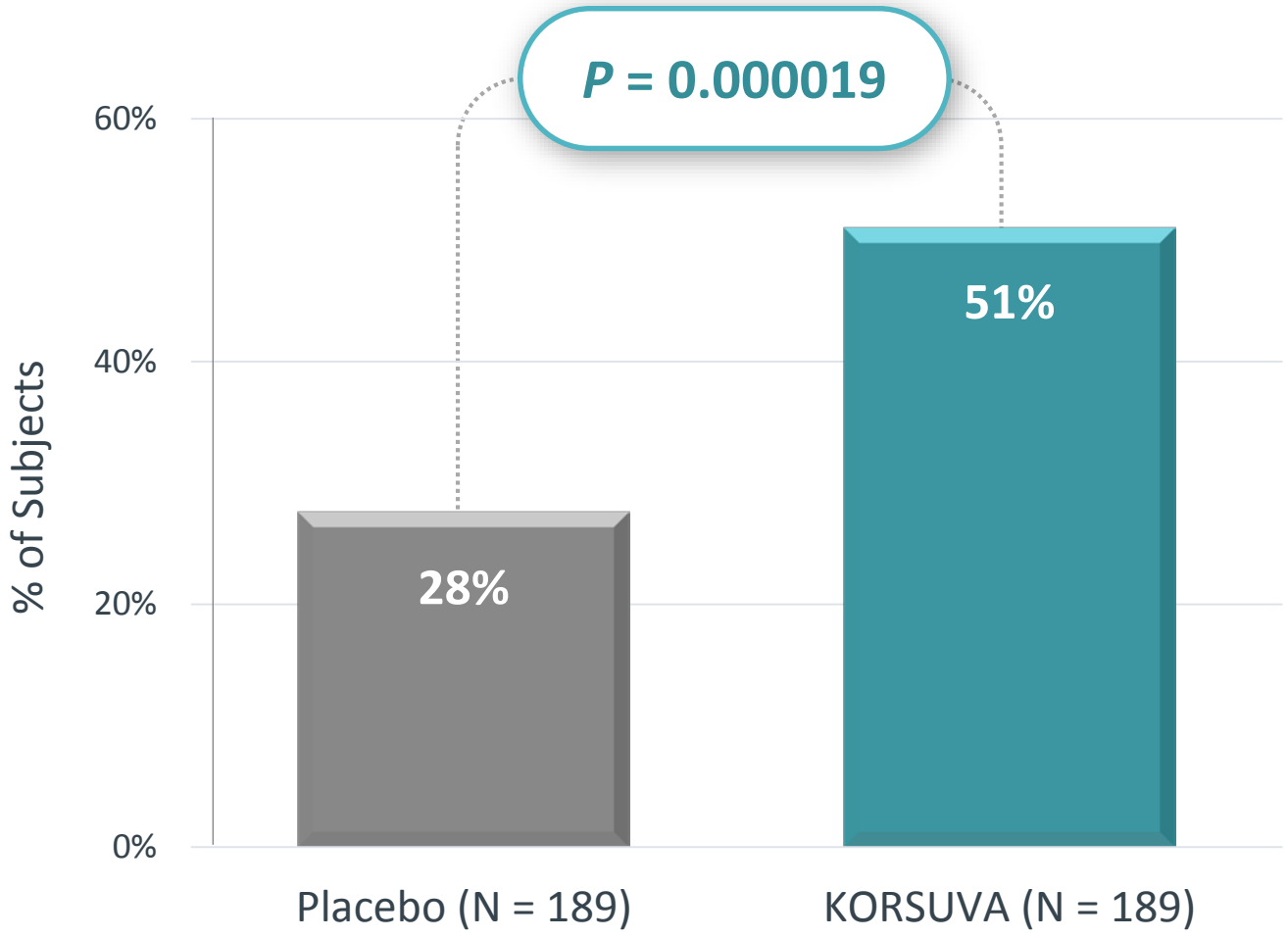
KALM-1 Phase 3 Primary Endpoint: ≥3 point improvement WI-NRS

TOP-LINE RESULTS:

KORSUVA subjects >2.5 times more likely to experience ≥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
Odd Ratio: 2.72

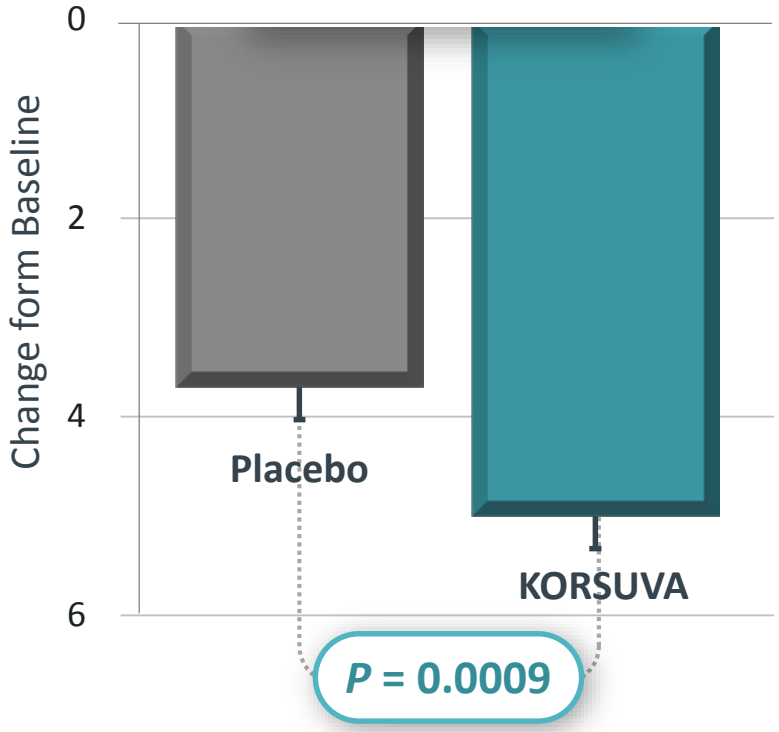
Secondary Endpoints: 5D-Itch and Skindex-10

TOP-LINE RESULTS:

Significant improvements in itch-related QoL measures

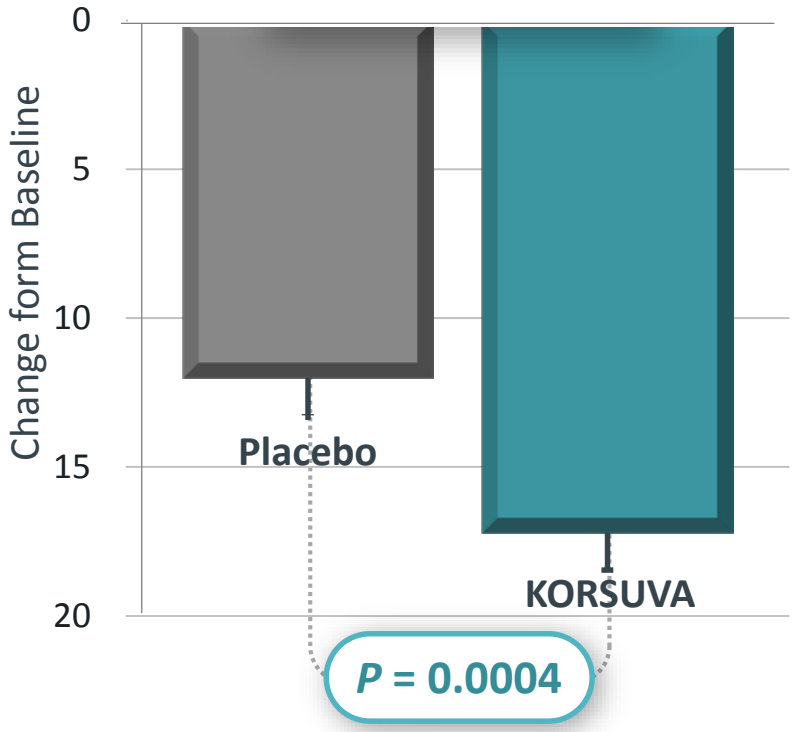
5-D

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-1 Phase 3 Pivotal Top-line Results Summary

Study met primary and all secondary endpoints

Endpoints at Week 12 KORSUVA 0.5 mcg/kg vs placebo	P Value
Primary Proportion subjects with ≥3 point improvement in weekly mean of daily WI-NRS	0.000019
Secondary	
1) Proportion subjects ≥4 point improvement in weekly mean of daily WI-NRS	0.000032
2) Change from baseline in 5-D Itch score	0.0009
3) Change from baseline in total Skindex-10 score	0.0004

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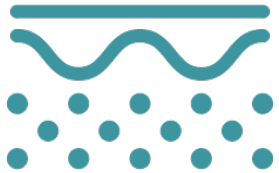
Development Programs for Oral KORSUVA™

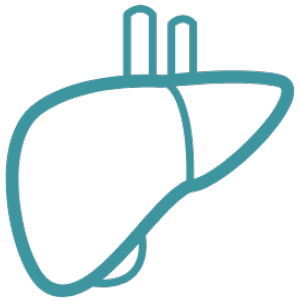
Phase 2 Trial
CKD-aP (Stage III-V)

~30% experience pruritus



Phase 2 Trial
Atopic Dermatitis

~87% to 100% experience pruritus



Phase 2 Trial
Chronic Liver Disease Pruritus

~30% experience pruritus

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US Market Opportunity in CKD-aP: Non-Dialysis

~7.3 million
diagnosed with CKD (IQVIA est)

33%
receive pruritus tx

Per NKF, CKD is a large under-recognized US public health issue

- ~30 million people affected (causes more deaths than breast/ prostate cancer)

No FDA approved therapies – large unmet medical need

- Commonly used medications: anti-histamines, corticosteroids, gabapentin, anti-depressants etc.

Oral KORSUVA™, if approved for pre-dialysis patients, would not fall under ESRD bundle payment system

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Projected Clinical Milestones – 2019/ 2020

	Pruritus / KORSUVA™ Injection	Pruritus / Oral KORSUVA™
4Q, 2019		Top-line data from Phase 2 Trial CKD-aP (Stage III-V)
2020	Top-line data from Global Ph 3 trial, KALM-2 (CKD-aP in dialysis pts)	Top-line data from Phase 2 Trial in AD & PBC patients with pruritus
2H, 2020	**NDA Submission**	

Financial Highlights

Cash and marketable securities

(Sept. 30, 2019)

$249.1M

Net loss

(Sept. 30, 2019)

($32.8M)

Shares outstanding

~46.7M

Options outstanding

~4.6M

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