CARA THERAPEUTICS

Corporate Presentation

November 2023

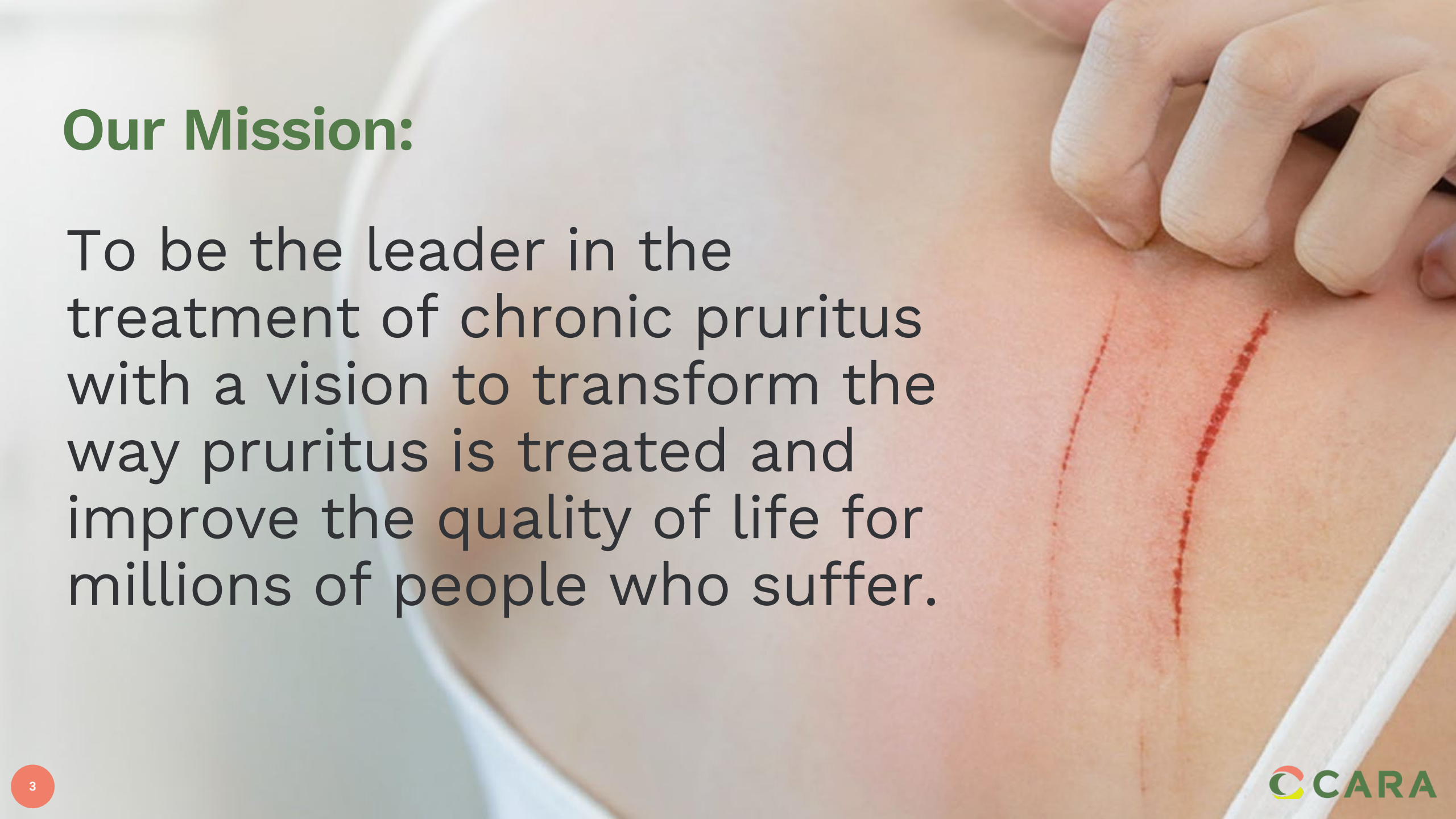
Forward-Looking Statements

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 the Company's ability to successfully commercialize KORSUVA injection and Kapruvia, future revenue and profit share from sales of KORSUVA and Kapruvia, planned future regulatory submissions and potential future regulatory approvals, potential for post-TDAPA reimbursement of KORSUVA, future product launches, the performance of the Company's commercial partners, including CSL Vifor, expected timing of the initiation, enrollment and data readouts from the Company's planned and ongoing clinical trials, the potential results of ongoing clinical trials, timing of future regulatory and development milestones for the Company's product candidates, the potential for the Company's product candidates to be alternatives in the therapeutic areas investigated and the potential for oral difelikefalin to address additional pruritic indications, the size and growth of the potential markets for pruritus management, the receipt of potential milestone payments pursuant to the Purchase and Sale Agreement with HCRX Investments Holdco, L.P. and Healthcare Royalty Partners IV, L.P., and the Company's expected cash reach. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These risks and uncertainties include the risks inherent in the launch of new products, including that our commercial partners, including CSL Vifor, may not perform as expected, risks inherent in the clinical and regulatory development of pharmaceutical products, and the risks 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 ending December 31, 2022 and its other documents subsequently filed with or furnished to the Securities and Exchange Commission, including its Form 10-Q for the quarter ended September 30, 2023. 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, except as required by law.

CARA

Our Mission:

To be the leader in the treatment of chronic pruritus with a vision to transform the way pruritus is treated and improve the quality of life for millions of people who suffer.



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Difelikefalin, a Pipeline in a Product

Novel, first-in-class selective and potent kappa opioid receptor agonist

Unique Chemical Structure and Features

- Synthetic peptide made of non-natural amino acids
- High hydrophilicity, high polar surface area and charge at physiological pH
- Does not readily cross the blood-brain-barrier

1

Differentiated MOA

- Acts on KORs on peripheral terminals of sensory nerves and immune cells
- Works downstream potentially as broad spectrum antipruritic

3

Attractive Pharmacology

- Highly selective and potent full agonist at KORs
- Does not produce classical mu opioid side effects (e.g., euphoria, addiction and respiratory depression)
- **Non-scheduled drug**

2

Strong Clinical Data in Multiple Therapeutic Areas

- IV formulation approved for chronic kidney disease-associated pruritus (CKD-aP) in hemodialysis patients
- Oral formulation has shown positive clinical data in the treatment of chronic pruritus
  - Advanced CKD
  - Atopic Dermatitis
  - Notalgia Paresthetica

4

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Strategic Focus on Moderate to Severe Chronic Pruritus

NEPHROLOGY

Advanced CKD Hemodialysis

APPROVED

~ 200K patients undergoing hemodialysis (HD) suffer from moderate-to-severe chronic pruritus

KORSUVA injection is the first-and-only FDA approved product to help these patients.

Advanced CKD Pre-Dialysis

PHASE 3

~ 300K patients with stage 4-5 advanced CKD suffer from moderate-to-severe chronic pruritus

There are no approved therapies.

DERMATOLOGY

Atopic Dermatitis

PHASE 3

~ 3M mild-to-moderate patients with Atopic Dermatitis (AD) suffer from moderate-to-severe chronic pruritus

Chronic pruritus is one of the defining features of AD.

Notalgia Paresthetica

PHASE 2/3

~ 650K patients with Notalgia Paresthetica (NP) are in the care of a healthcare provider for moderate-to-severe chronic pruritus

There are no approved therapies.

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KORSUVA® Injection Commercialization

KORSUVA®
(difelikefalin) Injection

First-and-only product approved for CKD-aP in HD in countries worldwide*

- US launch in 2Q22
- EU launch (Kapruvia) in 2H22
- AU, CA, SA, SG approvals in 2H22
- JP approval in 3Q23

CSL Vifor

Strong Commercial Partnership with Favorable Economics

- Leading commercial nephrology organization in US
- Strong relationships with US nephrology offices and dialysis centers
- Joint venture with Fresenius Medical Care* *

Only Current Product with TDAPA Designation

- During TDAPA period reimbursed at ASP for all patients on drug
- Following TDAPA period, add-on payment adjustment to bundle rate for 3 years
- TDAPA expiration on March 31, 2024

* Other countries where Korsuva/Kapruvia has been approved include Austria, Australia, Belgium, Bulgaria, Canada, Croatia, Cyprus, Czech Rep., Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Kuwait, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, The Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom, Switzerland, Singapore, and United Arab Emirates.

NOTE: In November 2023, Cara announced that it entered into a Purchase and Sale Agreement with HCRX Investments Holdco, L.P. and Healthcare Royalty Partners IV, L.P., or collectively HCR, in which HCR will receive all royalties due to Cara from KORSUVA® (difelikefalin) injection / Kapruvia® ex-U.S. license agreements with CSL Vifor and Maruishi Pharmaceutical Co.

** Vifor has contracted the sales force of Fresenius Renal Pharmaceuticals, a division of Fresenius Medical Care North America, to complement its sales force in selling into Fresenius clinics in the U.S.

NOTE: Korsuva is indicated for the treatment of moderate-to-severe pruritus associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis (HD). Limitations of Use Korsuva has not been studied in patients on peritoneal dialysis and is not recommended for use in this population

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Oral Difelikefalin: Expanding Reach in Advanced CKD-aP Market

Pruritis control is a significant unmet need among advanced CKD patients[1]

There are no FDA-approved therapies and current anti-pruritic approaches are inadequate[1,2]

Approximately 1.2 million US patients have advanced (stage 4-5) non-dialysis CKD[3-6]

~30% advanced CKD patients experience moderate to severe pruritus[7]

1. Makar M et al. Chronic kidney disease associated pruritus: a review. Kidney Blood Press Res 2021. 46:659-669. 2. Mettang T and Kremer AE. Uremic Pruritus. Kidney International. 2015. 87:685-691 3. Centers for Disease Control and Prevention https://nccd.cdc.gov/ckd/detail.aspx?Qnum=Q372. 4. DataMonitor 5. States Renal Data System https://adr.usrds.org/2020/chronic-kidney-disease/1-ckd-in-the-general-population. 6. Wong SJY et al. Decisions about Renal Replacement Therapy in Patients with Advanced Kidney Disease in the US Department of Veterans Affairs, 2000–2011. Clin Journal of Am Soc Neprol. 2016. 11(10): 1825-1833. 7. Sukul N et al. Pruritus and patient reported outcomes in non-dialysis CKD. Clin J Am Soc Nephrol 2019. 673-681.

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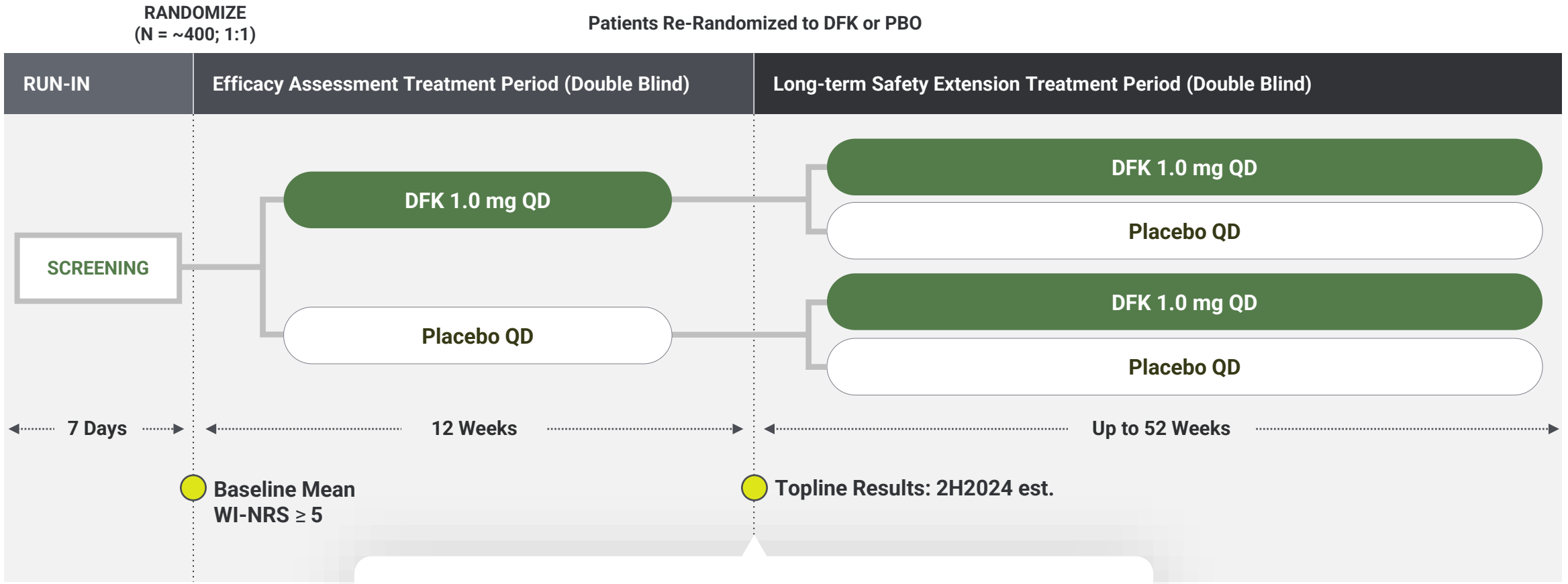
KICK 1 & KICK 2: Phase 3 Study Design in CKD

Program initiated in 1Q22, enrollment ongoing



PRIMARY ENDPOINT

- % of subjects with ≥4-point improvement from baseline in WI-NRS score at Week 12

ADDITIONAL ENDPOINTS

- Quality of life, including sleep
- Safety assessments

KICK1 US sites only, KICK 2 US and ex-US sites

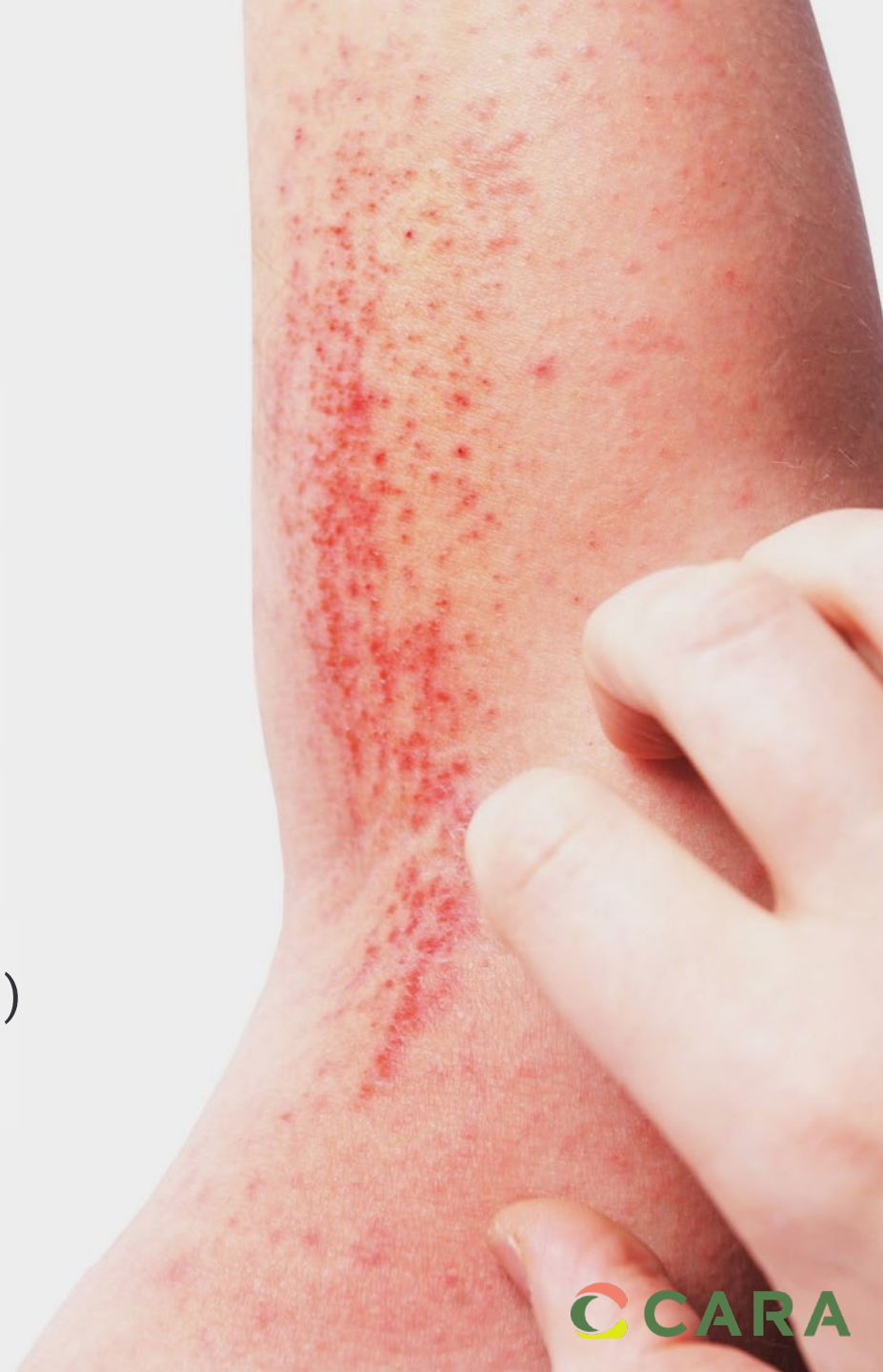
Oral Difelikefalin: Potential to Address Significant Need for an Oral Antipruritic in Atopic Dermatitis (AD)

Pruritus is a hallmark of AD, often called “the itch that rashes”[1]

Itch is considered the most burdensome AD symptom by patients[2], strongly and negatively impacts quality of life[3]

Pruritus in AD remains an unmet need

Target “itch dominant” adult AD patients (~25% of market or ~3M) with moderate to severe pruritus, but mild to moderate disease[4-6]



1. Correale CE et al. Atopic dermatitis: a review of diagnosis and treatment. Am Fam Physician. 1999. 60(4):1191-1198 2. Silverberg JI et al. Patient burden and quality of life in atopic dermatitis in US adults. Annals of Allergy, Asthma, and Immunology (2018). 121(3): 340-347 3. Legat FJ. Itch in atopic dermatitis – what is new? Front Med (Lausanne) 2021. 8:644760. 4. Barbarot S, Auziere S, Gadkari A, et al. Epidemiology of atopic dermatitis in adults: results from an international survey. Allergy. 2018;73(6):1284-1293. 5. United States Census Bureau 2020. 6. Raj Chovatiya MD, PhD , Donald Lei MS , Adnan Ahmed BS, Rajeev Chavda MD, Sylvie Gabriel MD, Jonathan I. Silverberg MD, PhD, MPH , Clinical phenotyping of atopic dermatitis using combined itch and lesional severity: A prospective observational study, Annals of Allergy, Asthma Immunology (2021).

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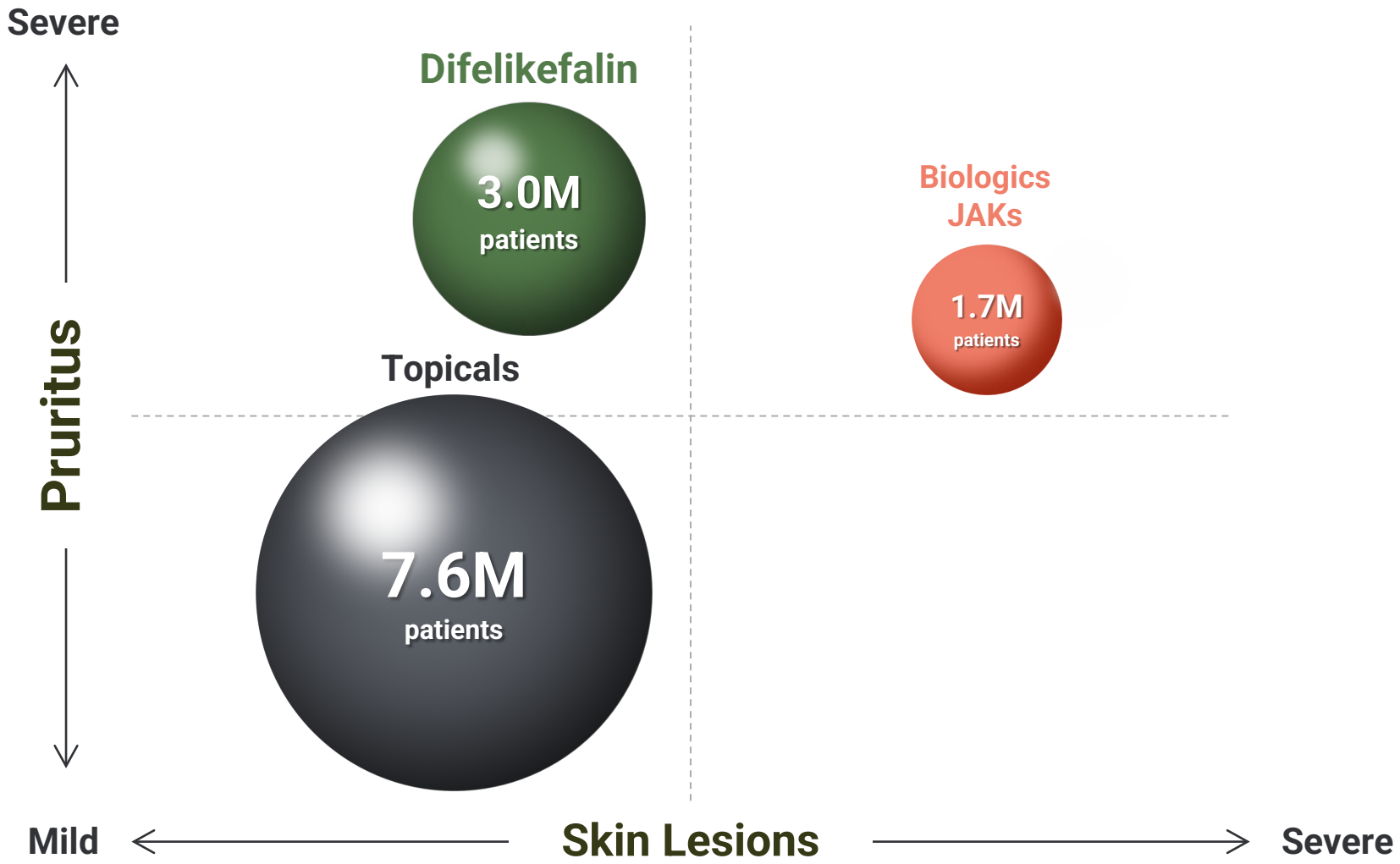
Oral Difelikefalin: Targeting Itch Dominant Adult AD Market

Differentiated positioning in a seemingly crowded market



- **Itch Dominant[1] AD Market**

  Significant Unmet Need

  Patients with mild to moderate lesions, but moderate to severe itching

- **Sizeable Target Market**

  12M adult AD patients

  80% mild-moderate AD

  30% moderate-severe itch

- **Preferable Product Characteristics**

  Oral, non-steroidal, non-biologic therapy

1. Raj Chovatiya MD, PhD , Donald Lei MS , Adnan Ahmed BS, Rajeev Chavda MD, Sylvie Gabriel MD, Jonathan I. Silverberg MD, PhD, MPH , Clinical phenotyping of atopic dermatitis using combined itch and lesional severity: A prospective observational study, Annals of Allergy, Asthma Immunology (2021).

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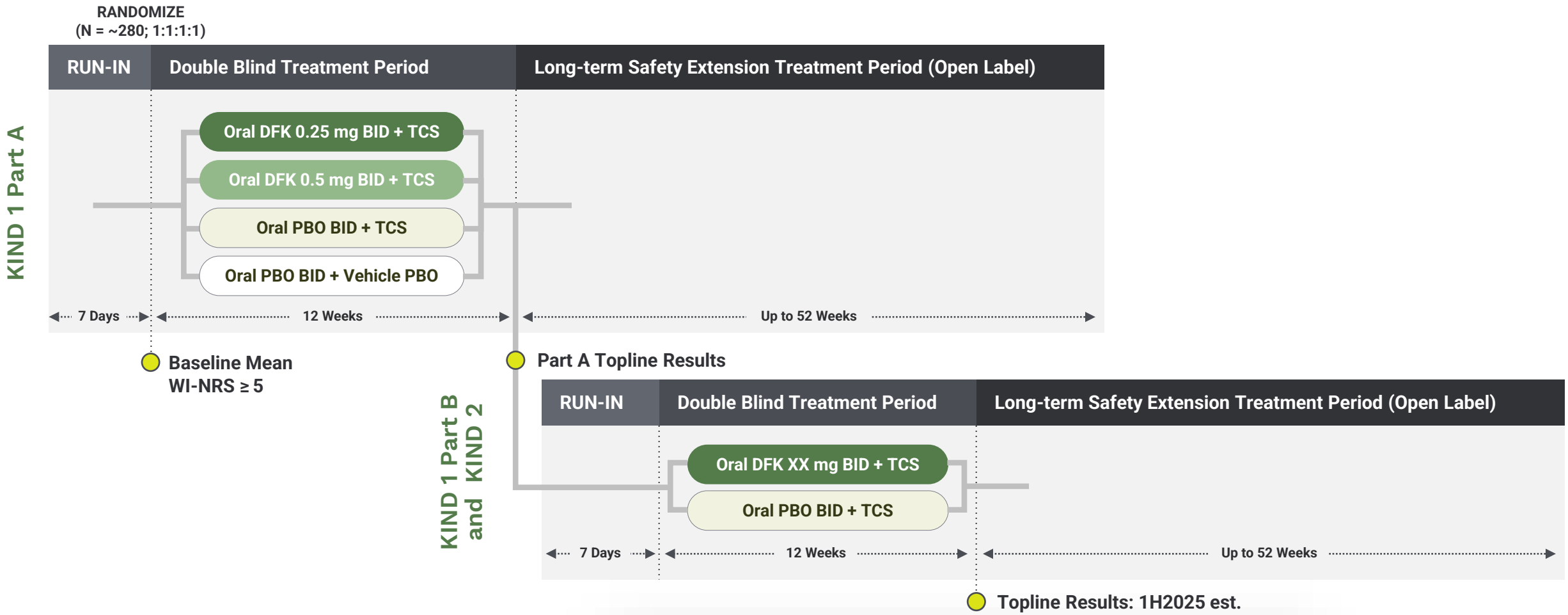
KIND 1 & KIND 2: Phase 3 Study Design in AD

Program initiated in 1Q22, enrollment ongoing



PRIMARY ENDPOINT

- % of subjects with ≥4-point improvement from baseline in WI-NRS score at Week 12

ADDITIONAL ENDPOINTS

- Quality of life, including sleep
- Skin assessment
- Safety assessments

KIND 1 Part A will include sites in USA only

KIND 1 Part B will include sites in North America only, while KIND 2 will include sites in North America and outside of North America

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Oral Difelikefalin: Potential to Address Significant Need in Notalgia Paresthetica (NP)

NP is a sensory neuropathic syndrome characterized by chronic pruritus[1]

Pruritus is burdensome and impairs quality of life[2]

Estimated >650K patients currently treated for NP[1, 3-5]

No FDA-approved treatments; off label treatments are either ineffective or have tolerability issues[2]

1. Pereira P. et al., Acta DV 2018 ; 98:82-88; 2. Howard M et al. Notalgia paresthetica: a review for dermatologists. Int J of Derm. 2017. 388-392. 3. US Census Bureau 2020 population projection; 4. Mollanazar N.K. et al., Acta Clin Croat 2018; 57:721-725; 5. Syneos Health qualitative primary research of US dermatologists, Feb 2022; 5. Syneos market research and Apollo claims database

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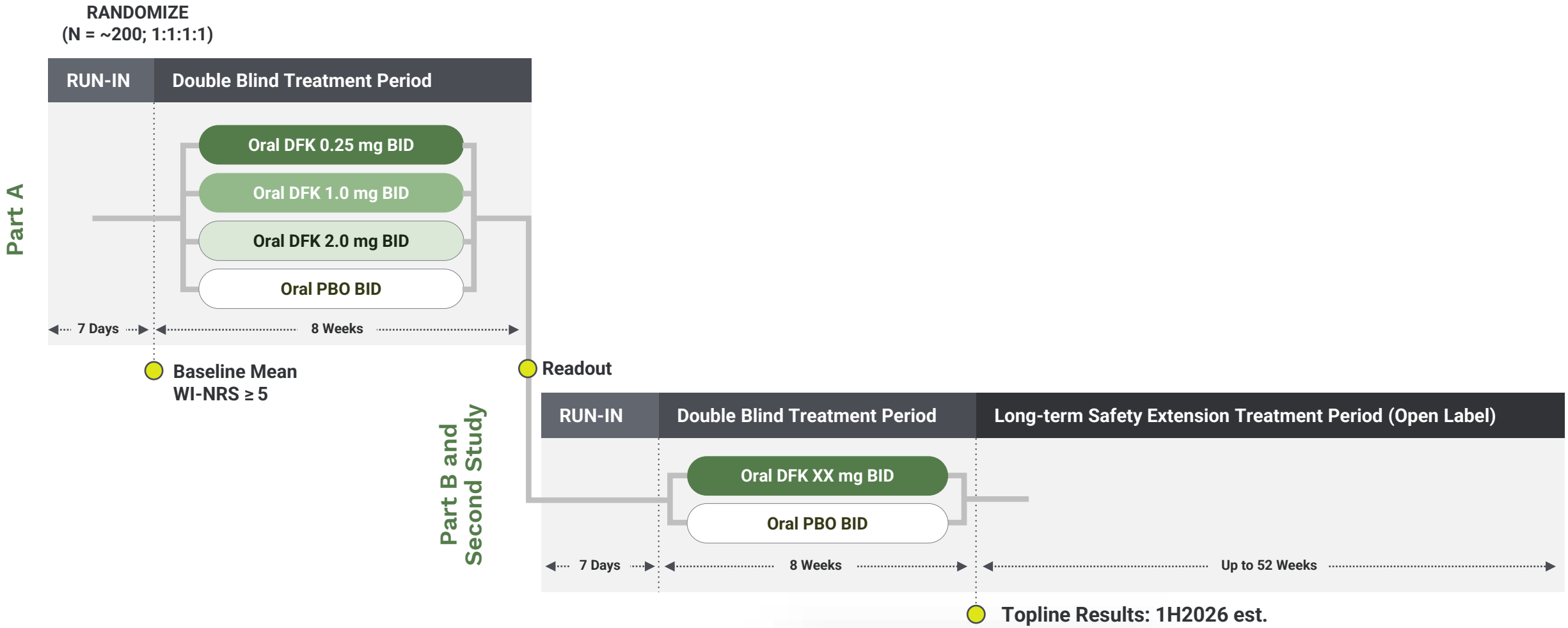
KOURAGE 1 and KOURAGE 2: Phase 2/3 Study Design in NP

Program initiated in 1Q23



PRIMARY ENDPOINT
% of subjects with ≥4-point improvement from baseline in WI-NRS score at Week 8

Catalysts to Drive Long-term Growth*

Initiation
KOURAGE 1 Part A
NP Phase 2/3
(1Q 2023)

KIND 1 Part A
AD Phase 3
Topline Data
(December 2023)

KORSUVA approved in Japan
(September 2023)

KICK 1 & 2
Advanced CKD Phase 3
Topline Data
(2H 2024)

KOURAGE 1 Part A
NP Phase 3
Readout
(2H 2024)

KIND 1B & 2
AD Phase 3
Topline Data
(1H 2025)

KOURAGE 1B & 2
NP Phase 3
Topline Data
(1H 2026)

KORSUVA® Injection US Commercialization - Launched April 2022

Kapruvia/KORSUVA International Commercialization - Launched September 2022**

2023 2024 2025 2026

*Anticipated Timelines
** In November 2023, Cara announced that it entered into a Purchase and Sale Agreement with HCRX Investments Holdco, L.P. and Healthcare Royalty Partners IV, L.P., or collectively HCR, in which HCR will receive all royalties due to Cara from KORSUVA® (difelikefalin) injection / Kapruvia® ex-U.S. license agreements with CSL Vifor and Maruishi Pharmaceutical Co.

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Strong Financial Foundation to Advance Pipeline and Drive Long-term Growth

1

Cash runway into 2025

- Entered into Royalty Interest Purchase and Sale Agreement with HealthCare Royalty (HCRx) for up to $40 million with $37.5M expected in total in the fourth quarter of 2023.

2

$83M cash position as of September 30, 2023

- 54M shares outstanding and no debt

3

Continued pipeline growth

- Sufficient resources to support development of oral difelikefalin across all three late-stage programs

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Thank You

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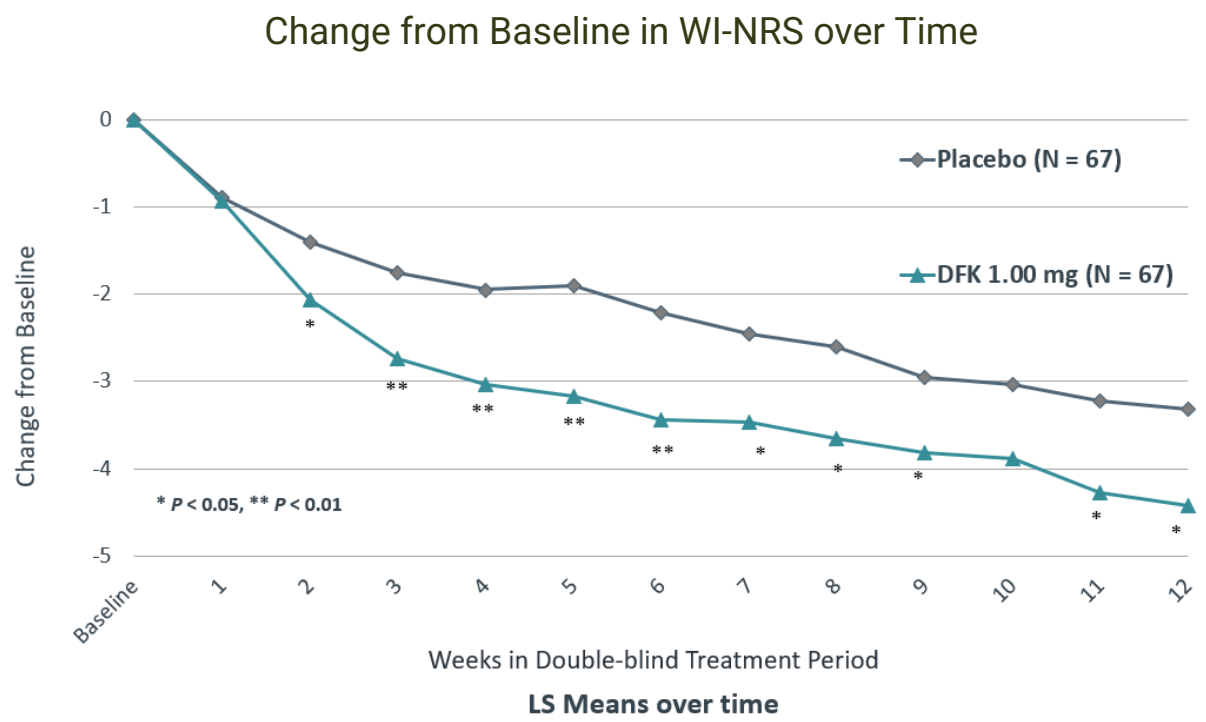
Appendix

Phase 2 Data Provides Path Forward into Phase 3 Advanced CKD

Primary Endpoint



- Significant difference achieved between 1mg oral difelikefalin and placebo in WI-NRS score at Week 12
- Generally well-tolerated with safety profile consistent with clinical development program
- Phase 2 findings and EOP2 discussion with FDA established dose and patient population in Advanced CKD for Phase 3 trial

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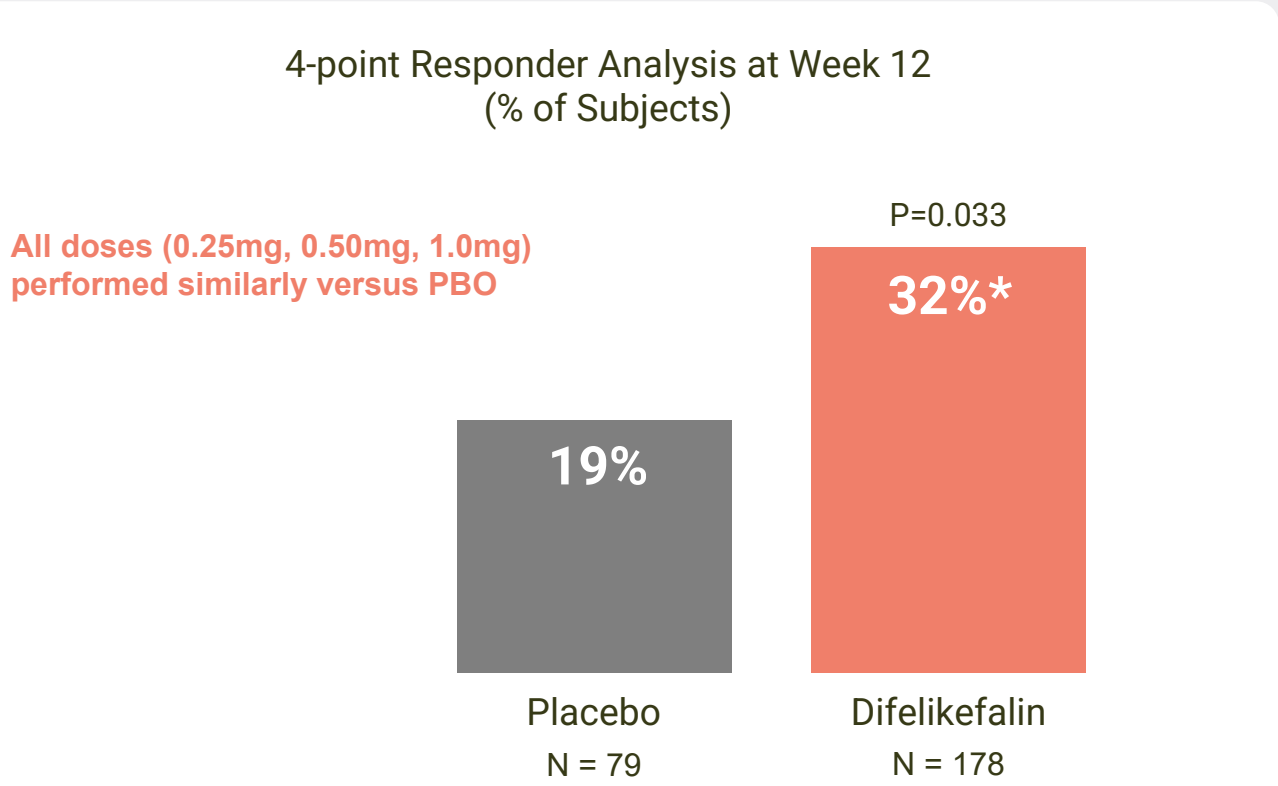
KARE STUDY: Phase 2 Data in Atopic Dermatitis (AD)

Population: Mild to Moderate AD (BSA <10)



- Anti-pruritic effect started at week 1 and was sustained through week 12
- Statistical significance achieved for the registration endpoint (4-point responder) in mild-to-moderate AD population
- The drug was generally well tolerated

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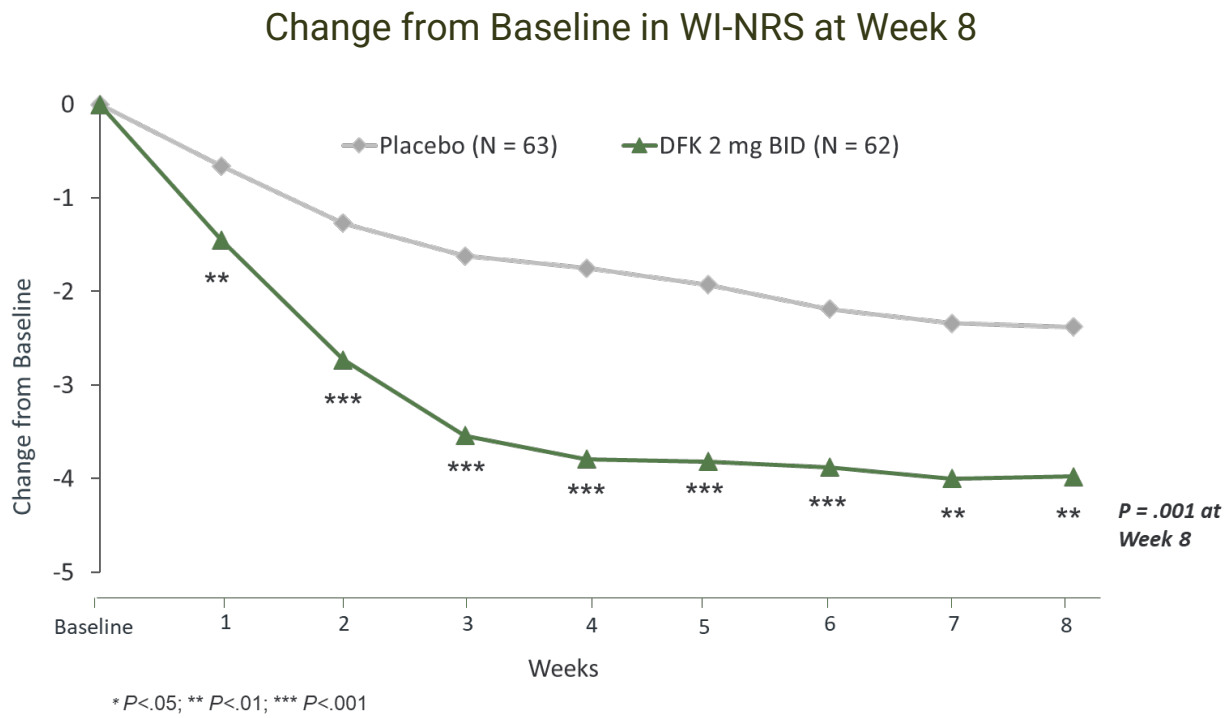
Encouraging Phase 2 Data in First Well-Controlled NP Study

Primary Endpoint



- Significant difference achieved between 2 mg BID oral difelikefalin and placebo in WI-NRS score at Week 8
- Rapid onset of action within Week 1 and sustained response through Week 8
- Significantly greater proportion of patients on difelikefalin with ≥ 4-point improvement starting Week 2
- Generally well-tolerated with safety profile consistent with other clinical development programs

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

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