UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d) of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **June 28, 2022**

CARA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-36279**	**75-3175693**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

4 Stamford Plaza	
107 Elm Street, 9th Floor	
Stamford, Connecticut	**06902**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(203) 406-3700**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2.):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	CARA	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On June 30, 2022, Cara Therapeutics, Inc. (the "Company") issued a press release (the "Press Release") announcing positive topline results from its KOMFORT Phase 2 clinical trial of oral difelikefalin for the treatment of moderate-to-severe pruritus associated with Notalgia Paresthetica ("NP") patients. The Company will hold a conference call to discuss the results at 8:30 a.m. ET on June 30, 2022. A copy of the Press Release and the presentation (the "NP Presentation") to be discussed on the conference call are furnished as Exhibit 99.1 and Exhibit 99.2, respectively, to this Current Report on Form 8-K and incorporated herein by reference.

On June 30, 2022, the Company made available an updated corporate presentation, which can be found on the Company's website (the "Corporate Presentation"). The Corporate Presentation is furnished as Exhibit 99.3 and incorporated herein by reference.

The information furnished under this Item 7.01, including Exhibit 99.1, Exhibit 99.2 and Exhibit 99.3, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or subject to the liabilities of that section, nor shall it be deemed to be incorporated by reference into any of the Company's filings with the Securities and Exchange Commission ("SEC") under the Exchange Act or the Securities Act of 1933, as amended, whether made before or after the date hereof, regardless of any general incorporation language in such a filing. The information shall not be deemed incorporated by reference into any other filing with the SEC made by the Company, regardless of any general incorporation language in such filing.

Item 8.01. Other Information.

On June 30, 2022, the Company issued the Press Release announcing positive topline results from its KOMFORT Phase 2 clinical trial of oral difelikefalin for the treatment of moderate-to-severe pruritus associated with NP patients.

The Phase 2 multicenter, randomized, double-blind, placebo-controlled, 8-week study was designed to evaluate the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in approximately 120 patients with NP. Patients were randomized to oral difelikefalin 2 mg taken twice daily versus placebo for 8 weeks, followed by a 4-week active extension period.

Primary Endpoint

The primary efficacy endpoint was the change from baseline in the weekly mean of the daily 24-hour Worst Itch-Numeric Rating Scale ("WI-NRS") score at Week 8. Other endpoints included the ≥4-point responder analysis, itch-related quality of life scores, and safety assessments.

Patients treated with oral difelikefalin achieved the primary endpoint (-4.0 difelikefalin versus -2.4 placebo, p=0.001) with significant improvement observed as early as Week 1 and sustained through Week 8.

Other Endpoints

A statistically significantly greater proportion of patients treated with oral difelikefalin achieved a ≥4-point improvement in WI-NRS score at Week 8 versus placebo (41% difelikefalin versus 18% placebo, p=0.007).

Safety and Tolerability

Oral difelikefalin was generally well tolerated with a safety profile consistent with that seen in earlier clinical trials. The most common treatment-emergent adverse events reported in ≥5% of patients treated with oral difelikefalin and greater than placebo were: nausea, headache, dizziness, constipation and urine output increased.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated June 30, 2022
99.2	NP Presentation, dated June 30, 2022
99.3	Corporate Presentation, dated June 30, 2022
104	Cover page interactive data file (formatted as Inline XBRL)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

CARA THERAPEUTICS, INC.

By: /s/ CHRISTOPHER POSNER
Christopher Posner
President and Chief Executive Officer

Date: June 30, 2022

Exhibit 99.1

Cara Therapeutics Announces Positive Topline Results from KOMFORT Phase 2 Trial of Oral Difelikefalin for the Treatment of Pruritus in Patients with Notalgia Paresthetica

– Study achieved primary endpoint of Worst Itch-Numeric Rating Scale score change from baseline at Week 8 (p=0.001) –

– Onset of action seen at Week 1 and sustained through Week 8 –

– Statistical significance achieved on the WI-NRS ≥4-point responder analysis at Week 8 (p=0.007) –

– Oral difelikefalin was well tolerated with a consistent safety profile –

– Conference call today at 8:30 a.m. ET –

STAMFORD, Conn., June 30, 2022 – Cara Therapeutics, Inc. (Nasdaq: CARA), a commercial-stage biopharmaceutical company leading a new treatment paradigm to improve the lives of patients suffering from pruritus, today announced positive topline results from its Phase 2 proof-of-concept clinical trial (KOMFORT) evaluating oral difelikefalin for the treatment of moderate-to-severe pruritus in patients with notalgia paresthetica (NP), a nerve disorder characterized by chronic pruritus of the upper to middle back.

"We are pleased to have demonstrated clinical proof of concept for oral difelikefalin in the treatment of pruritus associated with notalgia paresthetica," said Joana Goncalves, M.D., Chief Medical Officer at Cara Therapeutics. "These topline results coupled with the results from our other programs support the broad development of oral difelikefalin across disease areas regardless of the underlying cause of pruritus. We look forward to completing our data analyses and discussing next steps with the U.S. Food and Drug Administration."

"With no approved treatments available for notalgia paresthetica, the condition is challenging to manage and burdensome for patients," said Mark Lebwohl, M.D., the lead investigator and Professor and Dean for Clinical Therapeutics and Chairman Emeritus of the Department of Dermatology at Icahn School of Medicine at Mount Sinai. "These are encouraging results that underscore the potential for oral difelikefalin to be the first treatment option to address pruritus associated with notalgia paresthetica."

Phase 2 Proof-of-Concept Trial Design & Topline Results

The Phase 2 multicenter, randomized, double-blind, placebo-controlled, 8-week study was designed to evaluate the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in approximately 120 patients with NP. Patients were randomized to oral difelikefalin 2 mg taken twice daily versus placebo for 8 weeks, followed by a 4-week active extension period.

The primary efficacy endpoint was the change from baseline in the weekly mean of the daily 24-hour Worst Itch-Numeric Rating Scale (WI-NRS) score at Week 8. Other endpoints included the ≥4-point responder analysis, itch-related quality of life scores, and safety assessments.

Patients treated with oral difelikefalin achieved the primary endpoint (-4.0 difelikefalin vs. -2.4 placebo, p=0.001) with significant improvement observed as early as Week 1 and sustained through Week 8.

In addition, a statistically significantly greater proportion of patients treated with oral difelikefalin achieved a ≥4-point improvement in WI-NRS score at Week 8 vs. placebo (41% difelikefalin vs. 18% placebo, p=0.007).

Oral difelikefalin was generally well tolerated with a safety profile consistent with that seen in earlier clinical trials. The most common treatment-emergent adverse events reported in ≥5% of patients treated with oral difelikefalin and greater than placebo were: nausea, headache, dizziness, constipation and urine output increased.

Conference Call & Webcast

Cara management will host a conference call and live webcast today at 8:30 a.m. ET to discuss the positive topline results.

To participate in the conference call, please dial (855) 445-2816 (domestic) or (484) 756-4300 (international) and refer to conference ID 6999079. A live webcast of the call can be accessed under "Events & Presentations" in the News & Investors section of the Company's website at www.CaraTherapeutics.com.

An archived webcast recording will be available on the Cara website beginning approximately two hours after the call.

About Pruritus Associated with Notalgia Paresthetica

Notalgia paresthetica (NP) is a common, although under-recognized, chronic, sensory neuropathy affecting the upper back.[1] It is estimated that chronic pruritus affects up to 13% of the population in the United States, and about 8% of these patients suffer from neuropathic itch, including NP.[2,3] One of the hallmark features of NP is chronic pruritus, which can be significantly burdensome and undermines the affected patients' quality of life and overall well-being.[3] The exact etiology of NP still has not been fully elucidated; however, it is widely accepted that NP is a sensory neuropathy caused by alteration and damage to thoracic spinal nerves.[3]

The management of NP is challenging and is often resistant to multiple therapies. There is currently no approved treatment for NP and conventional treatments for pruritus, such as antihistamines and topical steroids, are largely ineffective.[4]

References:

1. Matthew Howard, Lukas Sahhar, Frank Andrews, Ralph Bergman and Douglas Gin. Notalgia paresthetica: a review for dermatologists. International J of Dermatology 2018,57, 388-392.
2. Manuel P. Pereira, Hannah Lüling, Annette Dieckhöfer, Sabine Steinke, Claudia Zeidler and Sonja Ständer. Brachioradial Pruritus and Notalgia Paraesthetica: A Comparative Observational Study of Clinical Presentation and Morphological Pathologies. Acta DV 2018; 98:82-88.
3. Mollanazar, N.K., Koch, S.D. & Yosipovitch, G. Epidemiology of Chronic Pruritus: Where Have We Been and Where Are We Going?. Curr Derm Rep 4, 20–29 (2015)
4. Mirna Šitum, Maja Kolić, Nika Franceschi and Marko Pećina. Notalgia Paresthetica. Acta Clin Croat 2018; 57:721-725.
5. Ahmed Ansari, David Weinstein & Naveed Sami. Notalgia paresthetica: treatment review and algorithmic approach. Journal of Dermatological Treatment 2019.

About Cara Therapeutics

Cara Therapeutics is a commercial-stage biopharmaceutical company leading a new treatment paradigm to improve the lives of patients suffering from pruritus. The Company's novel KORSUVA™ (difelikefalin) injection is the first and only FDA-approved treatment for moderate-to-severe pruritus associated with chronic kidney disease in adults undergoing hemodialysis. The Company is developing an oral formulation of difelikefalin and has initiated Phase 3 programs for the treatment of pruritus in patients with non-dialysis dependent advanced chronic kidney disease and atopic dermatitis. The Company has completed the placebo-controlled phase of a Phase 2 proof-of-concept trial of oral difelikefalin for the treatment of moderate-to-severe pruritus in patients with notalgia paresthetica. A Phase 2 proof-of-concept trial in primary biliary cholangitis patients with moderate-to-severe pruritus is ongoing. For more information, visit www.CaraTherapeutics.com and follow the company on Twitter, LinkedIn and Instagram.

Forward-looking Statements

Statements contained in this press release 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 planned future regulatory submissions and potential future regulatory approvals, 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, including NP, and the potential for oral difelikefalin to address additional pruritic indications, the size and growth of the potential markets for pruritus management, the Company's expected cash reach, and the potential impact of COVID-19 on the Company's clinical development and regulatory timelines and plans. 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 ending December 31, 2021 and its other documents subsequently filed with or furnished to the Securities and Exchange Commission. All forward-looking statements contained in this press release 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.

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Exhibit 99.2

KOMFORT Phase 2 Topline Data:

Oral Difelikefalin for Pruritus in Notalgia Pares

JUNE 2022

The KOMFORT Phase 2 study evaluated the efficacy and safety of oral difelikefalin for moderate to severe pruritus in adult subjects with notalgia paresthetica (NP). Oral difelikefalin is an investigational drug product and its safety and efficacy have not been fully evaluated by any regulatory authority. The FDA approved KORSUVA™ (difelikefalin) injection for the treatment of moderate-to-severe pruritus (itching) associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis (HD).

CA
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Forward Looking Statements

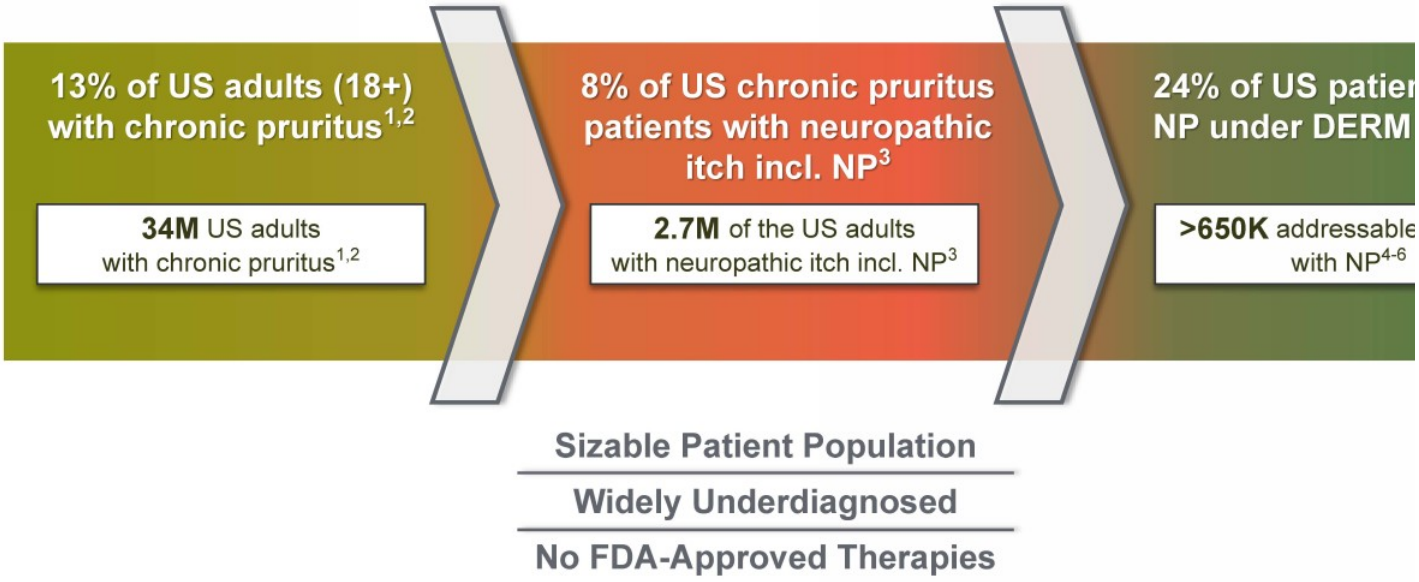
Statements contained in this presentation regarding matters that are not historical facts are "forward-lookin statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Examples of these looking statements include statements concerning the timing of the Company's planned clinical trials, poter of ongoing and planned clinical trials, the Company's planned future regulatory submissions and potential f regulatory approvals, timing of future regulatory and development milestones for the Company's product ca the potential for the Company's product candidates to be an alternative for Notalgia Paresthetica, the size a of the potential markets for Notalgia Paresthetica, the potential for oral difelikefalin to address additional pr indications, and the potential impact of COVID-19 on the Company's clinical development and regulatory ti plans. Because such statements are subject to risks and uncertainties, actual results may differ materially f expressed or implied by such forward-looking statements. Risks are described more fully in Cara Therapeu with the Securities and Exchange Commission, including the "Risk Factors" section of the Company's Annu Form 10-K for the year ending December 31, 2021 and its other documents subsequently filed with or furni Securities and Exchange Commission. All forward-looking statements contained in this presentation speak the date on which they were made. Cara Therapeutics undertakes no obligation to update such statements events that occur or circumstances that exist after the date on which they were made except as required b

Advancing our late-stage pipeline in multiple indications

Program	Indication	STAGE OF DEVELOPMENT: Phase 1	Phase 2	Phase 3	Approved
KORSUVA™ Injection[1]	Pruritus HD-CKD				
Oral difelikefalin	Pruritus NDD-CKD (stages IV-V)				
Oral difelikefalin	Pruritus Atopic Dermatitis				
Oral difelikefalin	Pruritus NP				
Oral difelikefalin	Pruritus PBC				

1. Approved in the EU with the tradename KapruviaTM. 2. Commercialization rights to difelikefalin in defined indications - Japan: Maruishi Pharmaceutical Co, LTD; South Korea: Chong Kun Dang Pharmaceuticals. 3. Vifor Fresenius Medical Care Renal Pharma (VFMCRP) has commercial rights under a profit-share arrangement in the US and a royalty arrangement ex-US.
HD CKD-aP: Hemodialysis Chronic Kidney Disease-associated Pruritus; NDD-CKD-aP: Non-Dialysis Dependent Chronic Kidney Disease associated Pruritus; Pruritus NP: Notalgia Paresthetica associated Pruritus; Pruritus PBC: Primary Biliary Cholangitis associated Pruritus

Notalgia Paresthetica: A Sizable Market Opportun



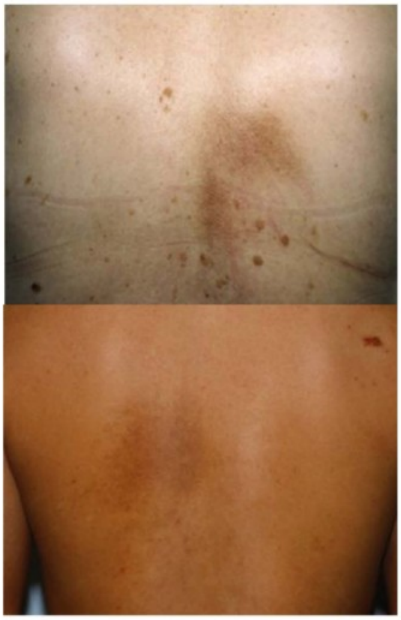
Sizable Patient Population

Widely Underdiagnosed

No FDA-Approved Therapies

 Source: 1. US Census Bureau 2020 population projection; 2. Mollanazar NK et al., Current Derm Report 2015: 4;20-29; 3. Pereira P. et al., Acta DV 2018; 98:82-88; 4. Syneos Health qualitative primary research of US dermatologists, Feb 2022; 5. Syneos Health quantitative research of derm office administrators, March 2022; 6. IQVIA, KOMODO, and RxDataScience Apollo claims database

Notalgia Paresthetica: A Significant Unmet Need



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

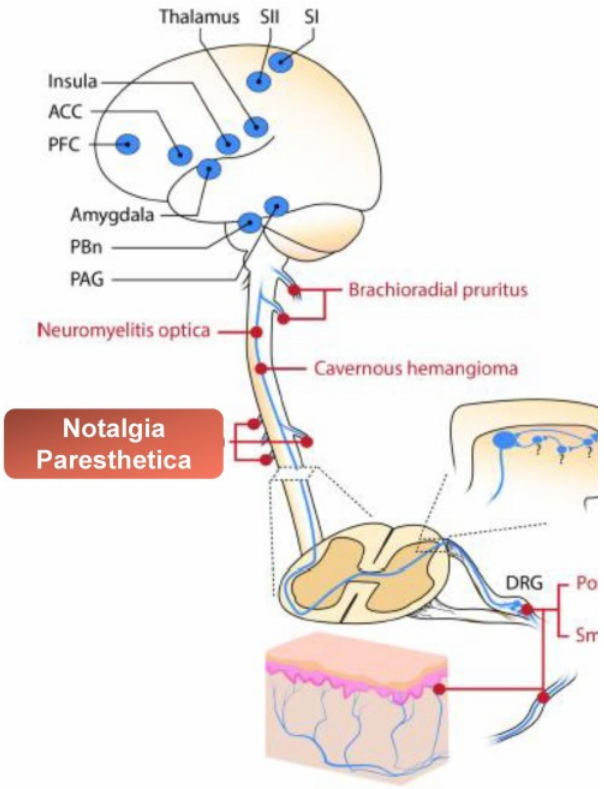
Pruritus is burdensome and impairs quality of life[1]

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

 Source: 1. Pereira Manuel et al ActaDV 2018; 98:82-88, 2. Howard et al Int J of Derm 2018; 57; 388- 392.

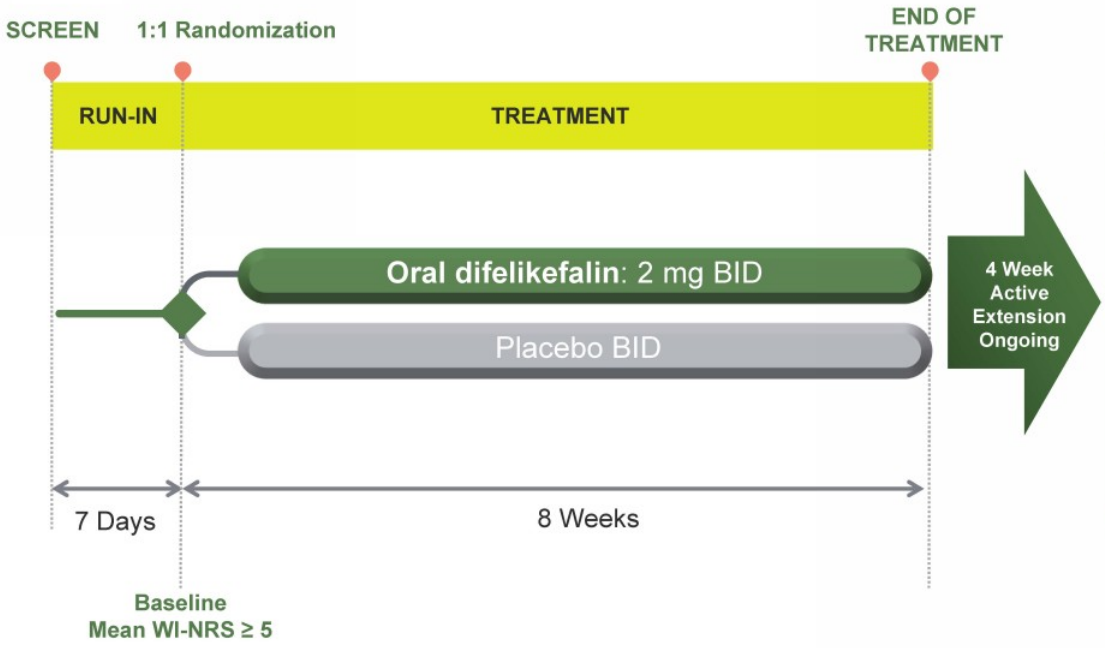
Notalgia Paresthetica

- Likely due to mechanical irritation along the spinal cord
- Believed to be caused by compression of the dorsal branches of the spinal nerves (T2-T6)
- Leads to circumscribed pruritus between the scapulae, usually unilateral but occasionally bilateral



 Source: Pereira Manuel et al ActaDV 2018; 98:82-88. Hachisuka et al Pain 2018; 159(3): 603-609.

KOMFORT: POC Phase 2 Study Design



Primary Endpoint

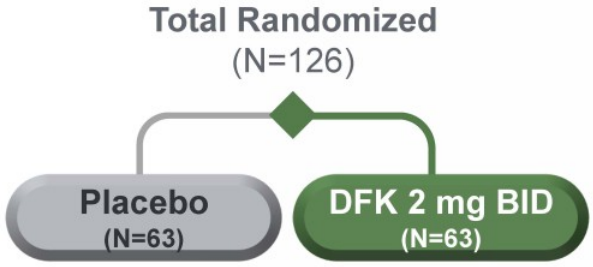
- **Change from bas**
  weekly mean of t
  Worst Itch-Numer
  (WI-NRS) at Week

Other Endpoints

- **Proportion of pat**
  ≥4-point improve
  at Week 8
- **Safety Assessme**
- **QoL assessments**

 Oral difelikefalin is an investigational drug product and its safety and efficacy have not been fully evaluated by any regulatory authority. The FDA approved KORSUVA™ (difelikefalin) injection for the treatment of moderate-to-severe pruritus (itching) associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis (HD).

Patient Disposition



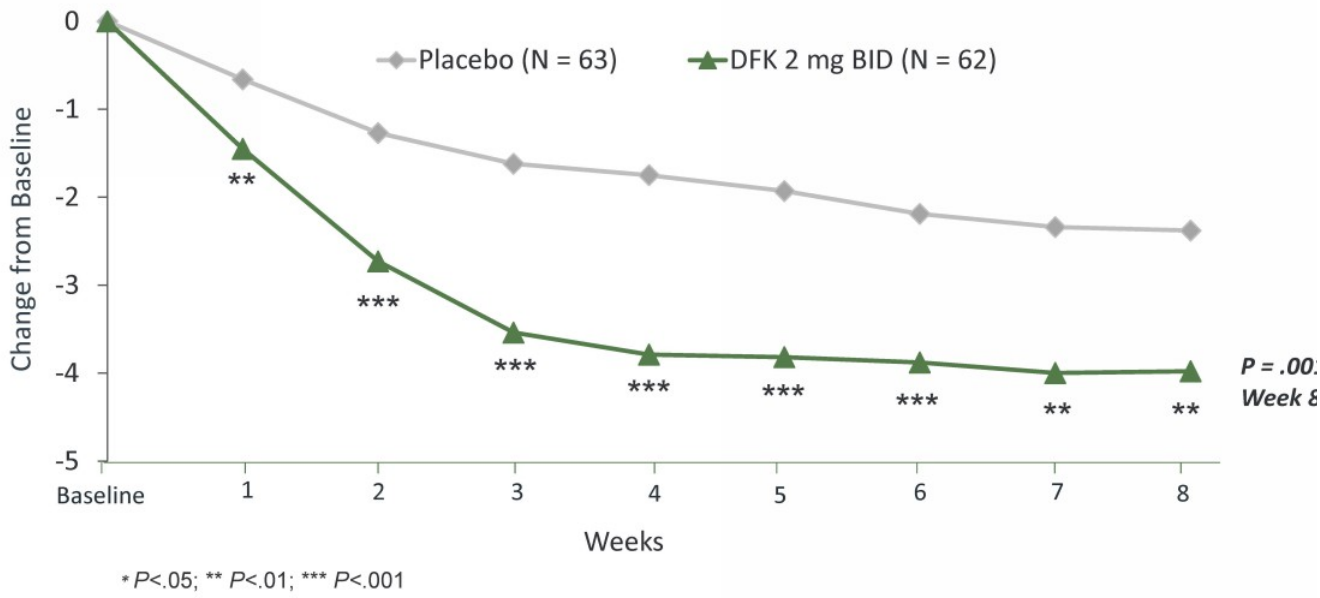
	Placebo (N=63)	DFK 2 mg BID (N=63)
Received Study Treatment	**63 (100%)**	**62 (98.4%)**
Completed	**57 (90.5%)**	**49 (77.8%)**
Discontinued	**6 (9.5%)**	**14 (22.2%)**
Adverse event	4 (6.3%)	12 (19.0%)
Lost to follow-up	2 (3.2%)	1 (1.6%)
Patient withdrew consent	0	1 (1.6%)

Patient Demographics & Disease Characteristics

	Placebo (N=63)	DFK 2 mg BID (N=62)
Female, n (%)	42 (66.7%)	48 (77.4%)
Age - Mean (SD)	60.2 (11.8)	59.3 (12.4)
Race, n (%)		
White	56 (88.9%)	49 (79.0%)
Black	4 (6.3%)	10 (16.1%)
Other	3 (4.8%)	3 (4.8%)
BMI – Mean (SD)	28.7 (5.2)	29.7 (5.8)
Duration of NP (yrs) – Mean (SD)	8.15 (7.4)	8.9 (10.4)
Baseline WI-NRS – Mean (SD)	7.6 (1.4)	7.6 (1.4)

Primary Endpoint: Change from Baseline in Daily WI-NRS at Week 8

Significant improvement observed with difelikefalin vs placebo at all timepoints

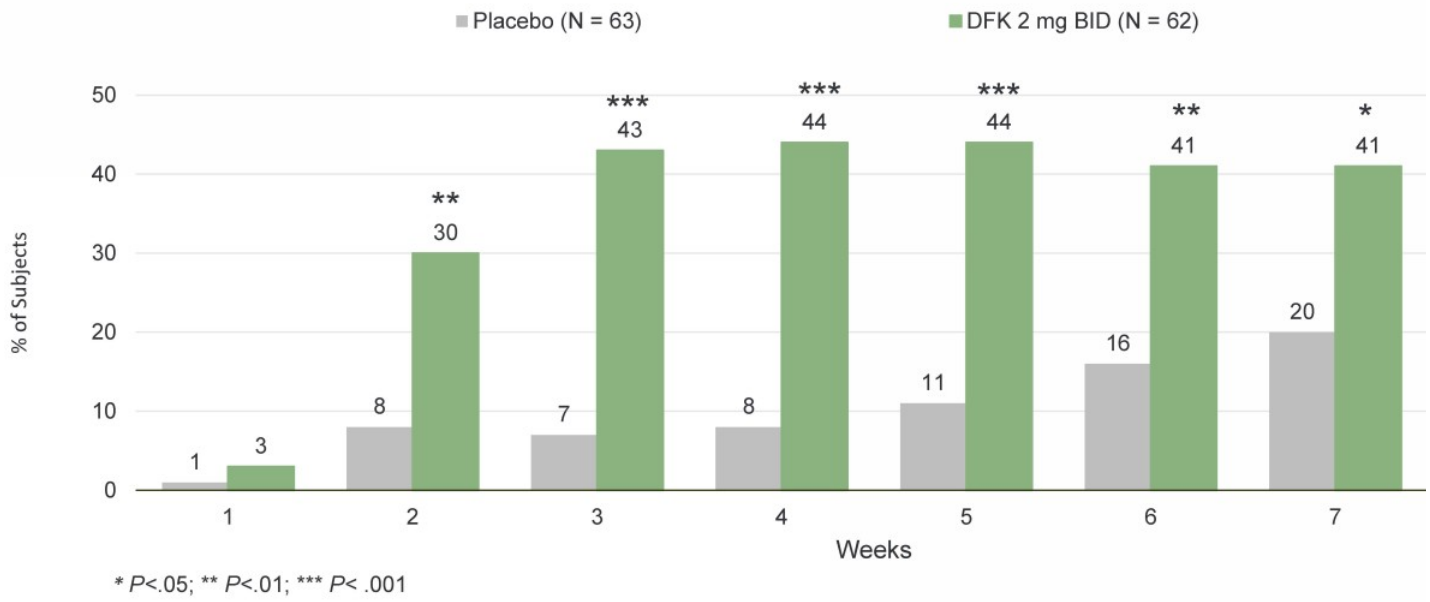


* *P*<.05; ** *P*<.01; *** *P*<.001

 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

≥ 4-point Improvement in WI-NRS (ITT)

Significant improvement observed with DFK vs placebo starting at Week 2



* *P*<.05; ** *P*<.01; *** *P*< .001

Estimated percentages & P-values from a logistic regression with terms for treatment and baseline WI-NRS score
Subjects with missing weekly WI-NRS scores for a particular week are categorized as non-responders

Summary of Adverse Events

	Placebo (N=63)	DFK 2 mg BID (N=62)
Patients with at least one TEAE, n (%)	32 (50.6%)	35 (56.5%)
Patients with at least one severe TEAE, n (%)	1 (1.6%)	0
Patients with at least one serious TEAE, n (%)	0	0
Patients with TEAE resulting in treatment discontinuation, n (%)	4 (6.3%)	12 (19.4%)

 Safety analyses performed in the safety population, defined as all randomized patients who received ≥1 dose of study drug based on actual treatment received.

Most Commonly Reported TEAEs

Treatment-emergent Adverse Events at ≥5% frequency; n (%)	Placebo (N=63)	DFK 2 mg BID (N=62)
Nausea	7 (11.1%)	8 (12.9%)
Abdominal pain*	8 (12.7%)	7 (11.3%)
Headache	3 (4.8%)	7 (11.3%)
Dizziness	2 (3.2%)	7 (11.3%)
Constipation	4 (6.3%)	6 (9.7%)
Urine output increased#	1 (1.6%)	5 (8.1%)

 Safety analyses performed in the safety population, defined as all randomized patients who received ≥1 dose of study drug based on actual treatment received.
*includes PTs abdominal pain, abdominal pain upper, abdominal discomfort, abdominal pain lower; #includes urine output increased and pollakiuria

KOMFORT Phase 2 Summary

- **Oral difelikefalin demonstrated strong anti-pruritic effect in patients v Notalgia Paresthetica**
  - Primary endpoint met demonstrating statistically significant superiority of difel versus placebo in Daily WI-NRS at Week 8
  - Rapid onset of action with significant improvements achieved at Week 1 and through Week 8
  - Significantly greater proportion of patients on difelikefalin had ≥ 4-point improv starting at Week 2

- **Oral difelikefalin was generally well tolerated with a consistent safety**

- **Next steps planned to include finalizing additional data analyses and engaging with FDA on path forward**

 Oral difelikefalin is an investigational drug product and its safety and efficacy have not been fully evaluated by any regulatory authority. The FDA approved KORSUVA™ (difelikefalin) injection for the treatment of moderate-to-severe pruritus (itching) associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis (HD).

Cara Therapeutics

CORPORATE PRESENTATION

JUNE 2022

Forward Looking Statements

Statements contained in this presentation regarding matters that are not historical facts are "forward-lookin statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Examples of these looking statements include statements concerning the Company's ability to successfully commercialize KO injection and Kapruvia, planned future regulatory submissions and potential future regulatory approvals, th ability to obtain and maintain coverage and adequate reimbursement for KORSUVA injection, the performa commercial partners, including Vifor Pharma, expected timing of the initiation, enrollment and data readout Company's planned and ongoing clinical trials, the potential results of ongoing clinical trials, timing of future and development milestones for the Company's product candidates, the potential for the Company's produ candidates to be alternatives in the therapeutic areas investigated, the size and growth of the potential mar pruritus management, the Company's expected cash reach, and the potential impact of COVID-19 on the C clinical development and regulatory timelines and plans. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking Risks are described more fully in Cara Therapeutics' filings with the Securities and Exchange Commission, the "Risk Factors" section of the Company's Annual Report on Form 10-K for the year ending December 31 its other documents subsequently filed with or furnished to the Securities and Exchange Commission. All fo looking statements contained in this presentation speak only as of the date on which they were made. Car Therapeutics undertakes no obligation to update such statements to reflect events that occur or circumstan exist after the date on which they were made, except as required by law.


OUR MISSION:
Transform the way pruritus is treated to bring quality to the lives of those who suffer.

Millions of US patients could benefit from a chron pruritus therapy

		Estimated US Pruritis Po
SYSTEMIC	HD-Dependent Chronic Kidney Disease (CKD)[1-2]	200
	Non-Dialysis Dependent CKD (Stage 4-5)[3-7]	300
	Chronic Liver Disease[8-12]	3M
DERMATOLOGICAL	Atopic Dermatitis[13-15]	12
NEUROLOGICAL	Notalgia Paresthetica[16-19]	>65

1..National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease. 2. Pisoni et al. Pruritus in haemodialysis patients: international results from the Dialysis Outcomes and Practice Patterns Study (DOPP Nephrology Dialysis Transplantation (2006); 21(12): 3495-3505. 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 reporte outcomes in non-dialysis CKD. Clin J Am Soc Neprhol 2019. 673-681. 8.Centers for Disease Control and Prevention https://www.cdc.gov/nchs/fastats/liver-disease.htm 9. Odea S et al. Prevalence of pruritus in patients with chronic liver disease: A multicenter study. Hepatology Research. 2018. 28(3): E252-E262. 10. Fujino H et al. Pruritus in patients with chronic liver disease and serum autotaxin levels in patients with primary biliary cholangitis. BMC Gastroenterology. 2019. 19:169. 11. Yoshikawa et al. Pruritus is common in patients with chronic liver disease and is improved by nalfurafine hydrochloride. Scientific Reports. 2021. 11:3015. 12. Data on file. 13. National Eczema Assocaition. https://nationaleczema.org/eczema/types-of-eczema/atopic-dermatitis/ 14. DRG Analysis. 15. Mollanazar NK, Smith PK, Yosipovitch G. Mediators of chronic pruritus in atopic dermatitis: getting the itch out? Clin Rev Allergy Immunol. (2016) 51:263–92. 16. US Census Bureau 2020 population projection; 17. Pereira P. et al., Acta DV 2018 ; 98:82-88; 18. Mollanazar N.K. et al., Acta Clin Croat 2018; 57:721-725e.; 19 Syneos market research and Apollo claims database

Cara is well positioned to seize the opportunity ar drive significant immediate and future growth

- First-and-only FDA-approved treatment for CKD-
- Robust R&D engine with multiple pipeline indicatio
- Significant market opportunity & strong financial foundation to deliver growth strategy

KORSUVA Injection is poised for rapid uptake

 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

KORSUVA Injection addresses significant unmet n
in US CKD-aP hemodialysis market

~500K

Patients on hemodialysis[1-2]

40%

With moderate-severe pruritus[2]

~200

Addressable Mar

1. National Institute of Diabetes and Digestive and Kidney Diseases. https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease.
2. URSDS. https://adr.usrds.org/2021/end-stage-renal-disease/1-incidence-prevalence-patient-characteristics-and-treatment-modalities
3. Pisoni et al. Pruritus in haemodialysis patients: international results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrology Dialysis Transplantation (2006); 21(12): 3495-3505.

Concentrated dialysis market dynamics can facili rapid uptake

2 Key Providers

- **Fresenius Medical Care and DaVita have a combined market share of ~75%[1]**

FRESENIUS MEDICAL CARE

Da Kidney

1 Major Payer

- **Medicare covers ~80% of CKD-HD patients[2]**
- **2nd drug in TDAPA**
  - 1st drug Parsabiv - $1.4B revenue in 3-yr period[3]

Medicar

1. https://healthcareappraisers.com/2020-outlook-dialysis-clinics-and-esrd/
2. https://adr.usrds.org/2020/end-stage-renal-disease/9-healthcare-expenditures-for-persons-with-esrd
3. Amgen Annual Report 2018, 2019, 2020

Partnership with Vifor Pharma can maximize laun potential

CARA™ THERAPEUTICS

VIFOR PHARMA

- Leading commercial nephrology organization with turnkey infrastructure, including 100+ sales FTEs
- Strong relationships with US nephrology offices and dialysis centers, including joint venture with Fresenius Medical Care
- Contractual economics bring near term profitability for KORSUVA Injection

KORSUVA injection U.S. launch commenced in Ap 2022 and is progressing well

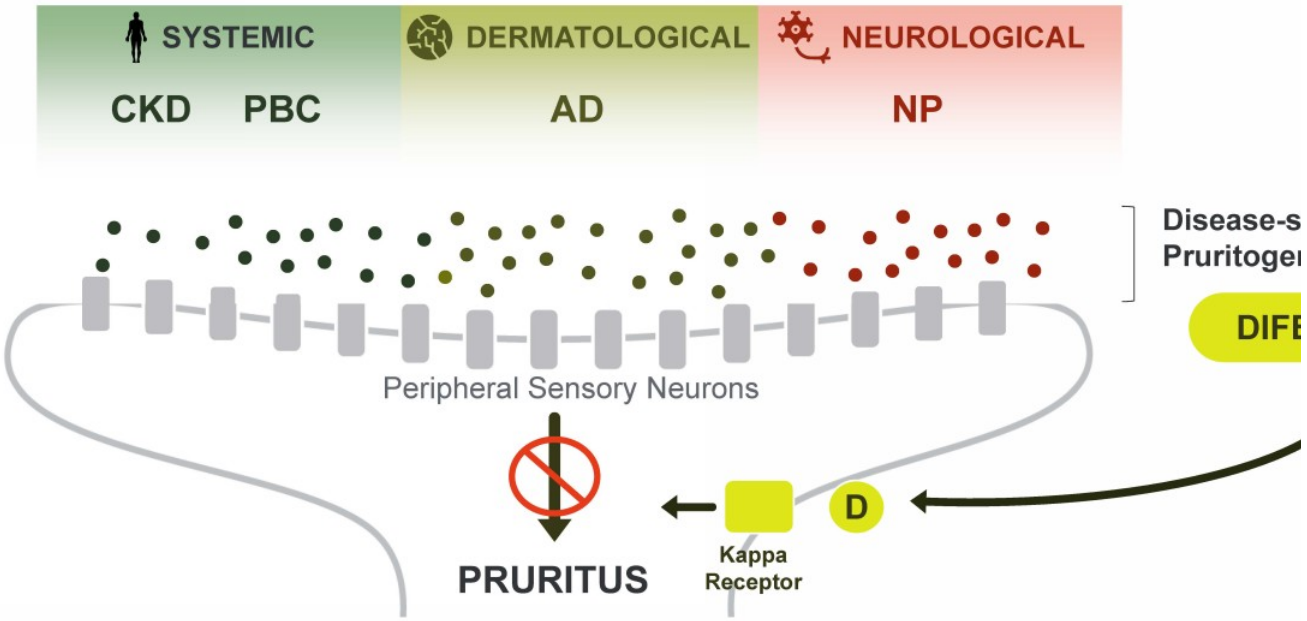
KORSUVA injection is available to order at all dialysis organizations nationwide

Healthcare Providers and Patients are being educated and activated

Product reimbursement via TDAPA is in place

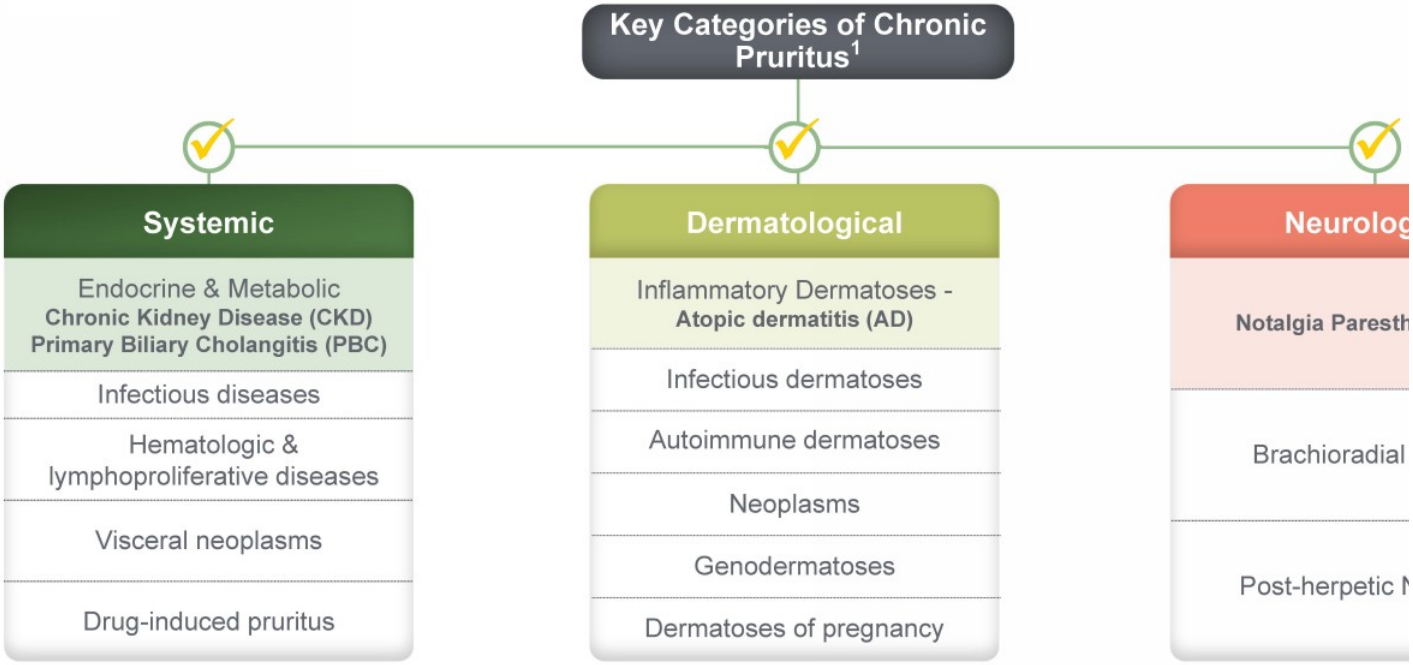
Difelikefalin MOA has potentially broad applicatio

Difelikefalin blocks itch response agnostic of itch trigger



 | Adapted from Pflugers Arch . 2013 December ; 465(12): doi:10.1007/s00424-013-1284-2.

Oral difelikefalin has potential for long-term growt

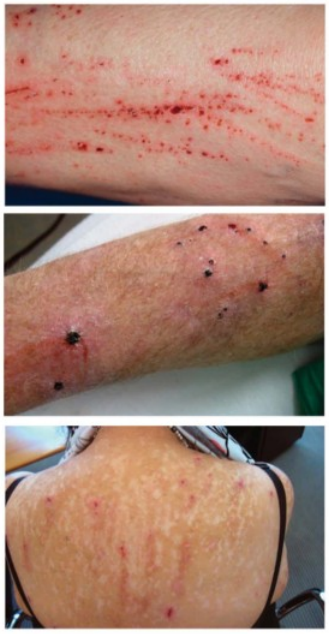


1. Matterne U. et al. Prevalence, correlates and characteristics of chronic pruritus: a population-based crosssectional study. Acta Derm Venereol. 2011;91(6):674-9.2. Matterne U et al. Incidence and determinants of chronic pruritus: a population-based cohort study. Acta Derm Venereol. 2013;93(5):532-7. 3. Adapted from: Stander S. et al. Clinical classification of itch: a position paper of the international forum for the study of itch. Acta Derm Venereol 2007. 87: 291-294.

Advancing our late-stage pipeline in multiple indications

1. Approved in the EU with the tradename Kapruvia™. 2. Commercialization rights to difelikefalin in defined indications - Japan: Maruishi Pharmaceutical Co, LTD; South Korea: Chong Kun Dang Pharmaceuticals
3. Vifor Fresenius Medical Care Renal Pharma (VFMCRP) has commercial rights under a profit-share arrangement in the US and a royalty arrangement ex-US.
HD CKD-aP: Hemodialysis Chronic Kidney Disease-associated Pruritus; NDD-CKD-aP: Non-Dialysis Dependent Chronic Kidney Disease associated Pruritus; Pruritus NP: Notalgia Paresthetica associated Pruritu
Pruritus PBC: Primary biliary cholangitis associated Pruritus

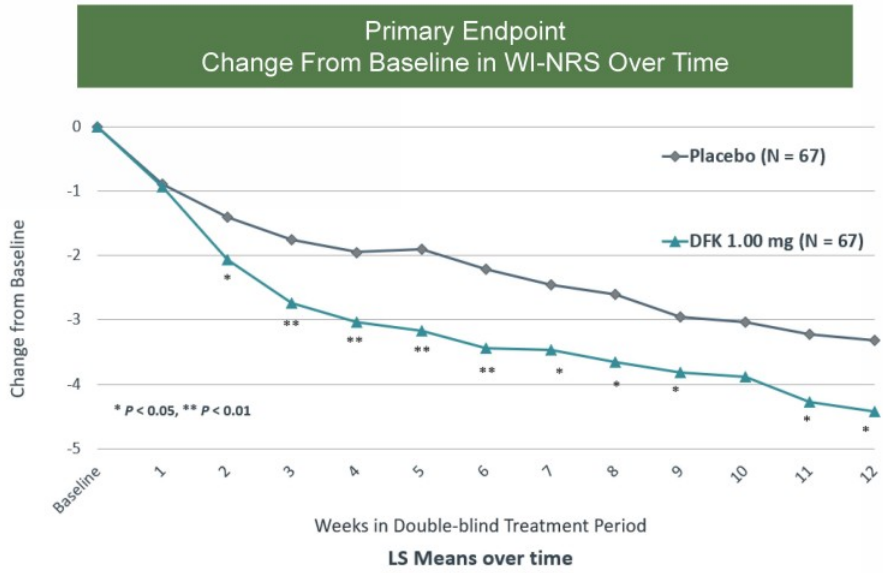
Oral difelikefalin: expanding reach in non-dialysis CKD market



- **Pruritis control is a significant unmet need among non CKD patients[1]**
- **There are no FDA-approved therapies and current anti- approaches are inadequate[1]**
- **Approximately 1.2 million US patients have advanced (non-dialysis CKD[2-5]**
- **~30% advanced non-dialysis CKD patients experience to severe pruritus[6]**

1. Makar M et al. Chronic kidney disease associated pruritus: a review. Kidney Blood Press Res 2021. 46:659-669. 2. Centers for Disease Control and Prevention https://nccd.cdc.gov/ckd/detail.aspx?Qnum=Q372. 3. DataMonitor 4. States Renal Data System https://adr.usrds.org/2020/chronic-kidney-disease/1-ckd-in-the-general-population. 5. 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. 6. Sukul N et al. Pruritus and patient reported outcomes in non-dialysis CKD. Clin J Am Soc Neprhol 2019. 673-681. 7. Mettang T and Kremer AE. Uremic Pruritus. Kidney International. 2015. 87:685-691

Phase 2 data provides path forward into Phase 3 NDD-CKD

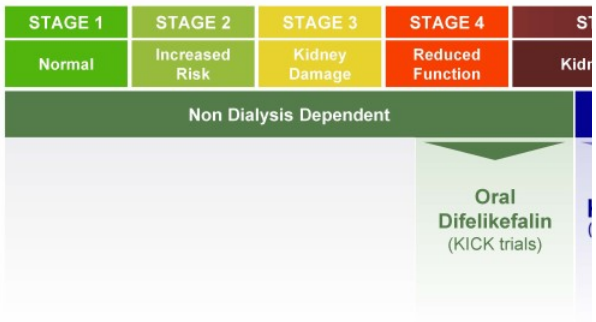


- ✓ **Significant difference achieve 1mg oral difelikefalin and plac NRS score at Week 12**
- ✓ **Generally well-tolerated with s profile consistent with clinica development program**
- ✓ **Phase 2 findings and EOP2 di with FDA established dose an population in Advanced CKD trial**

KICK 1 & KICK 2: Patient Population

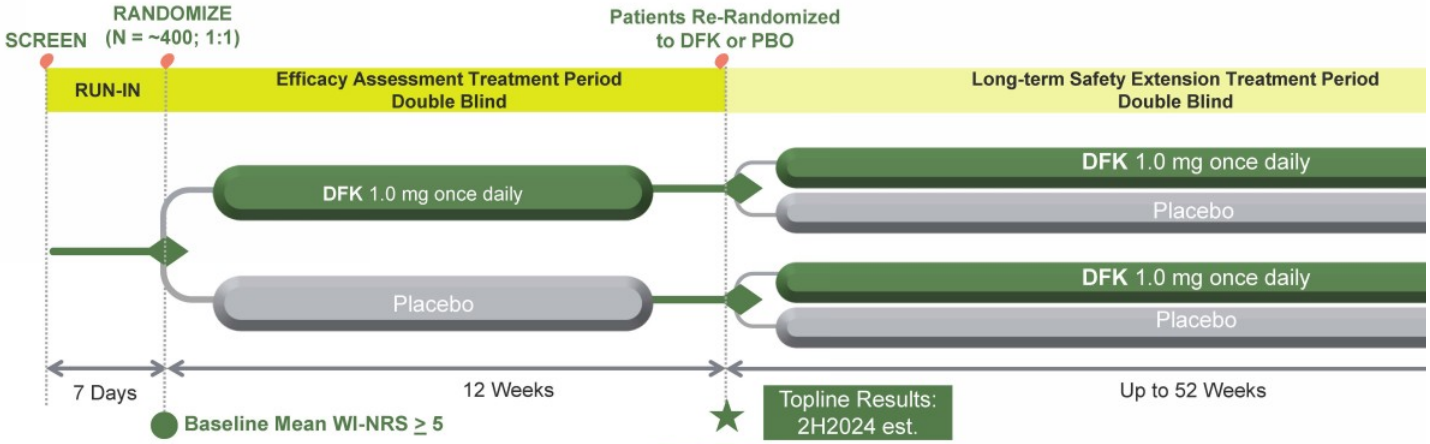
STUDY PATIENT POPULATION

- Adults with advanced stage 4 and 5 CKD
- Chronic Pruritus for at least 6 months prior to screening
- Moderate to Severe Pruritus at Baseline (WI-NRS ≥ 5)
- Allowed to be on stable treatment for itch including antihistamines and gabapentinoids



16 | *KICK1 US sites only, KICK 2 US and ex-US sites*

KICK 1 & KICK 2: Study Design



PRIMARY ENDPOINT

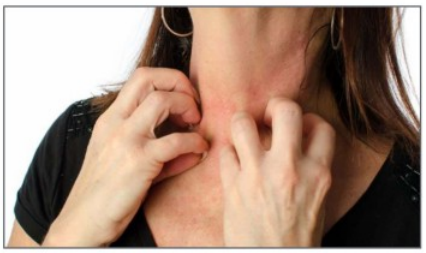
- **% of subjects with ≥4-point improvement from baseline in WI-NRS score at Week 12**

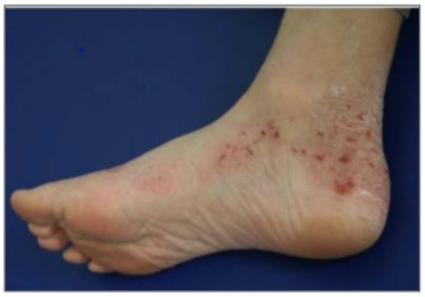
ADDITIONAL ENDPOINTS

- 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 (A





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

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

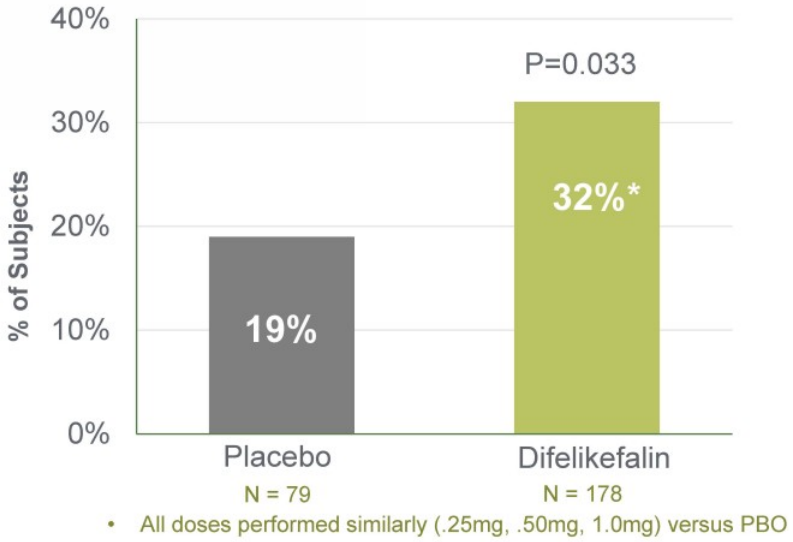
~12M diagnosed patients that experience chronic pru

Targeting pruritus in AD remains unmet need

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. National Eczema Assocaition. https://nationaleczema.org/eczema/types-of-eczema/atopic-dermatitis/ 5. DRG Analysis. 6. Mollanazar NK, Smith PK, Yosipovitch G. Mediators of chronic pruritus in atopic dermatitis: getting the itch out? *Clin Rev Allergy Immunol.* (2016) 51:263–92. 7. Lipman et al. Current clinical options for the management of itch in atopic dermatitis. Clin Cosmet Investig Dermatol. 2021. 14:959-969 8. Kapur S et al. Atopic dermatitis. Allergy Asthma and Clin Immunol. 2018. 14(Suppl2):52.

KARE STUDY: Phase 2 data in Atopic Dermatitis (

Population: Mild to Moderate AD (BSA <10)
4-point Responder Analysis at Week 12



- All doses performed similarly (.25mg, .50mg, 1.0mg) versus PBO

- ✓ **Anti-pruritic effect started at we was sustained through week 12**
- ✓ **Statistical significance achieved registration endpoint (4-point re in mild-to-moderate AD populati**
- ✓ **The drug was generally well tole**

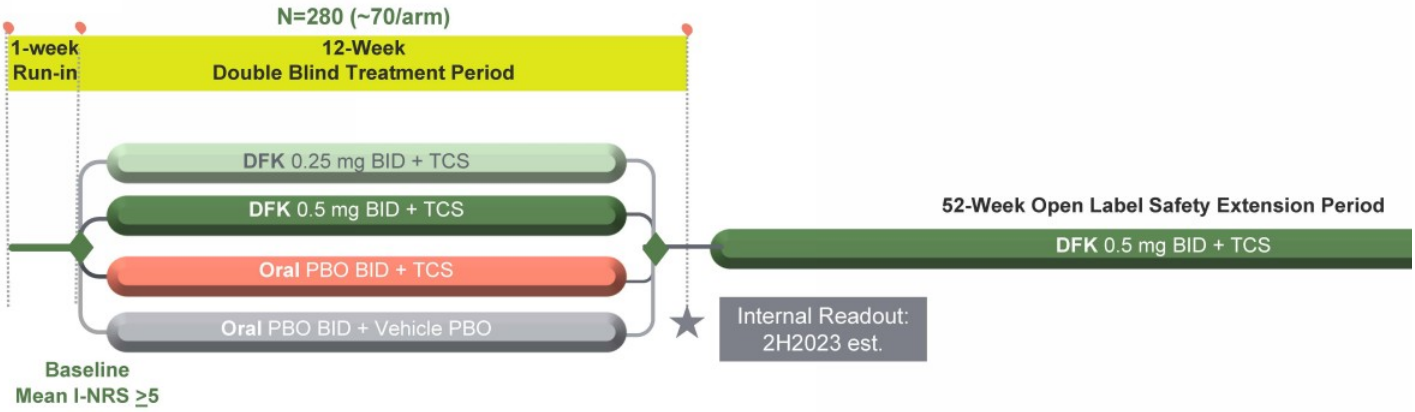
KIND 1 & KIND 2: Patient Population

STUDY PATIENT POPULATION

- Adults with AD-related pruritus not adequately controlled by topical therapy alone
- Chronic AD-related Pruritus ≥6 weeks
- Moderate to Severe Pruritus at Baseline (I-NRS ≥ 5)
- Mild to severe Atopic Dermatitis:
  - IGA ≥ 2, BSA ≤20%
- Patients need to be washed out of any medication that may impact itch and/or AD prior to screening
- Stratification to BSA <10% and ≥10%

Target Enrollment

KIND 1 Part A: Study Design



CRITERIA

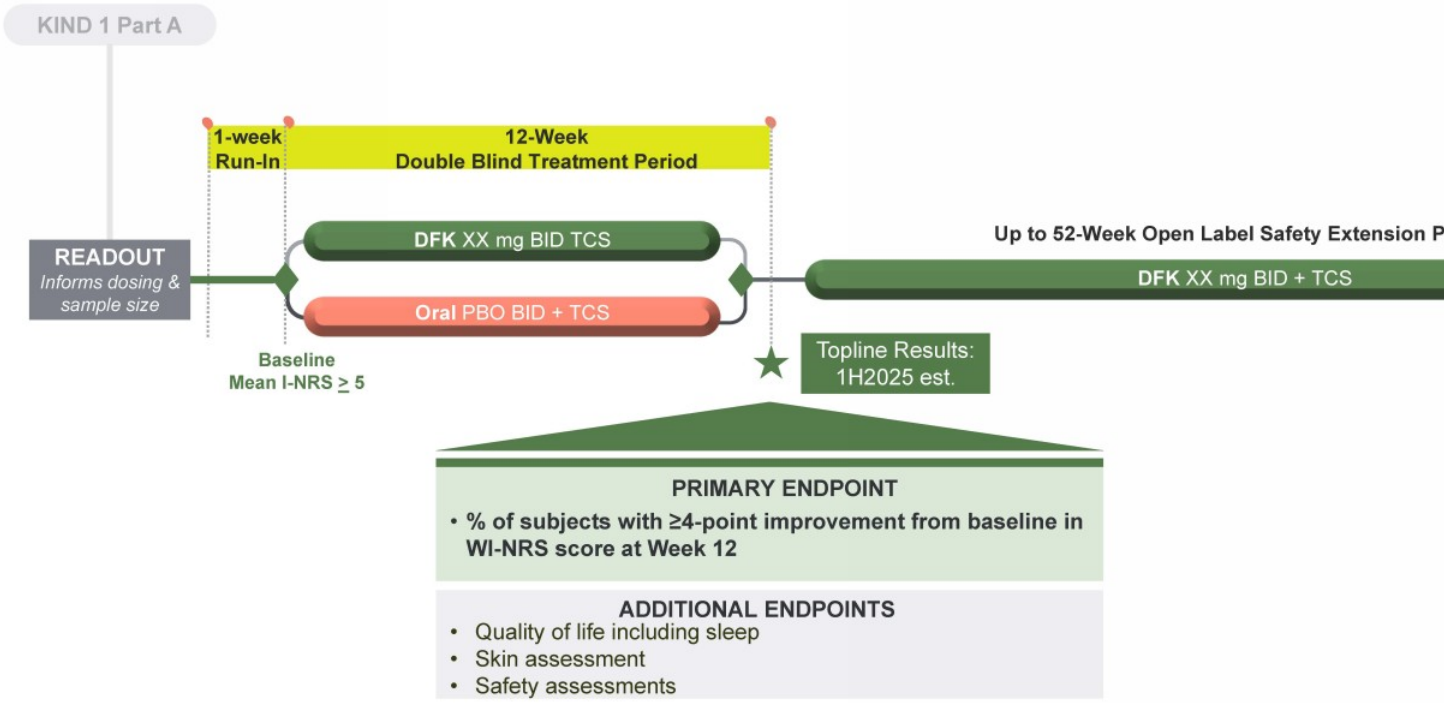
- % of subjects with ≥4-point improvement from baseline in WI-NRS score at Week 12
- Safety assessments

INFORMATION

- Dose
- Sample size

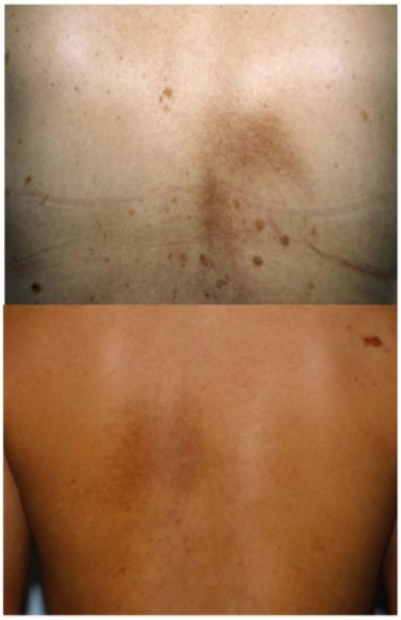
 KIND 1 Part A will include sites in North America only

KIND 1 Part B & KIND 2: Study Design



 | *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*

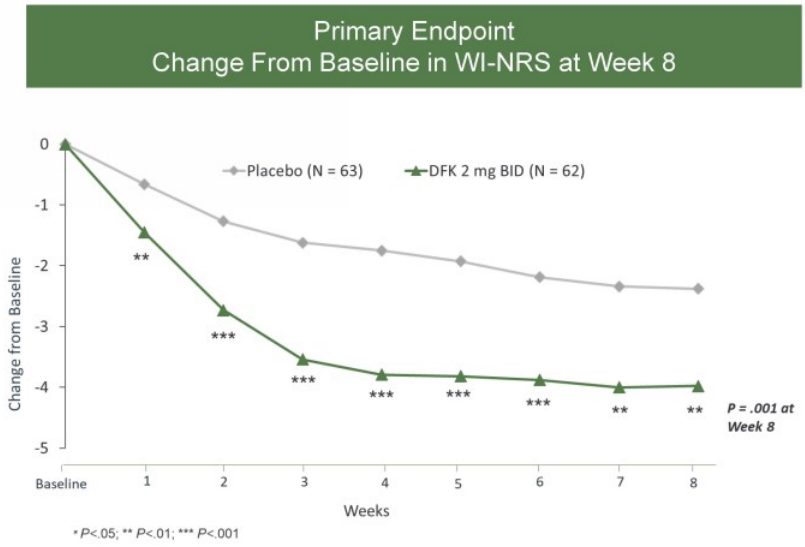
Oral difelikefalin: potential to address significant need in Notalgia Paresthetica (NP)



- **NP is a sensory neuropathic syndrome characterized chronic pruritus[3]**
- **Pruritus is burdensome and impairs quality of life[1]**
- **Estimated >650K patients currently treated for NP[2-5]**
- **No FDA-approved treatments; off label treatments are either ineffective or have tolerability issues[1]**

1. Howard M et al. Notalgia paresthetica: a review for dermatologists. Int J of Derm. 2017. 388-392. 2. US Census Bureau 2020 population projection; 3. Pereira P. et al., Acta DV 2018 ; 98:82-88; 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

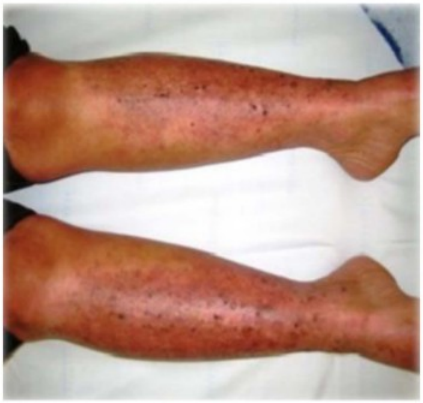
Promising Phase 2 Data in First Well Controlled NP Study



- ✓ **Significant difference achieved b 2 mg BID oral difelikefalin and pl in WI-NRS score at Week 8**
- ✓ **Rapid onset of action within Wee sustained response through Wee**
- ✓ **Significantly greater proportion patients on difelikefalin with ≥ 4- improvement starting Week 2**
- ✓ **Generally well-tolerated with saf profile consistent with other clin 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

Oral difelikefalin: potential in pruritus with Primar Biliary Cholangitis (PBC)



- **Pruritus is hallmark symptom of PBC and may be pers and debilitating[1]**
- **Associated with severe fatigue, sleep disturbance, an mental health issues[2]**
- **Addressable patient population of ~50K[3-4], with oppor to establish efficacy in other chronic liver diseases**
- **No FDA-approved treatments**

Phase 2 Readout Anticipated 2H 2022

1. Carrion AF et al. Understanding and treating pruritus in primary biliary cholangitis. Clin Liver Dis 2018. 22:517-532. 2. Pinheiro NC et al. Refractory pruritus in primary biliary cirrhosis. BMJ Case Rep. 2013. doi:10.1136/bcr-2013-200634 3. Lu M et al. Factors Associated with Prevalence and Treatment of Primary Biliary Cholangitis in United States Health Systems. Clin Gastroenterol Hepatol (2018 Aug);16(8):1333-1341.e6. 4. Trivedi HD et al. Management of Pruritus in Primary Biliary Cholangitis: A Narrative Review. The American Journal of Medicine (2017) 130, 744e1-744e7

Strong financial foundation to advance pipeline, e long-term growth

Cash runway into 1st half 2024

- Runway does not include potential near term revenue from KORSUVA Injection profit split or commercial milestones
- Contractual economics expected to bring near term profitability on KORSUVA Injection

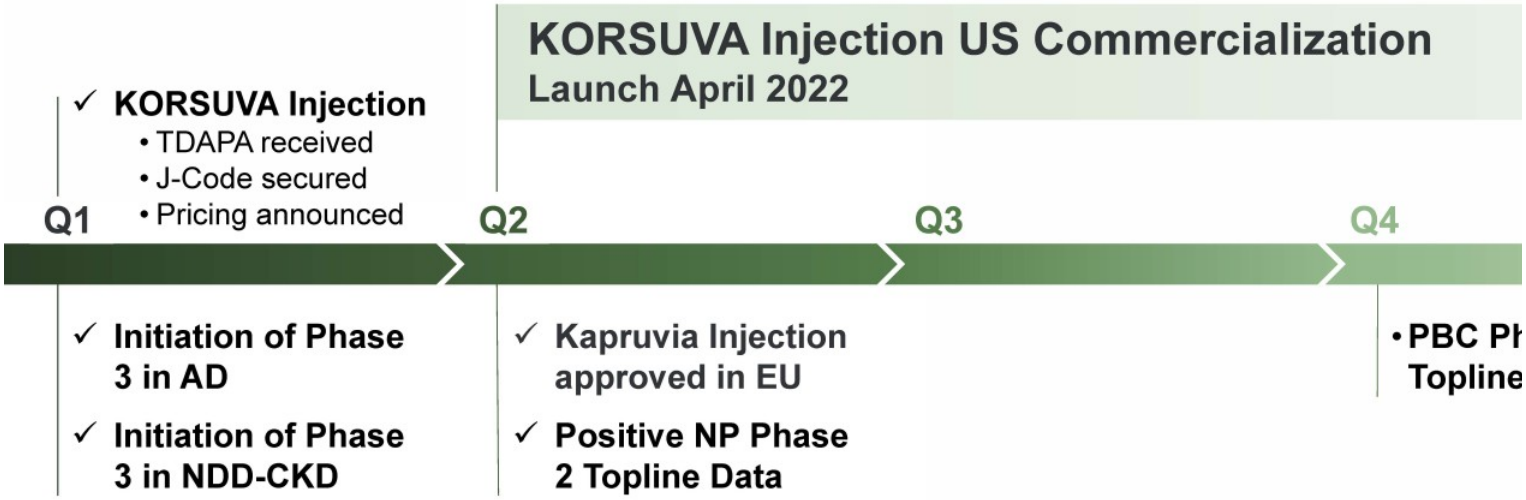
$210M cash position Mar 31, 2022

- 54M shares outstanding and no debt
- We do not expect to incur commercial costs related to KORSUVA Injec

Continued pipeline growth

- We have the resources to continue development of the oral difelikefalin program

2022 Value Catalysts to Drive Long-term Growth*



*Anticipated Timelines

THANK YOU