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

June 30, 2022

– 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 (GLOBE NEWSWIRE) -- 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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