Cara Therapeutics Announces Results from the KOMFORT Phase 2 Trial of Oral Difelikefalin for the Treatment of Pruritus in Notalgia Paresthetica Published in the New England Journal of Medicine

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Publication underscores the importance of data in underrecognized neuropathic itch disorder which lacks an approved treatment

STAMFORD, Conn., Feb. 08, 2023 (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 the *New England Journal of Medicine* (NEJM) has published results from the KOMFORT Phase 2 clinical trial of oral difelikefalin in patients with moderate-to-severe pruritus from notalgia paresthetica. The manuscript, titled "Phase 2 Trial of Difelikefalin in Notalgia Paresthetica," includes data from 126 patients randomized to receive oral difelikefalin 2 mg or placebo twice daily for 8 weeks.

"Notalgia paresthetica is an underrecognized neuropathic itch disorder characterized by pruritus of the upper back for which there is no approved treatment," said Brian Kim, M.D., MTR, lead author of the paper and Vice Chair of Research for the Kimberly and Eric J. Waldman Department of Dermatology, Icahn School of Medicine at Mount Sinai, NY. "In the KOMFORT Phase 2 trial, oral difelikefalin demonstrated encouraging potential to address the significant unmet need for an effective treatment option for this burdensome condition. I look forward to the continued evaluation of oral difelikefalin in a clinical trial program for the treatment of pruritus in patients with notalgia paresthetica."

The registrational Phase 2/3 program of oral difelikefalin will be enrolling notalgia paresthetica (NP) patients with moderate-to-severe pruritus. The program will be comprised of an 8-week Phase 2 dose-finding portion followed by two identical Phase 3 studies. Following selection of the optimal dose based on the Phase 2 portion of the study, that dose will be evaluated for safety and efficacy in the Phase 3 portion. Further details about the program will be released during a Capital Markets Day on February 16, 2023.

KOMFORT Phase 2 Trial Results

As previously announced and presented at the 31st European Academy of Dermatology and Venereology (EADV) Congress, the KOMFORT Phase 2 trial evaluating oral difelikefalin in patients with moderate-to-severe pruritus from notalgia paresthetica achieved the primary efficacy endpoint of change from baseline in the weekly mean of the daily 24-hour Worst Itch-Numeric Rating Scale (WI-NRS) score at Week 8 (-4.0 difelikefalin vs. -2.4 placebo, p=0.001).

A significantly greater proportion of patients achieved a ≥4-point improvement in WI-NRS score at Week 8 with oral difelikefalin vs. placebo (41% difelikefalin vs. 18% placebo, p=0.007). In addition, at Week 8, a significantly greater proportion of patients receiving oral difelikefalin vs. placebo achieved a complete response (22% difelikefalin vs. 5% placebo, p<0.01).

Secondary outcomes are reported in the NEJM manuscript and include itch-related quality-of-life and itch-related sleep measures. Oral difelikefalin was generally well tolerated, with all adverse events in difelikefalin-treated patients reported as mild or moderate in severity. Headache, dizziness, constipation, and increased urine output were more commonly reported in patients on difelikefalin.

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 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 a Phase 2 proof-of-concept trial of oral difelikefalin for the treatment of moderate-to-severe pruritus in patients with notalgia paresthetica and plans to initiate a Phase 2/3 clinical trial program in the first quarter of 2023. 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 future development of oral difelikefalin for treatment of pruritus in patients with notalgia paresthetica or to be a treatment option for those patients. 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 the Company's 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 ended December 31, 2021, the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 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, 2022. 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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