Cara Therapeutics Announces Difelikefalin (KORSUVA®) Injection New Drug Application Has Been Submitted in Japan

September 28, 2022

STAMFORD, Conn., Sept. 28, 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 that its licensing partner Maruishi Pharmaceutical Co., Ltd. submitted a New Drug Application (NDA) in Japan for approval of difelikefalin for the treatment of pruritus in hemodialysis patients.

“The NDA submission represents important progress toward bringing difelikefalin injection to hemodialysis patients suffering from pruritus in Japan,” said Christopher Posner, President and Chief Executive Officer of Cara Therapeutics. “In collaboration with our partners, we look forward to making difelikefalin injection available to healthcare providers and hemodialysis patients around the world who need a treatment option to relieve the burden of chronic kidney disease-associated pruritus.”

The NDA includes positive results of a Phase 3 study in Japan, jointly conducted by Maruishi and its sublicensee Kissei Pharmaceutical Co., Ltd., in which 178 patients were administered difelikefalin or placebo for 6 weeks followed by an open-label extension period of difelikefalin administration for 52 weeks. The primary endpoint, change in itch Numerical Rating Scale score, and the secondary endpoint, change in itching scores of Shiratori severity criteria, were significantly improved from baseline compared to the placebo group. Difelikefalin was well-tolerated.

KORSUVA (difelikefalin) injection is approved by the U.S. Food and Drug Administration for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adults undergoing hemodialysis. Cara’s U.S. commercial partner CSL Vifor has launched KORSUVA injection in the U.S. In addition, KORSUVA is approved by Health Canada and the Health Sciences Authority in Singapore. Under the brand name Kapruvia®, it is approved by the European Medicines Agency, the UK Medicines and Healthcare products Regulatory Agency, and the Swiss Agency for Therapeutic Products for the treatment of pruritus associated with chronic kidney disease in hemodialysis patients.

About Cara Therapeutics & Maruishi Pharmaceutical Co., Ltd. License Agreement

In April 2013, the companies entered into a license agreement under which Cara granted Maruishi an exclusive license to develop, manufacture, and commercialize drug products containing difelikefalin for acute pain and/or uremic pruritus in Japan. Maruishi has the right to grant sub-licenses in Japan, which entitles Cara to receive sub-license fees, net of prior payments made by Maruishi to Cara.

Under the terms of the agreement, Cara is eligible to receive milestone payments upon the achievement of defined clinical and regulatory events as well as tiered, double-digit royalties with respect to any sales of the licensed product sold in Japan by Maruishi, if any, and share in any sub-license fees.

About KORSUVA® Injection
KORSUVA is a kappa opioid receptor agonist developed in Cara laboratories and indicated for the treatment of moderate-to-severe pruritus associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis (HD). KORSUVA Injection is not a federally controlled substance.

Important Safety Information
Warnings and Precautions
Dizziness, Somnolence, Mental Status Changes, and Gait Disturbances: These adverse reactions, including falls, have occurred in patients taking KORSUVA and may subside with continued treatment. Concomitant use of centrally acting depressant medications, sedating antihistamines, and opioid analgesics may increase the likelihood of these adverse reactions and should be used with caution during treatment with KORSUVA.

Risk of Driving and Operating Machinery: Dizziness, somnolence, and mental status changes have occurred in patients taking KORSUVA. KORSUVA may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car and operating machinery. Advise patients not to drive or operate dangerous machinery until the effect of KORSUVA on their ability to do so is known.

Adverse Reactions
The most common adverse reactions (incidence ≥2% and ≥1% higher than placebo) were diarrhea (9.0%), dizziness (6.8%), nausea (6.6%), gait disturbances, including falls (6.6%), hyperkalemia (4.7%), headache (4.5%), somnolence (4.2%), and mental status changes (3.3%).

Use in Specific Populations
Severe Hepatic Impairment: The influence of severe hepatic impairment on the pharmacokinetics of KORSUVA in subjects undergoing hemodialysis (HD) has not been evaluated; therefore, use of KORSUVA in this population is not recommended.

Geriatric Use: The incidence of somnolence was higher in KORSUVA-treated subjects aged 65 years and older (7.0%) than in KORSUVA-treated subjects less than 65 years of age (2.8%). The incidence was comparable in both placebo age groups (3.0% and 2.1%, respectively).

Indication
KORSUVA is indicated for the treatment of moderate to severe pruritus associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis (HD).

Limitation of Use: KORSUVA has not been studied in patients on peritoneal dialysis and is not recommended for use in this population.

Please see KORSUVA® injection full **Prescribing Information** at **www.korsuva.com**.

About Chronic Kidney Disease-associated Pruritus

CKD-associated pruritus is an intractable systemic itch condition that occurs with high frequency and intensity in patients with chronic kidney disease undergoing dialysis. Pruritus has also been reported in patients with stage III-V CKD who are not on dialysis. The majority of dialysis patients (approximately 60 to 70%) report pruritus, with 30 to 40% reporting moderate or severe pruritus.[1,2,3] Recent data from the ITCH National Registry Study showed that among those with pruritus, approximately 59% experienced symptoms daily or nearly daily for more than a year. Given its association with CKD/ESRD, most afflicted patients will continue to have symptoms for months or years, with currently employed antipruritic treatments, such as antihistamines and corticosteroids, unable to provide consistent, adequate relief. Moderate-to-severe chronic pruritus has repeatedly been shown to directly decrease quality of life, contribute to symptoms that impair quality of life (such as poor sleep quality), and is associated with depression.[4] CKD-associated pruritus is also an independent predictor of mortality and the risk for hospitalization among hemodialysis patients.

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 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 potential regulatory approval of difelikefalin injection in Japan and the potential of difelikefalin injection to be a therapeutic option for CKD-aP in dialysis dependent 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 Cara's filings with the Securities and Exchange Commission, including the "Risk Factors" section of Cara's Annual Report on Form 10-K for the year ended 31 December 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. Except to the extent required by law, Cara undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

References:

[1] Pisoni RL, et al. Pruritus in haemodialysis patients: international results from the Dialysis Outcomes and Practice Patterns Study. Nephrol Dial Transplant. 2006; 21:3495-3505.

[2] Ramakrishnan K, et al. Clinical characteristics and outcomes of end-stage renal disease patients with self-reported pruritus symptoms. International Journal of Nephrology and Renovascular Disease. 2014; 7: 1-12.

[3] Sukul et al. Self-reported Pruritus and Clinical, Dialysis-Related, and Patient-Reported Outcomes in Hemodialysis Patients. Kidney Med. 2020 Nov 21;3(1):42-53.

[4] Mathur VS, et al. A longitudinal study of Uremic Pruritus in hemodialysis patients. Clin J Am Soc Nephrol. 2010; 5(8):1410-1419.

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Source: Cara Therapeutics, Inc.