Cara Therapeutics Announces Initiation of Phase 2 Trial of Oral KORSUVA™ (CR845/difelikefalin) for Pruritus in Patients with Primary Biliary Cholangitis (PBC)

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Completed Phase 1 trial in patients with hepatic impairment established Oral KORSUVA tablet strength

STAMFORD, Conn., June 26, 2019 (GLOBE NEWSWIRE) -- Cara Therapeutics, Inc. (Nasdaq:CARA), a biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pruritus by selectively targeting peripheral kappa opioid receptors, today announced the initiation of a Phase 2 trial of Oral KORSUVA (CR845/difelikefalin) for the treatment of pruritus in patients with hepatic impairment due to primary biliary cholangitis (PBC). Pruritus is a common symptom of cholestatic liver diseases with a prevalence of up to 70 percent in patients with PBC.[1,2]

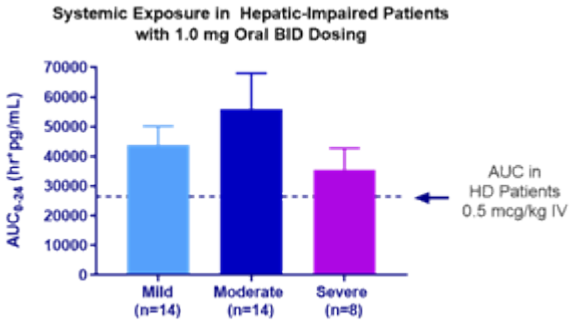
“Pruritus continues to be a significant comorbidity in patients with chronic cholestatic liver diseases and may be exacerbated by certain bile acid-related drugs,” said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. “We believe that Oral KORSUVA may provide a potential new, first-in-class therapeutic approach to treat this unmet clinical need.”

Phase 2 Trial Design

The Phase 2 multicenter, randomized, double-blind, placebo-controlled 16-week trial is designed to evaluate the safety and efficacy of 1 mg tablet of Oral KORSUVA taken twice daily (BID) versus placebo in approximately 60 patients with PBC and moderate-to-severe pruritus.

The primary efficacy endpoint is the change from baseline in the weekly mean of the daily 24-hour Worst Itch Numeric Rating Scale (WI-NRS) score at Week 16 of the treatment period. Secondary endpoints include change from baseline in itch-related quality of life scores at the end of Week 16 as assessed by the total Skindex-10 and 5-D itch scales, as well as the assessment of proportion of patients achieving an improvement from baseline of ≥3 points with respect to the weekly mean of the daily 24-hour WI-NRS score at week 16.

The dose of Oral KORSUVA (1 mg BID) in the Phase 2 trial is based on comparison to the exposure levels achieved with 0.5 mcg/kg dose of I.V. KORSUVA that exhibited statistically significant and clinically meaningful reduction in itch intensity in hemodialysis patients with moderate-to-severe pruritus in the Phase 2 and 3 trials.[3]



Data for oral dosing represent the arithmetic mean ± SEM.
Mean exposure (AUC) in patients with hepatic impairment is normalized to an equivalent 24-hour interval.

About Pruritus Associated with Primary Biliary Cholangitis

PBC is a rare, chronic, immune-mediated progressive liver disorder that usually appears in middle age and leads to inflammation as well as scarring of the small bile ducts. Pruritus has been commonly reported with varying severity in patients with PBC and contributes to a large symptomatic burden, including reduced quality of life. The underlying pathophysiology of pruritus in patients with liver disease is unclear; bile salts, histamine levels, opioids, serotonin, and female sex hormones have all been implicated as pruritogens.[4] Common pruritus treatments in patients with PBC include bile salt resins, such as cholestyramine, which has several side effects; rifampicin, which requires regular blood tests due to the risk of hepatoxicity and administration for more than two weeks is not recommended; mu-opioid receptor antagonists and sertraline. Despite these and other available

therapies, a significant proportion of patients do not respond to treatment.

References:

1. Rishe E, et al. Itch in primary biliary cirrhosis: a patient's perspective. Acta Derm Venereol 2008; 88: 34-37
2. Satoshi O, et al. Prevalence of pruritus in patients with chronic liver disease: A multicenter study. Hepatol Res. 2018; 48: E252-E262
3. Company data presented at the Kidney Week 2017 and Company press releases.
4. Bhalerao et al. Management of pruritus in chronic liver disease. Dermatol Res Pract. 2015; 295891

About KORSUVA for the Treatment of CKD-Associated Pruritus (CKD-aP)

The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to I.V. CR845 for the treatment of moderate-to-severe pruritus in CKD patients undergoing hemodialysis. Breakthrough Therapy designation is granted to expedite the development and review process for new therapies addressing serious or life-threatening conditions where preliminary clinical evidence indicates that the drug candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. There are currently no FDA-approved drugs for the treatment of CKD-aP.

The FDA has conditionally accepted KORSUVA™ as the trade name for difelikefalin injection. CR845/difelikefalin is an investigational drug product and its safety and efficacy have not been fully evaluated by any regulatory authority.

About Cara Therapeutics

Cara Therapeutics is a clinical-stage biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pruritus by selectively targeting peripheral kappa opioid receptors (KORs). Cara is developing a novel and proprietary class of product candidates, led by KORSUVA™ (CR845/difelikefalin), a first-in-class KOR agonist that targets the body's peripheral nervous system, as well as certain immune cells. In a Phase 3 trial and Phase 2 trials, KORSUVA Injection has demonstrated statistically significant reductions in itch intensity and concomitant improvement in quality of life measures in hemodialysis patients with moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP), and is currently being investigated in additional Phase 3 trials in hemodialysis patients with CKD-aP.

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 of KORSUVA (CR845/difelikefalin) as a treatment for pruritus in patients with hepatic impairment due to PBC or moderate-to-severe pruritus in stage III-V CKD 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 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 ended December 31, 2018, 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.

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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/c8c63b21-11d8-4b9b-a47b-3e28d6367a1b

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