Cara Therapeutics Announces Positive Results From KALM-1 Pivotal Phase 3 Trial of KORSUVA ™ Injection in Hemodialysis Patients with Pruritus

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- Statistically significant improvement in primary endpoint of proportion of patients with three point or greater reduction in mean worst itching intensity NRS score vs. placebo (p=0.000019) –

- Statistically significant improvement in key secondary endpoint of proportion of patients with four point or greater reduction in mean worst itching intensity NRS score vs. placebo (p=0.000032) –

- KORSUVA Injection well-tolerated through 12 weeks of treatment -

- Company to host conference call today at 8:30 a.m. ET -

STAMFORD, Conn., May 29, 2019 (GLOBE NEWSWIRE) -- Cara Therapeutics, Inc. (Nasdaq:CARA), a biopharmaceutical company focused on developing and commercializing new chemical entities with a primary focus on the treatment of pruritus by selectively targeting peripheral kappa opioid receptors, today announced positive topline data from the KALM-1 pivotal Phase 3 trial of KORSUVA™ (CR845/difelikefalin) Injection in hemodialysis patients with moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP).

"We are extremely pleased with the robust topline results from our first pivotal Phase 3 trial of KORSUVA Injection and are particularly encouraged by the early anti-pruritic response with KORSUVA Injection, which resulted in statistically significant separation from placebo after only one week of treatment and a sustained significant benefit through 12 weeks," said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. "We look forward to reporting topline data from our second global Phase 3 trial, KALM-2, in the second half of this year and, assuming positive results, moving towards an NDA submission as quickly as possible thereafter."

CKD-aP is an intractable systemic itch condition that occurs with high frequency and intensity in patients undergoing hemodialysis and peritoneal dialysis. Multiple studies estimate that at least 40 percent of patients with end-stage renal disease suffer from pruritus. The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to KORSUVA Injection for this indication.

"Itching is a significant problem for many of our hemodialysis patients and there is an unmet need for an effective treatment. I am impressed by the clinically meaningful efficacy demonstrated in this study," said Steven Fishbane, M.D., Chief, Division of Kidney Disease and Hypertension, Northwell Health, Professor of Medicine at Hofstra/Northwell and a KALM-1 clinical investigator. "Relative to the favorable safety data, these results suggest that, if approved, this can be an important drug that could help many of our patients."

KALM-1 Efficacy Data:

- *Primary Endpoint*: The proportion of patients on 0.5 mcg/kg of KORSUVA Injection achieving a three-point or greater improvement from baseline in the weekly mean of the daily 24 hour Worst Itching Intensity Numeric Rating Scale (WI-NRS) score at week 12 was 51% vs. 28% for patients on placebo (p= 0.000019)
- *Secondary Endpoints*:
    - The proportion of patients on 0.5 mcg/kg of KORSUVA Injection achieving a four-point or greater improvement from baseline in the weekly mean of the daily 24 hour WI-NRS score at week 12 was 39% vs. 18% for patients on placebo (p= 0.000032)
- *Itch-Related Quality of Life Measures*: The impact of KORSUVA Injection on itch-related quality of life measures associated with CKD-aP was measured using validated self-assessment Skindex-10 and 5-D itch scales:
    - Patients on KORSUVA Injection experienced a 43% improvement in the average total Skindex-10 score at week 12 vs. patients on placebo (p= 0.0004)
    - Patients on KORSUVA Injection experienced a 35% improvement in the average total 5-D Itch score at week 12 vs. patients on placebo (p= 0.0009)

KALM-1 Safety and Tolerability:

KORSUVA was generally well-tolerated with a safety profile consistent with that seen in earlier KORSUVA clinical trials. Overall, the incidence of adverse events (AEs) and serious AEs were similar across both KORSUVA and placebo groups. The most common treatment emergent AEs reported in >5% of patients were diarrhea (9.5% KORSUVA vs 3.7% placebo), dizziness (6.9% KORSUVA vs 1.1% placebo), nasopharyngitis (KORSUVA 5.3% vs 3.2% placebo) and vomiting (5.3% KORSUVA vs 3.2% placebo).

Conference Call

Cara management will host a conference call today at 8:30 a.m. ET to discuss the results of the study.

To participate in the conference call, please dial (855) 445-2816 (domestic) or (484) 756-4300 (international) and refer to conference ID 2987032. 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.

KALM-1 Phase 3 Trial Design

The Phase 3 U.S. study is a multicenter, randomized, double-blind, placebo-controlled 12-week treatment trial with a 52-week open label extension phase that is designed to evaluate the safety and efficacy of 0.5 mcg/kg KORSUVA (CR845/difelikefalin) Injection in 350 hemodialysis patients with moderate-to-severe pruritus.

The primary efficacy endpoint is the proportion of patients achieving at least a three-point improvement from baseline in the weekly mean of the daily 24-hour WI-NRS score at week 12.

Secondary endpoints include assessment of itch-related quality of life changes measured using the validated self-assessment 5-D itch and Skindex-10 scales, as well as the proportion of patients achieving at least a four-point improvement from baseline in weekly mean of the daily 24-hour WI-NRS score at week 12.

About CKD-aP

CKD-aP is an intractable systemic itch condition that occurs with high frequency and intensity in patients with chronic kidney disease undergoing hemodialysis and peritoneal dialysis. Pruritus has also been reported in patients with stage III-V CKD who are not on dialysis. Aggregate, longitudinal, multi-country studies estimate the weighted prevalence of CKD-aP to be approximately 40 percent in patients with end-stage renal disease (ESRD), with approximately 25 percent of patients reporting severe pruritus. The majority of dialysis patients (approximately 60-70 percent) report pruritus, with 30 to 40 percent reporting moderate or severe pruritus.[1,2] Recent data from the ITCH National Registry Study showed that among those with pruritus, approximately 59 percent 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.[3] CKD-aP is also an independent predictor of mortality among hemodialysis patients, mainly related to increased risk of inflammation and infections.

References:

1. Pisoni RL, et al. Pruritus in haemodialysis patients: international results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). 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. Mathur VS, et al. A longitudinal study of Uremic Pruritus in hemodialysis patients. Clin J Am Soc Nephrol. 2010; 5(8):1410-1419.

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 Phase 3 trials in hemodialysis patients with 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.

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 plans, strategies and expectations for the future, including the potential results of ongoing and planned clinical trials, future regulatory submissions; the size of the potential markets that are potentially addressable for the Company's product candidates, including the pruritus market, the potential for KORSUVA Injection to be a therapeutic option for CKD-aP, and the expected timing for announcement of the results of other ongoing clinical trials. 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 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. 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.

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