



Cara Therapeutics and Vifor Fresenius Medical Care Renal Pharma Announce Positive Results From Global KALM-2 Pivotal Phase 3 Trial of KORSUVATM Injection in Hemodialysis Patients with Pruritus

April 21, 2020

- **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 ($p=0.02$) -**
- **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 ($p=0.01$) -**
- **KORSUVA Injection NDA and MAA submission expected in the second half of 2020 -**
- **Cara to host conference call today at 8:30 a.m. ET -**

STAMFORD, Conn. and ST. GALLEN, Switzerland, April 21, 2020 (GLOBE NEWSWIRE) -- Cara Therapeutics, Inc. (Nasdaq:CARA) and Vifor Fresenius Medical Care Renal Pharma (VFMCPR), today announced positive topline data from Cara's KALM-2 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 very pleased with the positive topline data from our global, pivotal Phase 3 trial of KORSUVA Injection, which reinforce the robust results we reported from our U.S. KALM-1 Phase 3 trial last year," said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. "With these data in hand, we remain on track to submit our New Drug Application (NDA) for KORSUVA Injection in the second half of this year to the U.S. Food and Drug Administration (FDA) and, working with our partner Vifor Fresenius Medical Care Renal Pharma, plan to submit for Marketing Authorization Approval (MAA) to the European Medicines Agency (EMA) shortly thereafter."

"I continue to be very impressed by the robust efficacy of KORSUVA for the treatment of pruritus in our patients undergoing hemodialysis," said Steven Fishbane, M.D., Chief, Division of Kidney Disease and Hypertension, Northwell Health and Professor of Medicine at Hofstra/Northwell. "Itching is a real issue for our hemodialysis patients and there are no approved treatments in the U.S. or Europe so I am encouraged by the potential of this drug to address a significant unmet need for our patients."

"We are delighted with this outcome and congratulate the Cara team on the positive topline Phase 3 data on KORSUVA Injection in hemodialysis patients with moderate-to-severe pruritus," said Stefan Schulze, Vifor Pharma President of Executive Committee and Chief Operating Officer. "KORSUVA Injection has the potential to serve as a breakthrough therapeutic for treating this serious itching condition in hemodialysis patients, and is a natural fit to our leading nephrology-focused product portfolio. We are committed to making KORSUVA Injection available as quickly as possible to hemodialysis patients, who urgently need effective therapy."

CKD-aP is an intractable systemic itch condition that occurs with high frequency and intensity in patients undergoing hemodialysis. Multiple studies estimate that at least 40% of dialysis patients suffer from pruritus. The FDA has granted Breakthrough Therapy designation to KORSUVA Injection for this indication.

KALM-2 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 54% versus 42% for patients on placebo ($p= 0.02$).
- **Key Secondary Endpoint:** 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 41% versus 28% for patients on placebo ($p= 0.01$).
- **Itch-Related Quality of Life Measures:** Patients on KORSUVA Injection experienced a 12% and 29% numerical improvement in the average total Skindex-10 and total 5-D Itch scores, respectively, which did not meet statistical significance.

KALM-2 Safety and Tolerability:

KORSUVA Injection was generally well-tolerated with a safety profile consistent with that seen in KALM-1 and the KORSUVA clinical program in patients with CKD-aP. 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 (8.1% KORSUVA versus 5.5% placebo), falling (6.8% KORSUVA

versus 5.1% placebo), vomiting (6.4% KORSUVA versus 5.9% placebo), nausea (6.4% KORSUVA versus 4.2% placebo) and dizziness (5.5% KORSUVA versus 5.1 % placebo).

VFMCPR License Agreement

In May 2018, Cara licensed worldwide rights, except in the U.S., Japan and South Korea, to commercialize KORSUVA Injection for the treatment of CKD-aP in dialysis patients to VFMCPR, a company that specializes in nephrology therapies. Cara retains full development and commercialization rights for KORSUVA Injection for the treatment of CKD-aP in the U.S. except in the dialysis clinics of Fresenius Medical Care North America (FMCNA), where VFMCPR and Cara will promote KORSUVA Injection under a profit-sharing arrangement based on net FMCNA clinic sales recorded by Cara. Cara will solely promote KORSUVA Injection in all non-FMC clinics in the U.S. and retain all profits from those sales.

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 1681438. A live webcast of the call can be accessed under "Events & Presentations" in the News & Investors section of Cara'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-2 Phase 3 Trial Design

KALM-2 is a Phase 3, global, multicenter, randomized, double-blind, placebo-controlled, 12-week trial (with a 52-week open label extension phase) designed to evaluate the safety and efficacy of 0.5 mcg/kg KORSUVA (CR845/difelikefalin) Injection in 473 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 the proportion of patients achieving four-point or greater improvement from baseline in weekly mean of the daily 24-hour WI-NRS score at week 12, as well as itch-related quality of life changes measured using the validated self-assessment 5-D itch and Skindex-10 scales.

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 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% in patients with end-stage renal disease (ESRD), with approximately 25% of patients reporting severe pruritus. The majority of dialysis patients (approximately 60 to 70%) report pruritus, with 30 to 40% reporting moderate or severe pruritus.^{1,2} 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.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. *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 two Phase 3 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 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 Vifor Pharma and Vifor Fresenius Medical Care Renal Pharma Ltd (VFMCPR)

Vifor Pharma Group is a global specialty pharmaceuticals company. It aims to become the global leader in iron deficiency, nephrology and cardio-renal therapies. Vifor Pharma Group consists of the following companies: Vifor Pharma; Vifor Fresenius Medical Care Renal Pharma, a joint company with Fresenius Medical Care; Relypsa; and OM Pharma. Vifor Pharma Group is listed on the Swiss Stock Exchange (SIX Swiss Exchange, VIFN, ISIN: CH0364749348).

Vifor Fresenius Medical Care Renal Pharma Ltd., a common company of Vifor Pharma Group and Fresenius Medical Care, develops and commercialises innovative and high quality therapies to improve the life of patients suffering from chronic kidney disease (CKD) worldwide. The company was founded at the end of 2010 and is owned 55% by Vifor Pharma Group and 45% by Fresenius Medical Care.

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 planned timing of future regulatory submissions; the size of the potential markets that are potentially addressable for Cara's product candidates, including the pruritus market and the potential for KORSUVA Injection to be a therapeutic option for CKD-aP. 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, 2019 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.

MEDIA CONTACT:

Annie Starr
6 Degrees
973-415-8838
astarr@6degreespr.com

INVESTOR CONTACT:

Jane Urheim
Stern Investor Relations, Inc.
212-362-1200
jane.urheim@sternir.com



Source: Cara Therapeutics, Inc.