Press Release

VFMCRP and Cara Therapeutics announce positive results from global KALM-2 pivotal phase-III trial of KORSUVA™ injection in haemodialysis patients with Pruritus

- **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**

St Gallen and STAMFORD, Conn., April 21, 2020 – Vifor Fresenius Medical Care Renal Pharma (VFMCRP) and Cara Therapeutics, Inc. (Nasdaq:CARA) today announced positive topline data from Cara's KALM-2 pivotal phase-III trial of KORSUVA™ (CR845/difelikefalin) Injection in haemodialysis patients with moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP).

"We are delighted with this outcome and congratulate the Cara team on the positive topline phase-III data on KORSUVA Injection in haemodialysis 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 an innovative therapeutic for treating this serious itching condition in haemodialysis 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 haemodialysis patients, who urgently need effective therapy."

"We are very pleased with the positive topline data from our global, pivotal phase-III trial of KORSUVA Injection, which reinforce the robust results we reported from our U.S. KALM-1 phase-III 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 VFMRCP, to submit a Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) shortly thereafter."

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 percent 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% vs.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% vs. 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 didn't meet statistical significance.

KALM-2 Safety and Tolerability:

KORSUVA was generally well-tolerated with a safety profile consistent with that seen in KALM-1 and in 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 vs 5.5% placebo), fall (6.8% KORSUVA vs 5.1% placebo), vomiting (6.4% KORSUVA vs 5.9% placebo), nausea (6.4% KORSUVA vs 4.2% placebo) and dizziness (5.5% KORSUVA vs 5.1 % placebo)

VFMRCP 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 VFMCRP, specialises in nephrology therapies. Cara retains full development and commercialisation 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 VFMCRP 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.

KALM-2 phase-III Trial Design

KALM-2 is a phase-III, 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 3-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 >4-point 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 percent in patients on dialysis, 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 Vifor Pharma and Vifor Fresenius Medical Care Renal Pharma

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). For more information, visit www.viforpharma.com.

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. For more information about Vifor Fresenius Medical Care Renal Pharma and its parent companies, please visit www.vfmcrp.com, www.viforpharma.com and www.freseniusmedicalcare.com

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 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. 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 and

VFMCRP undertake 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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