# C-28

## Longer-Term Paltusotine Treatment in Patients With Carcinoid Syndrome: Safety and Exploratory Efficacy Results From a 2-Year Open-Label Extension Study

*Mary A. Maluccio, MD, MPH[1], Rachel Riechelmann, MD, PhD[2], Michael J. Demeure, MD, MBA[3], Joseph S. Dillon, MD[4], Juan Manuel O'Connor, MD, MSc[5], Shagufta Shaheen, MD[6], Ana Oviedo, MD[7], Lowell Anthony, MD[8], Łukasz Hajac, MD, PhD[9], Juliana Lorenzoni Althoff, MD[10], Mariano Dioca, MD[11], Thorvardur R. Halfdanarson, MD[12], Andrew E. Hendifar, MD[13], Ana Rosa Pinto Quidute, MD, PhD[14], Mariana Scandizzo, MD[15], Denka Markova, PhD[16], Hui Tian, PhD[16], Zhimin Xiao, MD[16], Bin Zhang, MD, MSc[16], Alan Krasner, MD[16], Aman Chauhan, MD[17], Simron Singh, MD, MPH[18], Amr Mohamed, MD[19]*

*[1]LSU Health Sciences Center, New Orleans, LA, USA; [2]AC Camargo Cancer Center, São Paulo, Brazil; [3]Hoag Family Cancer Institute, Newport Beach, CA, USA; [4]University of Iowa, Carver College of Medicine, Iowa City, IA, USA; [5]Instituto Alexander Fleming, Buenos Aires, Argentina; [6]Stanford Medicine, Stanford, CA, USA; [7]Hospital de Gastroenterología Dr. Carlos Bonorino Udaondo, Buenos Aires, Argentina; [8]University of Kentucky, Lexington, KY, USA; [9]Neuroendocrine Cancer Unit, Lower Silesian Oncology Center, Wrocław, Poland; [10]Hospital São José, Criciúma, Brazil; [11]Instituto de Oncología Ángel H. Roffo, Buenos Aires, Argentina; [12]Mayo Clinic, Rochester, MN, USA; [13]Cedars-Sinai Medical Center, Los Angeles, California, USA; [14]Department of Physiology and Pharmacology, Drug Research and Development Center (NPDM), Faculty of Medicine, Federal University of Ceará (UFC), Fortaleza, Brazil; [15]Hospital Universitario Sanatorio Güemes, Buenos Aires, Argentina; [16]Crinetics Pharmaceuticals, Inc., San Diego, CA, USA; [17]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, CA, USA; [18]Sunnybrook Health Sciences Center, Toronto, Canada; [19]University Hospitals Seidman Cancer Center, Case Western Reserve University, Cleveland, OH, USA*

### BACKGROUND

Paltusotine is a once-daily, nonpeptide, selective somatostatin 2 receptor agonist in development as an oral treatment for patients with carcinoid syndrome (CS).

### METHODS

This phase 2, multicenter study examined the safety, tolerabilty, and exploratory efficacy of paltusotine in patients with CS. The study included an 8-week randomized treatment period (RTP) and a 102-week open-label extension (OLE). Patients were adults with a locally advanced or metastatic grade 1 or 2 neuroendocrine tumor (NET) and actively symptomatic CS, either untreated with somatostatin receptor ligand (SRL) therapy (average of ≥4 bowel movements/day or >2 flushing episodes/day on ≥2 days over a 2-week period) or washed out of SRL (symptoms previously controlled on SRL) with

demonstrated symptom worsening after washout. This analysis evaluated the effects of paltusotine treatment through the end of the 2-year OLE.

## RESULTS

Thirty-six patients (n=9 untreated; n=27 SRL washout) were enrolled; mean age was 60.8 years (range 35-83), 52.8% were female, and 47.2% had a grade 2 NET. Of 30 RTP completers, 26 continued into the OLE. The mean±SD number of flushing episodes per day was 2.4±1.9 at baseline (n=36), 0.9±1.1 at week 8 (n=30; end of RTP), 0.4±0.6 at week 58 (n=15), and 0.3±0.4 at week 110 (n=12; end of OLE). The mean±SD daily worst flushing severity score (numeric rating scale from 0-10) was 3.4±2.3, 1.5±1.7, 0.5±0.7, and 0.7±1.1, respectively. The mean±SD number of bowel movements per day was 3.6±1.7 at baseline, 2.6±1.3 at week 8 (end of RTP), 2.0±1.0 at week 58, and 2.1±1.2 at week 110 (end of OLE). At the last available assessment (end of RTP, end of OLE, or early discontinuation), the paltusotine dose was 40 mg/day in 11 patients, 80 mg/day in 18 patients, and 120 mg/day in 7 patients. The most common treatment-related adverse events (AEs) were diarrhea (RTP: 25.0%; OLE: 7.7%), abdominal pain (RTP: 16.7%; OLE: 3.8%), and nausea (RTP: 11.1%; OLE: 11.5%). Across the entire study period, no serious AEs were considered treatment-related. Three patients (RTP, n=1; OLE; n=2) had AEs that led to treatment discontinuation; none were considered treatment-related.

## CONCLUSIONS

In this phase 2 study, once-daily oral paltusotine reduced the frequency and severity of CS symptoms, and improvements were sustained during longer-term (up to 2 years) treatment. Paltusotine was well tolerated, and the incidence of AEs decreased over the study period. A phase 3, randomized, placebo-controlled trial of paltusotine in the treatment of patients with CS (CAREFNDR; carefndr.com) is currently ongoing.

## ABSTRACT ID #36520