# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, D.C. 20549**

# FORM 8-K

## CURRENT REPORT

**Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): December 18, 2023**

# Crinetics Pharmaceuticals, Inc.

**(Exact name of Registrant as Specified in Its Charter)**

| **Delaware** | **001-38583** | **26-3744114** |
|---|---|---|
| **(State or Other Jurisdiction of Incorporation)** | **(Commission File Number)** | **(IRS Employer Identification No.)** |

| | |
|---|---|
| **6055 Lusk Boulevard**<br>**San Diego, California**<br>**(Address of Principal Executive Offices)** | **92121**<br>**(Zip Code)** |

**Registrant's Telephone Number, Including Area Code: (858) 450-6464**

**10222 Barnes Canyon Road, Bldg. #2**
**San Diego, California 92121**
**(Former Name or Former Address, if Changed Since Last Report)**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Securities registered pursuant to Section 12(b) of the Act:**

| **Title of each class** | **Trading Symbol(s)** | **Name of each exchange on which registered** |
|---|---|---|
| Common Stock, par value $0.001 per share | CRNX | Nasdaq Global Select Market |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 7.01 Regulation FD Disclosure.**

On December 18, 2023, Crinetics Pharmaceuticals, Inc. (the "Company" or "Crinetics") issued a press release and made available a corporate presentation announcing positive initial findings from its ongoing open-label Phase 2 carcinoid syndrome ("CS") study (NCT05361668) of paltusotine, an oral, once-daily investigational compound being developed for the treatment of acromegaly and CS. Copies of the press release and corporate presentation are attached as Exhibits 99.1 and 99.2, respectively, to this report, and are incorporated herein by reference. The press release and corporate presentation will also be available under the "Investors" section of the Company's website. The Company intends to deliver the corporate presentation during a conference call and live webcast with the investment community on December 18, 2023, at 5:00 p.m. Eastern Time.

The information contained in this Item 7.01, including in Exhibits 99.1 and 99.2 hereto, is being "furnished" and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, is not subject to the liabilities of that section and is not deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except as shall be expressly set forth by specific reference in such a filing.

**Item 8.01 Other Events.**

On December 18, 2023, Crinetics announced positive initial findings from its ongoing open-label Phase 2 CS study (NCT05361668) of paltusotine, an oral, once-daily investigational compound being developed for the treatment of acromegaly and CS.

The Phase 2 study is a randomized, open-label, parallel group, multi-center study evaluating the safety, tolerability, pharmacokinetics, and efficacy of paltusotine in people living with carcinoid syndrome. Participants were randomized to receive either 40 mg or 80 mg of paltusotine, with the ability to dose titrate based on tolerability or inadequate control of symptoms during the first four weeks of treatment. At the time of this initial data snapshot, safety data were available for 27 participants, 23 of whom had completed at least two weeks of the randomized treatment period and 15 of whom had completed the full 8-week randomized treatment period. Thirteen of the 15 participants (87%) who completed the randomized treatment phase enrolled in the long-term extension phase of the study.

The initial findings indicate that:

- Administration of paltusotine resulted in rapid and sustained reductions in bowel movement ("BM") frequency and flushing episodes:
  - 65% reduction of excess bowel movements (defined as daily bowel movements above the upper limit of normal, 3/day) for patients with >3/day at baseline
  - 65% reduction of flushing frequency for patients with >1/day at baseline
- Exposure of paltusotine in people with carcinoid syndrome was consistent with prior clinical studies
- Paltusotine was generally well-tolerated with a safety profile consistent with prior clinical studies
  - There were no treatment-related severe or serious adverse events ("AEs"), with the majority of treatment-related AEs being mild-to-moderate.
  - The most frequently reported AEs included diarrhea, headache, and abdominal pain.
- Enrollment in the study is complete, with a total of 36 participants enrolled. Topline data from the complete study is expected in the first half of 2024.

**Forward-Looking Statements**

This report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this report are forward-looking statements, including statements regarding the plans and timelines for the clinical development of paltusotine, including the therapeutic potential and clinical benefits or safety profile thereof; the expected timing of topline data from the ongoing Phase 2 study of paltusotine in CS; and the potential for any of our ongoing clinical studies to show safety or efficacy. These forward-looking statements speak only as of the date of this report and are subject to a number of known and unknown risks, uncertainties and assumptions, including, without limitation, initial findings and topline results that we report may change following a more comprehensive review of the data related to the clinical studies and such data may not accurately reflect the complete results of a clinical study, the possibility of unfavorable new clinical data and further analyses of existing clinical data, and the FDA and other regulatory authorities may not agree with our interpretation of such results; and the other risks and uncertainties described in the company's periodic filings with the SEC. The events and circumstances reflected in the Company's forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Additional information on risks facing Crinetics can be found under the heading "Risk Factors" in Crinetics' periodic filings with the SEC, including its annual report on Form 10-K for the year ended December 31, 2022. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by applicable law, Crinetics does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release dated December 18, 2023 |
| 99.2 | Corporate Presentation |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Crinetics Pharmaceuticals, Inc.

Date: December 18, 2023

By: /s/ R. Scott Struthers, Ph. D.
R. Scott Struthers, Ph. D.
President and Chief Executive Officer

**Exhibit 99.1**

# Crinetics Announces Positive Initial Findings from Ongoing Open-Label Phase 2 Study of Paltusotine for the Treatment of Carcinoid Syndrome

*Significant Reductions in Frequency and Intensity of Both Bowel Movements and Flushing Episodes Were Observed*

*Paltusotine was Well-Tolerated with an Overall Pharmacokinetic Profile that was Consistent with Prior Studies*

*Phase 2 Study Enrollment is Complete (N=36), and Topline Results Expected in 1H 2024*

*Management to Host a Conference Call Today at 5:00 p.m. Eastern Time*

**SAN DIEGO – December 18, 2023** – Crinetics Pharmaceuticals, Inc. (Nasdaq: CRNX) today announced positive initial findings from its ongoing open-label Phase 2 carcinoid syndrome (CS) study of paltusotine, an oral, once-daily investigational compound being developed for the treatment of acromegaly and CS.

"We are very encouraged by these strong initial findings in our Phase 2 study of paltusotine in people with carcinoid syndrome," said Scott Struthers, Ph.D., founder and chief executive officer of Crinetics. "These initial results show the potential of paltusotine to significantly reduce both frequency and intensity of bowel movements and flushing, the key carcinoid syndrome symptoms. Further, paltusotine was well-tolerated and the overall pharmacokinetic profile was consistent with prior studies. After completing this Phase 2 study next quarter, we anticipate sharing the results with the FDA to align on the design of a Phase 3 program."

**Key Highlights from Ongoing Open-label Phase 2 Study of Paltusotine in Carcinoid Syndrome:**

The Phase 2 study is a randomized, open-label, parallel group, multi-center study evaluating the safety, tolerability, pharmacokinetics, and efficacy of paltusotine in people living with carcinoid syndrome. Participants were randomized to receive either 40 mg or 80 mg of paltusotine, with the ability to dose titrate based on tolerability or inadequate control of symptoms during the first four weeks of treatment. At the time of this initial data snapshot, safety data were available for 27 participants, 23 of whom had completed at least two weeks of the randomized treatment period and 15 of whom had completed the full 8-week randomized treatment period. Thirteen of the 15 participants (87%) who completed the randomized treatment phase enrolled in the long-term extension phase of the study.

The initial findings indicate that:

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- Exposure of paltusotine in people with carcinoid syndrome was consistent with prior clinical studies
- Paltusotine was generally well-tolerated with a safety profile consistent with prior clinical studies
  - There were no treatment-related severe or serious adverse events (AEs), with the majority of treatment-related AEs being mild-to-moderate.
  - The most frequently reported AEs included diarrhea, headache, and abdominal pain.
- Enrollment in the study is complete, with a total of 36 participants enrolled. Topline data from the complete study is expected in the first half of 2024.

**Data Review Conference Call**
Crinetics will hold a conference call and live webcast on Monday, December 18 at 5:00 p.m. Eastern Time to discuss the initial findings from the Phase 2 study. To participate, please dial 1-877-451-6152 (domestic), 1-201-389-0879 (international), or request a callback here and refer to conference ID 13742964. To access the webcast, click here. Following the live event, a replay will be available on the Investors section of the Company's website.

**About the Phase 2 Study**
The Phase 2 study is a randomized, open-label, parallel group, multi-center study evaluating the safety, tolerability, pharmacokinetics and efficacy of paltusotine in people living with carcinoid syndrome. This study consists of a randomized treatment phase followed by a long-term extension phase. Enrollment in the study is complete, and a total of 36 patients with documented carcinoid syndrome requiring medical therapy were randomized to receive either 40 mg or 80 mg of daily oral paltusotine. The treatment phase of the study is expected to be completed in the first quarter of 2024. For additional information, please visit clinicaltrials.gov (NCT05361668).

**About Carcinoid Syndrome**
Carcinoid syndrome is found in approximately 20% of patients with neuroendocrine tumors (NETs). NETs are a rare, slow-growing type of cancer that arise most often in the digestive tract. When these tumors metastasize to the liver, carcinoid syndrome can occur and is most commonly characterized by diarrhea and flushing. While injectable depot somatostatin receptor ligand (SRL) therapies are mainstay treatments for carcinoid syndrome, these injections are associated with considerable treatment burden and offer inadequate relief of carcinoid syndrome symptoms for many patients.

**About Paltusotine**
Paltusotine is the first oral, once-daily selectively-targeted somatostatin receptor type 2 (SST2) agonist and is currently in investigational Phase 3 studies for acromegaly and a Phase 2 study for carcinoid syndrome. It was designed by the Crinetics discovery team to provide an efficacious and convenient once-daily option for people living with acromegaly and neuroendocrine tumors. In Phase 2 studies and the recently completed PATHFNDR-1 Phase 3 study, paltusotine maintained IGF-1 levels in acromegaly patients who switched from monthly injectable medications to paltusotine. IGF-1 is the primary biomarker endocrinologists use to manage acromegaly patients. Initial findings from an ongoing Phase 2 study in carcinoid syndrome further support paltusotine's potential beyond acromegaly.

**About Crinetics Pharmaceuticals**
Crinetics Pharmaceuticals is a clinical stage pharmaceutical company focused on the discovery, development, and commercialization of novel therapeutics for endocrine diseases and endocrine-related tumors. Paltusotine, an investigational, first-in-class, oral somatostatin receptor type 2 (SST2) agonist, is in Phase 3 clinical development for acromegaly and Phase 2 clinical development for carcinoid syndrome associated with neuroendocrine tumors. Crinetics has demonstrated pharmacologic proof-of-concept in a Phase 1 clinical study for CRN04894, a first-in-class, investigational, oral ACTH antagonist, that is currently in Phase 2 clinical studies for the treatment of Cushing's disease and congenital adrenal hyperplasia. All of the company's drug candidates are orally delivered, small molecule new chemical entities resulting from in-house drug discovery efforts, including additional discovery programs addressing a variety of endocrine conditions such as hyperparathyroidism, polycystic kidney disease, Graves' disease, thyroid eye disease, hyperinsulinism, diabetes and obesity.

**Forward-Looking Statements**

*This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this press release are forward-looking statements, including statements regarding the plans and timelines for the clinical development of paltusotine and CRN04894, including the therapeutic potential and clinical benefits or safety profile thereof; the expected timing of topline data from the ongoing Phase 2 study of paltusotine in carcinoid syndrome; plans and timing for the full results of the Phase 2 study of paltusotine in carcinoid syndrome and sharing the results with the FDA to align on and design a Phase 3 program; plans and timing to further develop paltusotine in carcinoid syndrome or to conduct Phase 3 studies of paltusotine in carcinoid syndrome; the potential benefits of CRN04894 in patients with Cushing's disease or Congenital Adrenal Hyperplasia and the expected plans and timing for data from ongoing clinical studies; the potential for any of our ongoing clinical studies to show safety or efficacy; the potential for our discovery program for endocrine diseases including hyperparathyroidism, polycystic kidney disease, Graves' disease, thyroid eye disease, hyperinsulinism, diabetes and obesity to progress to drug candidates and show safety or efficacy and our plans to identify and create new drug candidates for additional diseases. These forward-looking statements speak only as of the date of this press release and are subject to a number of known and unknown risks, uncertainties and assumptions, including, without limitation, initial findings and topline results that we report may change following a more comprehensive review of the data related to the clinical studies and such data may not accurately reflect the complete results of a clinical study, the possibility of unfavorable new clinical data and further analyses of existing clinical data, and the FDA and other regulatory authorities may not agree with our interpretation of such results; and the other risks and uncertainties described in the company's periodic filings with the SEC. The events and circumstances reflected in the company's forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Additional information on risks facing Crinetics can be found under the heading "Risk Factors" in Crinetics' periodic filings with the SEC, including its annual report on Form 10-K for the year ended December 31, 2022. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by applicable law, Crinetics does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.*

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Exhibit 99.2

Crinetics Pharmaceuticals

# INITIAL RESULTS FROM ONGOING PALTUSOTINE CARCINOID SYNDROME OPEN LABEL PHASE 2 STUDY

A Randomized, Parallel Group Study to Evaluate the Safety, Pharmacokinetics, and Dose Response of Paltusotine Treatment in Subjects with Carcinoid Syndrome

# SAFE HARBOR STATEMENT

This presentation contains forward-looking statements. Crinetics Pharmaceuticals, Inc. ("Crinetics," the "company," "we," "us," or "our") cautions you that statements contained in this presentation regarding matters that are not historical facts are forward-looking statements. These statements are based on the company's current beliefs and expectations. Such forward-looking statements include, but are not limited to, statements regarding: the plans and timelines for the clinical development of paltusotine and CRN04894, including the therapeutic potential and clinical benefits or safety profile thereof; the expected timing of topline results data from the ongoing Phase 3 clinical study of paltusotine in acromegaly and Phase 2 study of paltusotine in carcinoid syndrome; the expected timing of the submission of a new drug application for paltusotine for the treatment of acromegaly and related open label extension studies; plans and timing for the full results of the Phase 2 study of paltusotine in carcinoid syndrome and sharing the results with the FDA to align on and design a Phase 3 program; plans and timing to further develop paltusotine in carcinoid syndrome or to conduct Phase 3 studies of paltusotine in carcinoid syndrome; the potential for any of our ongoing clinical studies to show safety or efficacy; and our plans to identify and create new drug candidates for additional diseases. In some cases, you can identify forward-looking statements by terms such as "may," "believe," "anticipate," "could," "should," "estimate," "expect," "intend," "plan," "project," "will," "contemplate," "predict," "continue," "forecast," "aspire," "goal," "potential," "target" or the negative of or other similar terms.

These statements speak only as of the date of this presentation, involve known and unknown risks, uncertainties, assumptions, and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, without limitation: topline and initial data that we report may change following a more comprehensive review of the data related to the clinical studies and such data may not accurately reflect the complete results of a clinical study, and the FDA and other regulatory authorities may not agree with our interpretation of such results; the risk that preliminary results of preclinical studies or clinical studies do not necessarily predict final results and that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, and as more patient data become available, the possibility of unfavorable new clinical data and further analyses of existing clinical data; potential delays in the commencement, enrollment and completion of clinical studies and the reporting of data therefrom; the FDA or other regulatory agencies may require additional clinical studies of paltusotine or suggest changes to our planned Phase 3 clinical studies prior to and in support of the approval of a New Drug Application or applicable foreign regulatory approval; international conflicts may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our clinical studies and preclinical studies, manufacturing and supply chain, or impairing employee productivity; our dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of our clinical studies, nonclinical studies and preclinical studies for paltusotine; regulatory developments or price restrictions in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval and/or commercialization; our ability to obtain and maintain intellectual property protection for our product candidates; we may use our capital resources sooner than we expect; and other risks described under the heading "Risk Factors" in documents we file from time to time with the Securities and Exchange Commission ("SEC"). Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and, except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. This presentation also contains estimates made by independent parties and by us relating to addressable patients and addressable market size. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.

# Once Daily Oral Paltusotine Showed Strong Initial Results in Carcinoid Syndrome Patients

## SAFETY

- Paltusotine was well-tolerated with no severe or serious treatment related adverse events and consistent with prior studies

## PHARMACOKINETICS

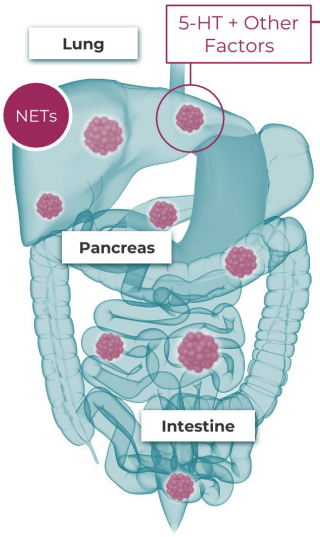
- Overall PK was generally consistent with expectations from healthy volunteers

## EFFICACY

- Significant reductions in frequency and severity of bowel movements and flushing with 40mg and 80mg

**Safety profile and efficacy observed to date with paltusotine supports progressing to Phase 3 study in carcinoid syndrome (pending complete data, expected 1H 2024)**

# Carcinoid Syndrome is a Serious Disease and Patients Need Better Treatment Options




## Carcinoid Syndrome

**~33,000** Patients Diagnosed with Carcinoid Syndrome (US)

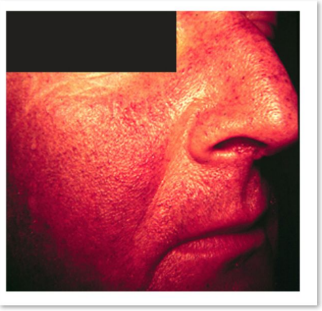
**Excess bowel movements (>3/day) are highly disruptive**
***Goal:*** *reduce frequency and urgency (normal is ≤3/day)*

**Severe Flushing episodes can be debilitating and potentially dangerous**
***Goal:*** *reduce frequency and severity (normal is < 1/day)*

**Severe and life-threatening complications: carcinoid heart disease (found in up to 50% of patients) & carcinoid crisis**
***Goal:*** *prevent severe complications*

**Injected SRLs Impose a high burden of care and frequently don't last all month**
***Goal:*** *eliminate depot and rescue injections and provide consistent control throughout the month*

**Facial Flushing in a patient with carcinoid syndrome**



*Courtesy of*
*Stephen E Goldfinger, MD* UpToDate®

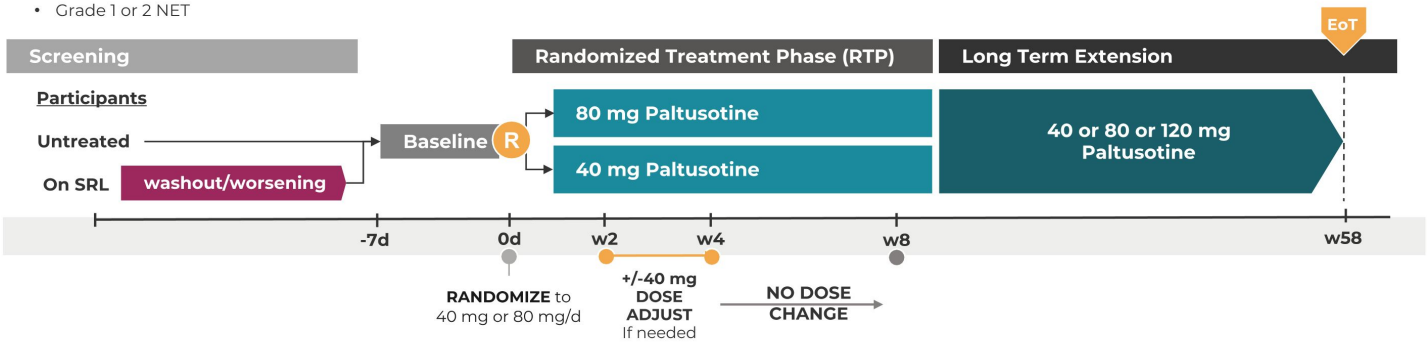
5-HT = Serotonin; NETs = Neuroendocrine tumors
SRL = somatostatin receptor ligand

# Phase 2 Study Design: Evaluating Safety, PK and Efficacy of Paltusotine in Carcinoid Syndrome Patients

**Protocol:** 8-week, open label parallel, randomized 2-dose study followed by Long Term Extension

**Key Eligibility Criteria:**

- Treatment naïve or currently untreated and actively symptomatic – *OR* – controlled on SRL therapy and symptom worsening upon washing out of treatment.
- Positive SSTR expression
- Grade 1 or 2 NET




**1 Primary Endpoint**

Safety and tolerability of Paltusotine

**2 Secondary Endpoint**

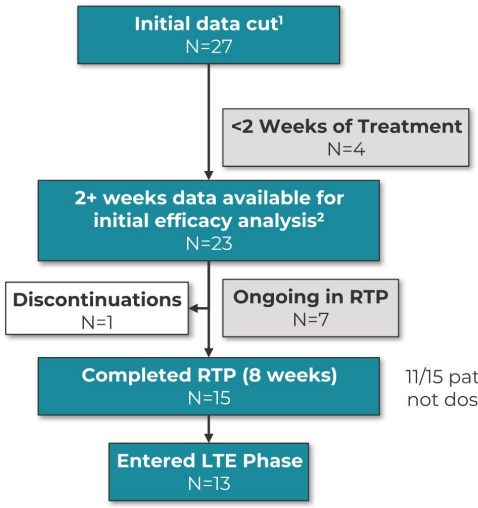
Pharmacokinetics of Paltusotine at 40, 80 and 120 mg doses

**Exploratory Endpoints**

Bowel movement and flushing frequency, octreotide rescue use, biomarkers, stool consistency, abdominal pain, PRO measures

SSTR = somatostatin receptor; SRL = somatostatin receptor ligand
EoT = end of treatment; PRO = patient reported outcome

# Disposition and Dosing for the Initial Data Cut (N=27)




11/15 patients were not dose adjusted

**Dose at Randomization (N=27 initial data cut)**

| | 40mg | 80mg | Total |
|---|---|---|---|
| Naïve/ Untreated | 5 | 4 | 9 |
| Switching | 8 | 10 | 18 |
| Total | 13 | 14 | 27 |

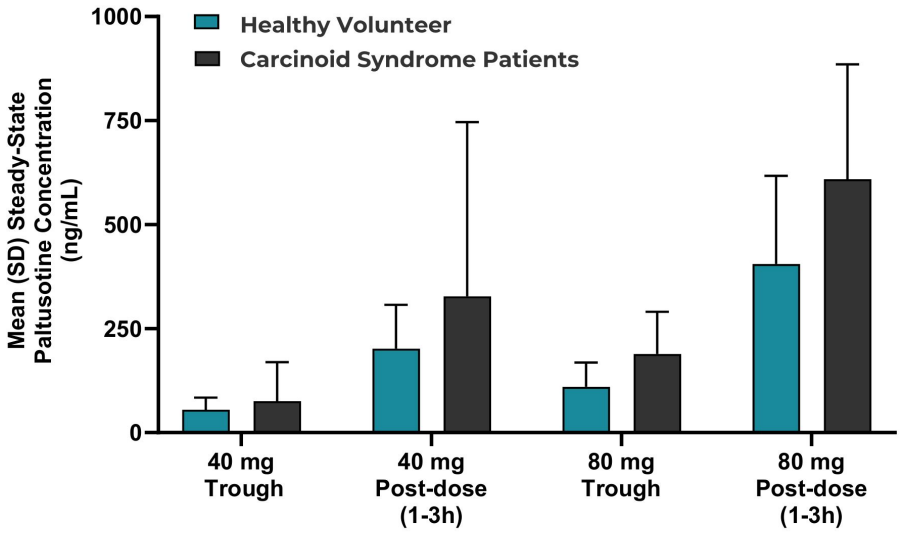
RTP = Randomized treatment phase (8 weeks); LTE = Long Term Extension

1. Safety analysis as of November 27, 2023 initial data cutoff
2. Efficacy analysis based on a minimum of 2 weeks of data available as of the November 27, 2023 data cutoff

# Baseline Demographics and Disease Characteristics

| | Naïve/Untreated Symptomatic N=9 | Switching from SRL N=18 | Overall N=27 |
|---|---|---|---|
| **Female, n(%)** | **6(67)** | **9(50)** | **15(56)** |
| **Male, n(%)** | **3(33)** | **9(50)** | **12(44)** |
| **Age at informed consent - Mean (SD), years** | **58.2 (19.5)** | **60.6(8.1)** | **59.8(12.7)** |
| **BMI - Mean (SD), kg/m²** | **30.0(14.0)** | **29.6(5.7)** | **29.8(9.1)** |
| **Geographic Region** | | | |
| North America, n(%) | 4(44) | 11(61) | 15(55) |
| Europe, n(%) | 1(11) | 0 | 1(3) |
| Latin America , n(%) | 4(44) | 7(38) | 11(40) |
| **Duration since Carcinoid Syndrome diagnosis – Median, months** | **8.2** | **64.4** | **60.2** |
| **NET Tumor Grade 1, n(%)** | **5(56)** | **8(44)** | **13(48)** |
| **NET Tumor Grade 2, n(%)** | **4(44)** | **10(56)** | **14(52)** |

# Paltusotine Exposure in Patients with Carcinoid Syndrome was Consistent with Expectations from Healthy Volunteers




Healthy volunteer data is from paltusotine population PK model sampling at steady-state trough and 2-hour post-dose.
Carcinoid Syndrome patients: N=7, N=4, N=9, and N=9 for 40 mg trough, 40 mg post-dose, 80 mg trough, and 80 mg post-dose, respectively.

# Paltusotine was Well-Tolerated with No Severe or Serious Treatment-Related Adverse Events

| Treatment-Emergent Adverse Events | Paltusotine N = 27 |
|---|---|
| **Any** | **18(66.7)** |
| Mild | 9(33.3) |
| Moderate | 7(25.9) |
| Severe | 2(7.4) |
| **Serious** | **3(11.1)** |
| **Death** | **1(3.7)*** |
| **Treatment-related** | **15(55.6)** |
| Mild | 9(33.3) |
| Moderate | 6(22.2) |
| Severe | 0 |
| **Serious** | **0** |
| **Death** | **0** |

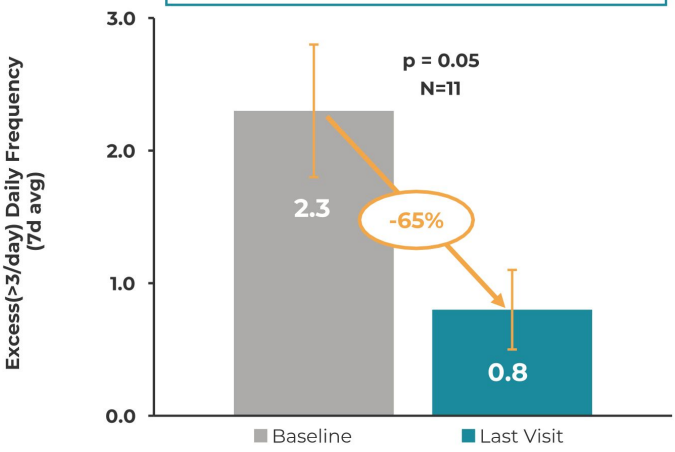
**Preliminary Safety Summary from Ongoing Carcinoid Syndrome Phase 2 Study**

- Paltusotine was well-tolerated with no treatment related severe or serious treatment related adverse events
- The most frequently reported adverse events included diarrhea, headache and abdominal pain
- Adverse event findings were similar across paltusotine dosing of 40 and 80 mg
- No new safety signals have been observed during study monitoring of vital signs, ECGs, or safety laboratory values

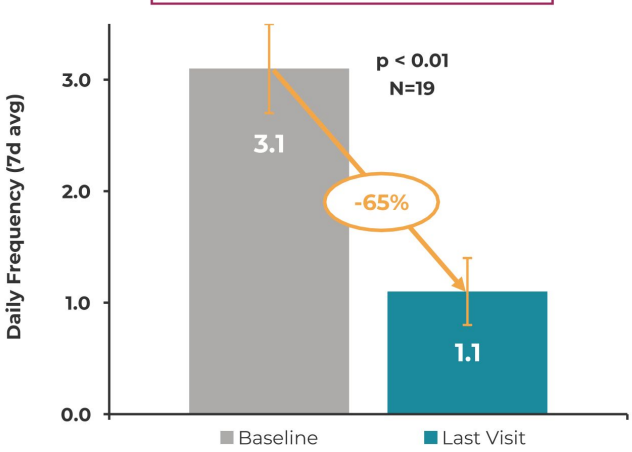
* The fatal outcome of one SAE (cardiac failure, most likely secondary to carcinoid heart disease) occurred 26 days after treatment discontinuation and was not treatment related.

# Paltusotine Reduced the Frequency of Both Key Carcinoid Syndrome Core Symptoms: Excess BM and Flushing

**Excess Bowel Movement* Frequency For Patients with >3/day at Baseline**



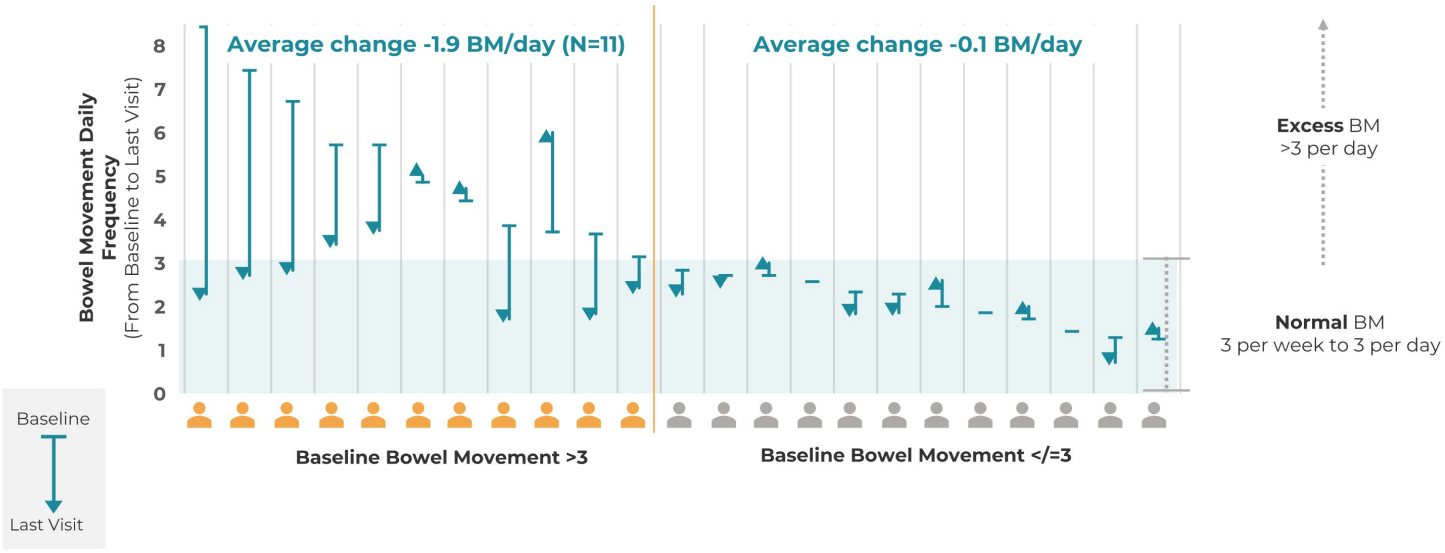

**Flushing Frequency for Patients with ≥1/day at Baseline**




*Excess bowel movements (BM) were defined as daily bowel movements above the upper limit of normal (3 per day)
Exploratory analysis of last visit prior to the preliminary data cut off includes 23 subjects: 15 subjects completed the week 8 visit, 4 subjects completed week 6 visit, 3 subjects completed week 4 visit and 1 subject completed week 2 visit.

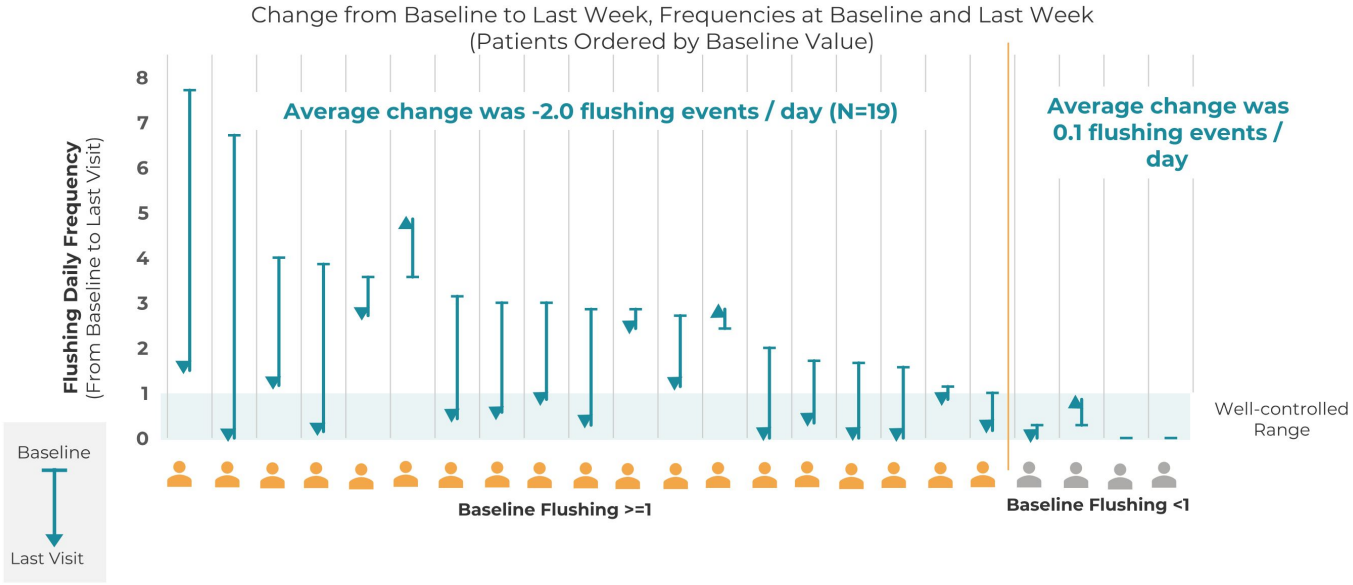
# Paltusotine had Clear Benefit on Subjects with Elevated Bowel Movement Frequency

Change from Baseline to Last Week of Treatment
(Patients Ordered by Baseline Value)




(1) End of each arrow represents the data from the last available week of treatment for each of the 23 subjects. 15 subjects completed the week 8 visit, 4 subjects completed week 6 visit, 3 subjects completed week 4 visit and 1 subject completed week 2 visit.

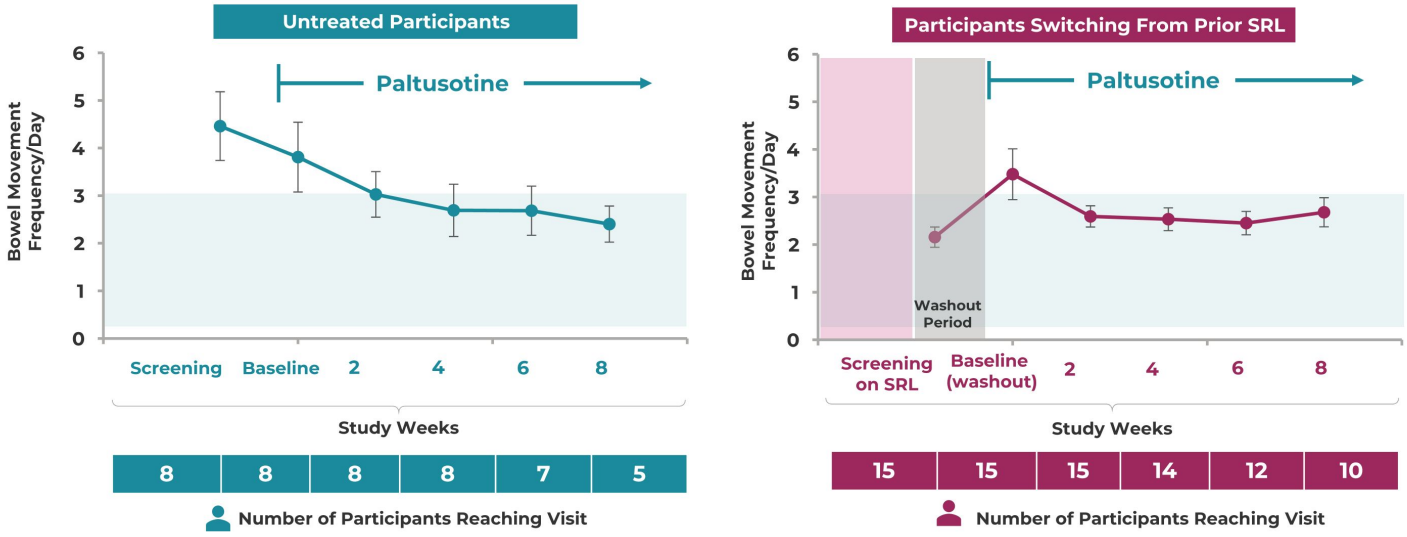
# Paltusotine Showed Improvements in Flushing Frequencies in Majority of Subjects




(1) End of each arrow represents the data from the last available week of treatment for each of the 23 subjects. 15 subjects completed the week 8 visit, 4 subjects completed week 6 visit, 3 subjects completed week 4 visit and 1 subject completed week 2 visit.

# Rapid Improvements in Bowel Movement Frequency were Observed within 2 Weeks of Treatment

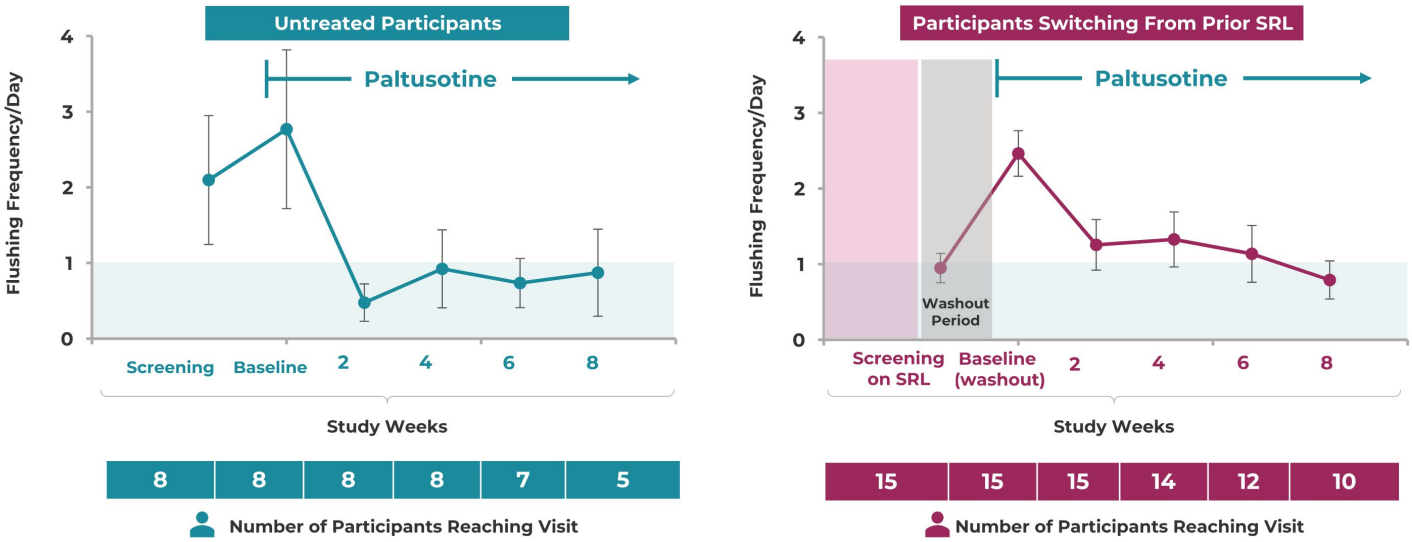
**Bowel Movement Frequency of All Participants (N=23) Whether Experiencing Excess BMs at Baseline or Not**




Frequency measure is based on the 14-day average during the screening period and 7-day average prior to baseline on all other timepoints
SRL = somatostatin receptor ligand

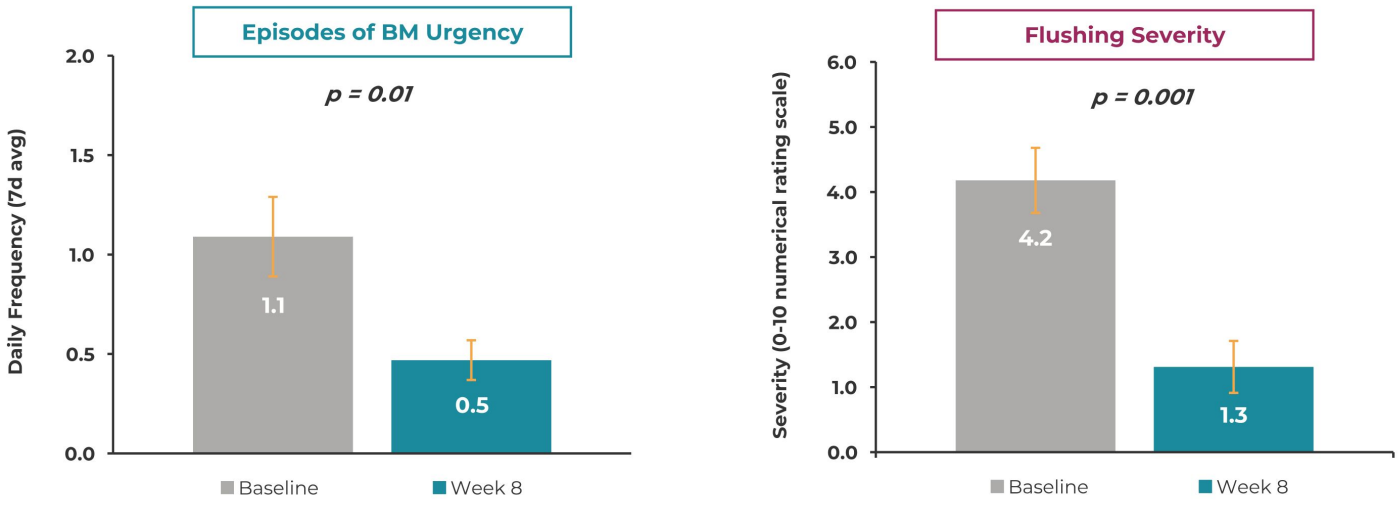
# Rapid Improvements in Flushing Frequency were Observed within 2 Weeks of Treatment

**Flushing Frequency of All Participants (N=23) Whether Experiencing Flushing at Baseline or Not**



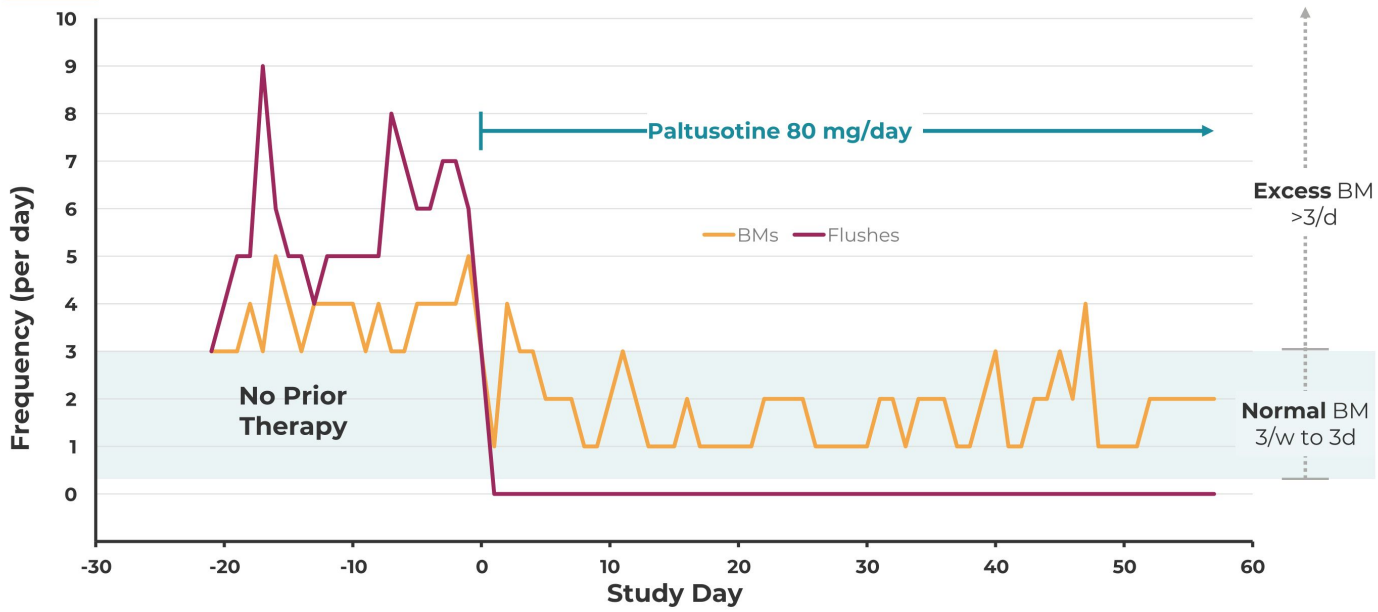

Frequency measure is based on the 14-day average during the screening period and 7-day average prior to baseline on all other timepoints
SRL = somatostatin receptor ligand

# Paltusotine Also Reduced the Severity of Key Carcinoid Syndrome Symptoms



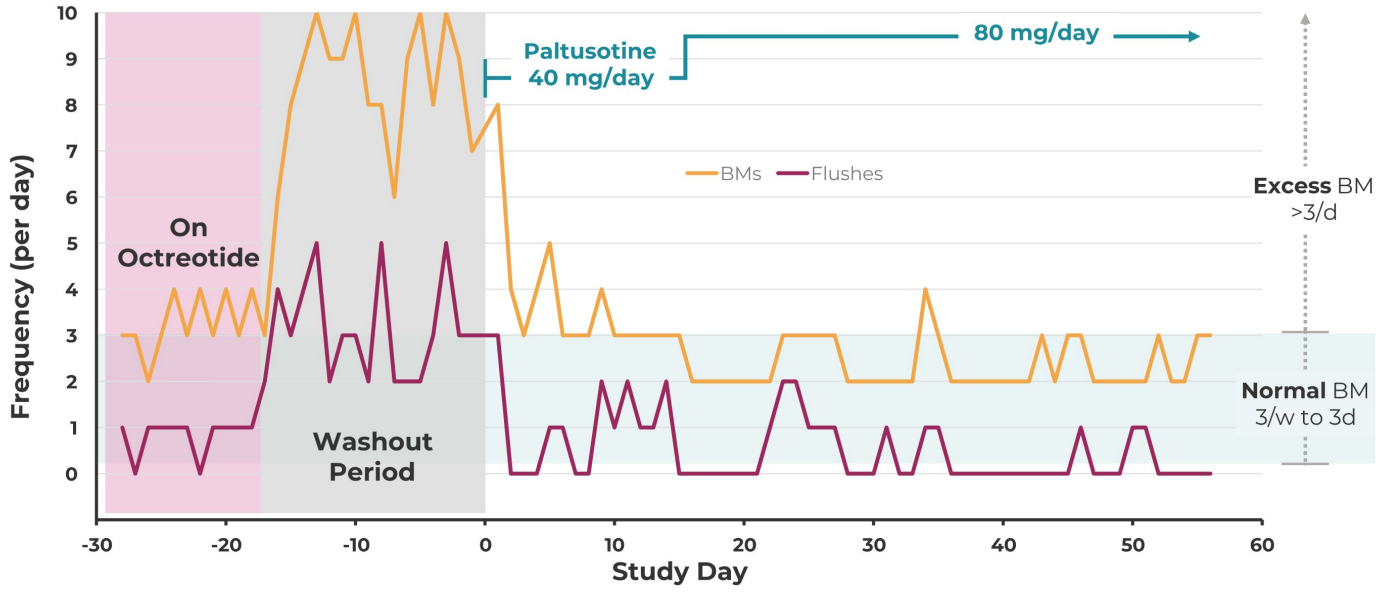

N=15 who completed the Randomized Treatment Period
BM = bowel movement

# Example Study Participant #1: Elimination of Flushing and Normalization of BMs




BM = bowel movement

# Example Study Participant #2: Meaningful Improvements in BM and Flushing Frequencies




BM = bowel movement

# Once Daily Oral Paltusotine Showed Strong Initial Results in Carcinoid Syndrome Patients

## Summary: Exceeded Initial Goals for the Study

- Significant reductions of frequency and severity of bowel movements and flushing with 40mg and 80mg
- Paltusotine was well-tolerated with no severe or serious treatment related adverse events
- Overall PK was generally consistent with expectations from healthy volunteers

## Next Steps: Initial Data Supports Preparation for Phase 3

- Analysis of biomarker and supplemental patient reported outcome data
- The study has completed enrollment (N=36), and the topline data from the complete study is expected in 1H 2024
- Expect to submit complete data set and engage with FDA first half of 2024

# Anticipated Paltusotine Milestones


**1Q24**
- Results from PATHFNDR-2 Phase 3 study in untreated acromegaly patients

**1H24**
- Topline results from carcinoid syndrome Phase 2 study (N=36)

**2H24**
- Acromegaly NDA submission
- Carcinoid syndrome Phase 3 start pending alignment with FDA

**Ongoing Open Label Extension Studies**
- N > 175 participants and increasing
- 26 patients from Phase 2 extension study have been treated with paltusotine for >3 years, 35 patients for >2 years

# Q&A

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**Dana Pizzuti, M.D.**
Chief Medical & Development Officer

**Alan Krasner, M.D.**
Chief Endocrinologist