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): March 12, 2024

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 **San Diego, California**	**92121**
(Address of Principal Executive Offices)	**(Zip Code)**

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

(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 March 12, 2024, Crinetics Pharmaceuticals, Inc. (the "Company," "Crinetics," "we," "us," or "our") issued a press release and made available a corporate presentation announcing positive topline results from its 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 March 12, 2024, at 4:30 p.m. Eastern Time.

The information that is solely contained in this Item 7.01 of this Current Report on Form 8-K, including in Exhibit 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.

The information regarding the press release referred to in Item 7.01 of this Current Report on Form 8-K is incorporated herein by reference. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

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 and CRN04894, including the therapeutic potential and clinical benefits or safety profile thereof; plans and timing for sharing the full results of the Phase 2 study of paltusotine in CS 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 Congenital Adrenal Hyperplasia or Cushing's disease 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, 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 report and are subject to a number of known and unknown risks, uncertainties and assumptions, including, without limitation, 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, 2023. 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 March 12, 2024
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: March 12, 2024

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

Exhibit 99.1

Crinetics Announces Positive Topline Results from Phase 2 Trial of Paltusotine for the Treatment of Carcinoid Syndrome

Paltusotine Treatment Demonstrated Rapid and Sustained Reductions in Frequency and Severity of Flushing Episodes and Bowel Movements

Paltusotine was Generally Well-Tolerated and Showed an Overall PK Profile Consistent with Prior Studies

Results Confirm Initial Positive Data Previously Reported

Management to Host a Conference Call Today at 4:30 p.m. Eastern Time

SAN DIEGO – March 12, 2024 –Crinetics Pharmaceuticals, Inc. (Nasdaq: CRNX) a clinical stage pharmaceutical company focused on the discovery, development and commercialization of novel therapeutics for endocrine diseases and endocrine-related tumors, today announced positive topline results from its open-label Phase 2 carcinoid syndrome study of paltusotine, an oral, once-daily investigational compound being developed for the treatment of acromegaly and carcinoid syndrome.

"We are very pleased that these results from our Phase 2 study of paltusotine in carcinoid syndrome confirm our decision to move expeditiously toward Phase 3," said Scott Struthers, Ph.D., founder and chief executive officer of Crinetics. "These results highlight the potential of paltusotine to deliver significant benefits to patients living with the debilitating symptoms of carcinoid syndrome. We plan to engage with the FDA to align on a Phase 3 study design and have begun preparations to enable the initiation of a Phase 3 program by the end of the year."

Key Highlights from the Phase 2 Study:

The Phase 2 trial was a randomized, open-label, parallel group, multi-center study evaluating the safety, tolerability, pharmacokinetics, and efficacy of paltusotine in people living with carcinoid syndrome. A total of 36 participants were randomized to receive either 40 mg (n=18) or 80 mg (n=18) of paltusotine for 8 weeks, with the ability to dose titrate based on tolerability or inadequate control of symptoms during the first four weeks of treatment. Six participants in the 40 mg group increased their dose to 80 mg, and 3 participants in the 80 mg group increased to 120 mg. Thirty patients completed the randomized treatment phase, with 1 patient from the 40 mg group and 5 patients from the 80 mg group discontinuing treatment. Twenty-six of the 30 participants who completed the randomized treatment phase enrolled in the long-term extension phase of the study.

Results demonstrated:

- Rapid and sustained reductions in flushing episodes and bowel movement (BM)
  - 63% reduction in mean flushing frequency for patients with >1/day at baseline (n=24; p<0.0001)
  - 60% reduction in mean excess BM frequency (defined as daily bowel movements above the upper limit of normal, 3/day) in patients with >3/day at baseline (n=16; p=0.02)
  - 61% reduction in mean flushing severity (n=31; p<0.0001) and 64% reduction in mean BM urgency (n=31; p<0.0001)

    - Reductions in frequency and severity of symptoms were observed within 2 weeks of paltusotine treatment and sustained through 8 weeks in both naïve/untreated patients and those switching from prior somatostatin receptor ligand (SRL) therapy
- Overall pharmacokinetic profile of paltusotine in patients with carcinoid syndrome was consistent with expectations from healthy volunteers
- 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)
    - The most frequently reported AEs included diarrhea, abdominal pain, nausea and headache
    - AE findings were similar across 40 mg and 80 mg dosing groups
- Levels of biomarkers serotonin and 5HIAA provide additional evidence of paltusotine activity in carcinoid syndrome

“I am excited about the clinical improvements that paltusotine demonstrated for patients with carcinoid syndrome in this study,” said Aman Chauhan, M.D., Sylvester Comprehensive Cancer Center, University of Miami and an investigator on the study. “There is a critical need for better treatment options for patients with neuroendocrine tumors who experience carcinoid syndrome. The results from this study of paltusotine are highly encouraging and I look forward to the next stage in its development.”

Data Review Conference Call

Crinetics will hold a conference call and live webcast today, Tuesday, March 12 at 4:30 p.m. Eastern Time to discuss the results from the Phase 2 study. To participate, please dial 1-888-886-7786 (domestic), 1-416-764-8658 (international), or request a callback here and refer to conference ID 02300008. 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. 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 for 8 weeks. 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 carcinoid syndrome. 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. Results from the Phase 2 study in carcinoid syndrome further support paltusotine’s potential use 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 in 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, an investigational, first-in-class, oral ACTH antagonist, that is currently in Phase 2 clinical studies for the treatment of congenital adrenal hyperplasia and Cushing's disease. 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, 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; plans and timing for sharing the full results of the Phase 2 study of paltusotine in carcinoid syndrome 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 Congenital Adrenal Hyperplasia or Cushing's disease 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, 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, 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, 2023. 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

Results from 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 strategic objectives for paltusotine; 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 results data from the ongoing Phase 3 clinical study of paltusotine in acromegaly; 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 sharing the full results of the Phase 2 study of paltusotine in carcinoid syndrome with the FDA to align on a Phase 3 program and the plans and enrollment in related open label extension studies; the potential benefits of CRN04894 in patients with Congenital Adrenal Hyperplasia or Cushing's Disease and the expected plans and timing for data and topline data readouts from ongoing clinical studies; the potential benefits of PTH receptor antagonists for patients with hyperparathyroidism, the potential benefits of TSH antagonist for Graves' Disease or thyroid eye disease; the potential for any of our ongoing clinical studies to show safety or efficacy; the potential of our ongoing discovery efforts to target future indications for hyperparathyroidism, polycystic kidney disease, Graves diseases, thyroid eye disease, or diabetes/obesity, and the expected plans and timing for candidate selection and clinical development of such candidates; our plans to identify and create new drug candidates for additional diseases or the potential for any such new drug candidates to show safety or efficacy; the direction or trajectory of the Company's potential future growth, the receipt of any revenues from product sales and the ability of such revenues to support continued growth, and our expected plans and timing for commercialization of paltusotine and other product candidates pending regulatory approval. 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," "lead to," "designed to," "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. 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 information gathered from market research, estimates and other statistical data made by independent parties and by us relating to addressable patients, addressable market size and other data about our industry or the potential market opportunity for our product, including academic and community medical oncologist and other HCP opinions collected during market research. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to the opinions gathered in market research or to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Once Daily Oral Paltusotine Showed Positive Results in Carcinoid Syndrome Patients

EFFICACY FINDINGS: Rapid and Sustained Reductions in Patient Symptoms

- ☑ **Flushing:** 63% reduction in frequency for patients with >1/day ($p < 0.0001$)
- ☑ **Flushing Severity:** 61% reduction in severity of episodes ($p<0.0001$)
- ☑ **Excess Bowel Movement:** 60% reduction in frequency for patients with >3/day ($p=0.02$)
- ☑ **Bowel Movement Urgency:** 64% reduction in urgent episodes ($p<0.0001$)

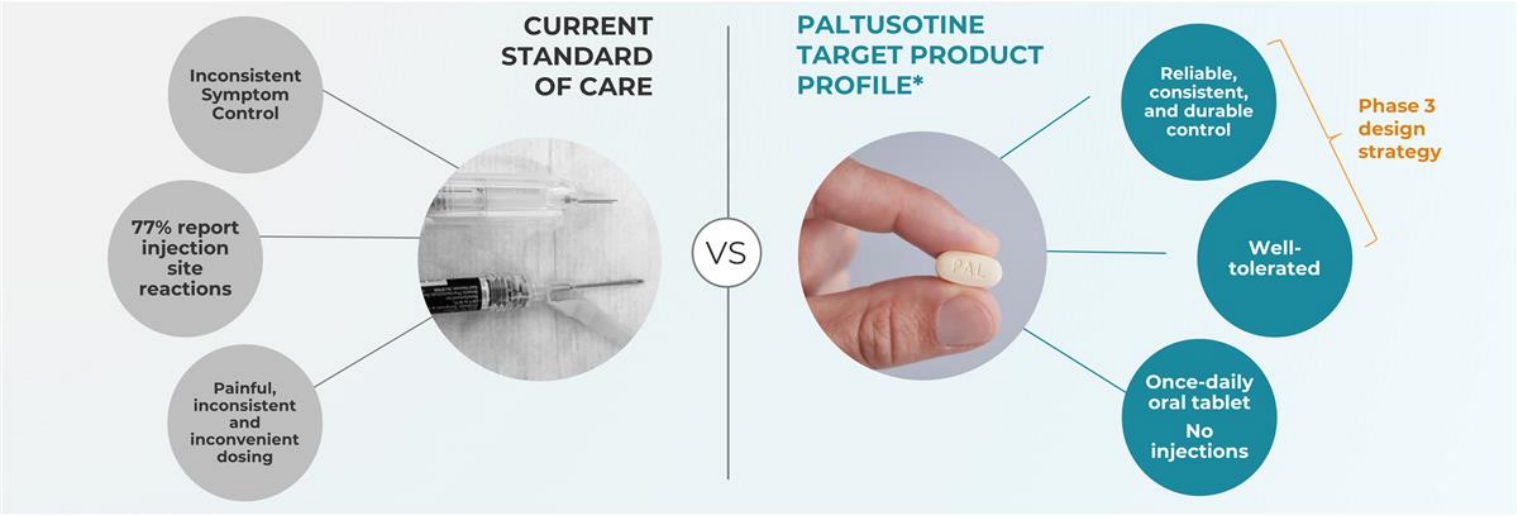
SAFETY

- ☑ Paltusotine was generally well-tolerated with no treatment-related severe or serious adverse events
- ☑ Paltusotine demonstrated no new safety signals

Efficacy and safety findings support progressing to a pivotal phase 3 trial
(pending discussions with the FDA)

Paltusotine is an investigational drug in clinical studies for the treatment of acromegaly and carcinoid syndrome.

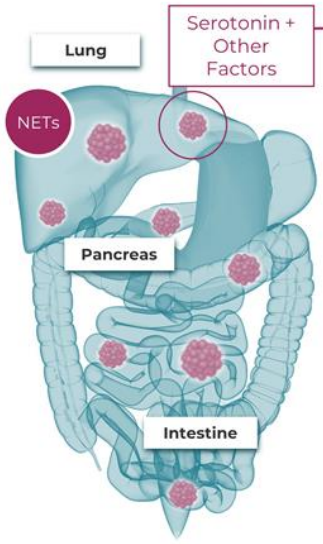
Paltusotine: Designed to Allow People with Acromegaly and Carcinoid Syndrome to Focus on Living



*Pending alignment with FDA on phase 3 study for Carcinoid Syndrome. Paltusotine is an investigational drug in clinical studies for the treatment of acromegaly and carcinoid syndrome.

References 1. Geer EB, Sisco J, Adelman DT, et al. Patient reported outcome data from acromegaly patients treated with injectable somatostatin receptor ligands (SRLs) in routine clinical practice. *BMC Endocr Disord*. 2020;20(1):117. doi:10.1186/s12902-020-00595-4; 2. Strasburger CJ, Karavitaki N, Störmann S, et al. Patient-reported outcomes of parenteral somatostatin analogue injections in 195 patients with acromegaly. *Eur J Endocrinol*. 2016;174(3):355-62. doi:10.1530/EJE-15-1042; 3. Fleseriu et al. Frontiers in Endocrinology; March 2021, Vol.12; 4. Boyd et al. Pancreas 2013;42: 878—882.

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



Carcinoid Syndrome

~**33,000** Patients Diagnosed with Carcinoid Syndrome (U.S.)

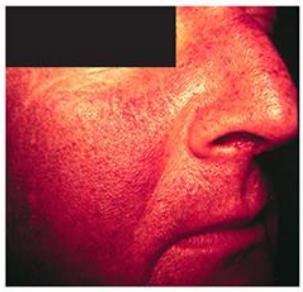
Excess bowel movements (>3/day) are highly disruptive
Goal: *reduce frequency and urgency (normal is ≤3/day)*

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 lose effectiveness before next injection
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®

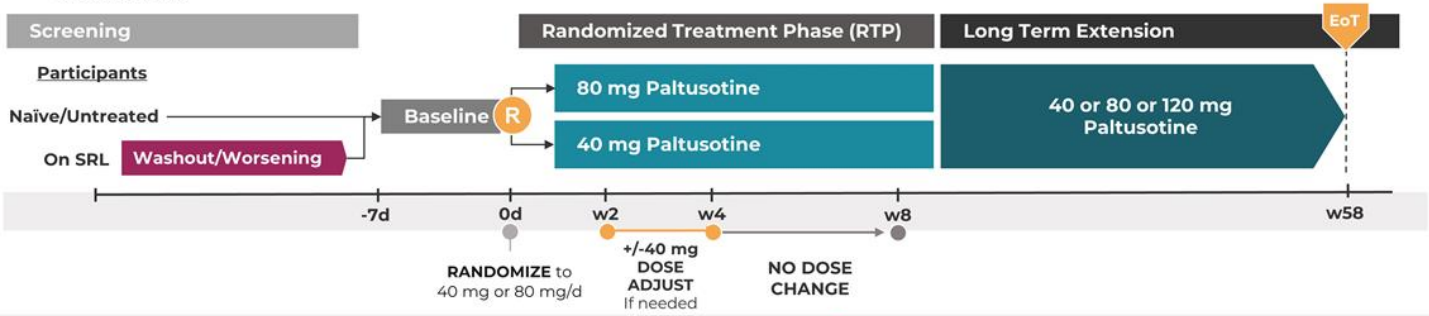
NETs = Neuroendocrine tumors; SRL = somatostatin receptor ligand.

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 a Long Term Extension phase

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

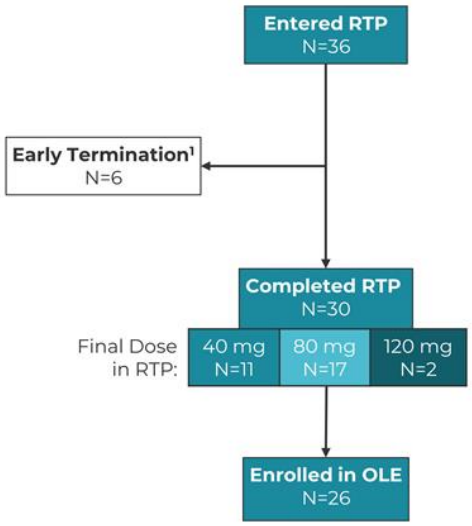
Pharmacokinetics of Paltusotine

Exploratory Efficacy Endpoints

Bowel movement and flushing frequency and severity markers, octreotide rescue use, biomarkers, PRO measures

EoT = end of treatment; NET = Neuroendocrine tumor; PK = Pharmacokinetics; PRO = patient reported outcome; SRL = somatostatin receptor ligand; SSTR = somatostatin receptor.

Subject Disposition and Dosing



	Total n (%)
Entered RTP	**36**
Naïve/Untreated	9
Switching	27
Discontinued	6 (17)
Withdrawal by subject	1 (3)
Adverse event	2 (6)
Investigator decision	2 (6)
Need for administration of a prohibited concomitant medication	1 (3)
Increased dose at Week 2 or 4	9
Completed RTP	**30 (83)**
Naïve/Untreated	8
Switching	22
Enrolled in OLE	**26 (87)**

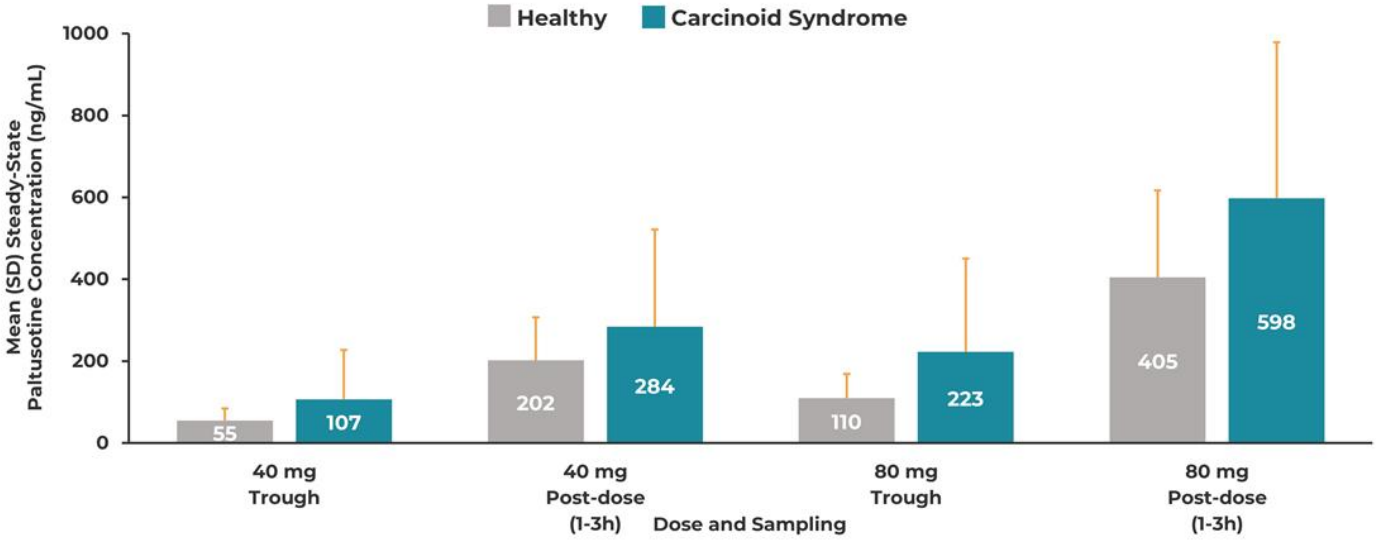
RTP = Randomized treatment phase (8 weeks); OLE=Open-label extension.
1. One subject who discontinued in the RTP dosed with paltusotine and had diary data through week 8 of the RTP.

Baseline Demographics and Disease Characteristics were Consistent Across Patient Groups

	Naïve/Untreated Symptomatic N=9	Switching from SRL N=27	Overall N=36
Female, n (%)	**6 (67)**	**13 (48)**	**19 (53)**
Male, n (%)	**3 (33)**	**14 (52)**	**17 (47)**
Age - Mean (SD), years	**58.2 (19.5)**	**61.6 (10.3)**	**60.8 (13.0)**
BMI - Mean (SD), kg/m²	**30.0 (14.0)**	**28.4 (5.3)**	**28.8 (8.1)**
Geographic Region			
North America, n (%)	4 (44)	15 (56)	19 (53)
Europe, n (%)	1 (11)	1 (4)	2 (6)
Latin America , n (%)	4 (44)	11 (41)	15 (42)
Duration Since Carcinoid Syndrome Diagnosis – Median, months	**8.2**	**72.1**	**69.4**
NET Tumor Grade 1, n (%)	**5 (56)**	**14 (52)**	**19 (53)**
NET Tumor Grade 2, n (%)	**4 (44)**	**13 (48)**	**17 (47)**

BMI=Body Mass Index; NET = Neuroendocrine tumor.

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



Healthy volunteers: simulated (n=1000) using paltusotine population PK model, sampling at steady-state trough and 2h post-dose. Carcinoid Syndrome patients: 40 mg trough (n=17), 40 mg post-dose (n=15), 80 mg trough (n=21), 80 mg post-dose (n=18), 120 mg trough (n=2), and 120 mg post-dose (n=2). 120 mg data omitted due to small sample size.

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

Treatment-Emergent Adverse Events, n (%)	Paltusotine N=36
Any	**26 (72.2)**
Mild/Moderate	22 (61.1)
Severe	4 (11.1)
Leading to discontinuation	2 (5.6)
Serious	4 (11.1)
Death	1 (2.8)*
Treatment-related	**16 (44.4)**
Mild/Moderate	16 (44.4)
Severe	0
Leading to discontinuation	0
Serious	0
Death	0

Preliminary Safety Summary from Ongoing Carcinoid Syndrome Phase 2 Study

- Paltusotine was generally well-tolerated with no treatment related severe or serious adverse events
- 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.
ECG = Electrocardiogram; SAE = Serious Adverse Event.

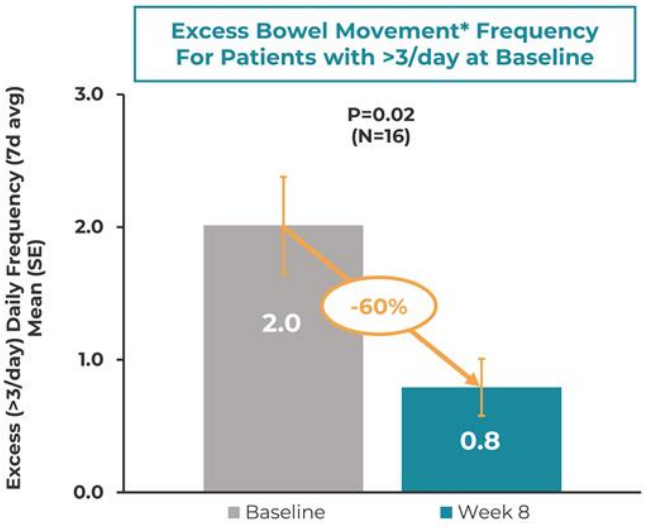
Most Frequent Treatment-Emergent Adverse Events Observed were Mild to Moderate

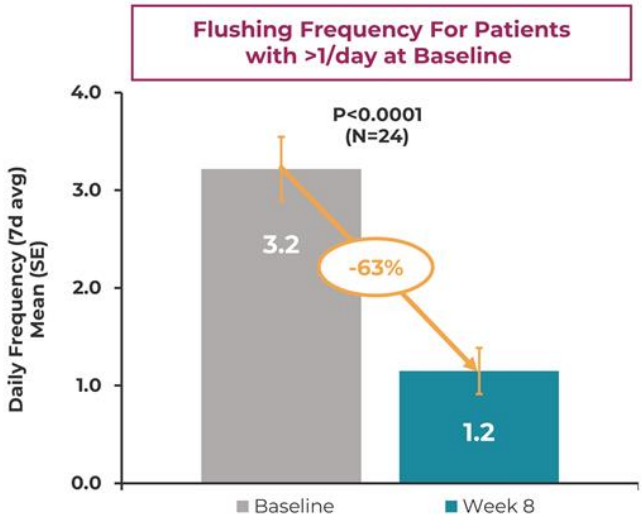
Treatment-Emergent Adverse Events, n (%)	Paltusotine N=36
Diarrhea	14 (38.9)
Abdominal Pain	7 (19.4)
Nausea	6 (16.7)
Headache	6 (16.7)
Flushing	5 (13.9)
Fatigue	4 (11.1)
Asthenia	3 (8.3)
ALT Elevation	2 (5.6)*
Vomiting	2 (5.6)
Hypertension	2 (5.6)
Myalgia	2 (5.6)
Pyrexia	2 (5.6)
Somnolence	2 (5.6)
Urinary tract infection	2 (5.6)

- Adverse event frequency was similar across both dose groups
- Most adverse events were mild to moderate in severity and transient
- Safety profile consistent with symptoms of carcinoid syndrome and SRL treatment effects

*The two cases of ALT elevation were < 3X ULN and not associated with elevated bilirubin or alkaline phosphatase.

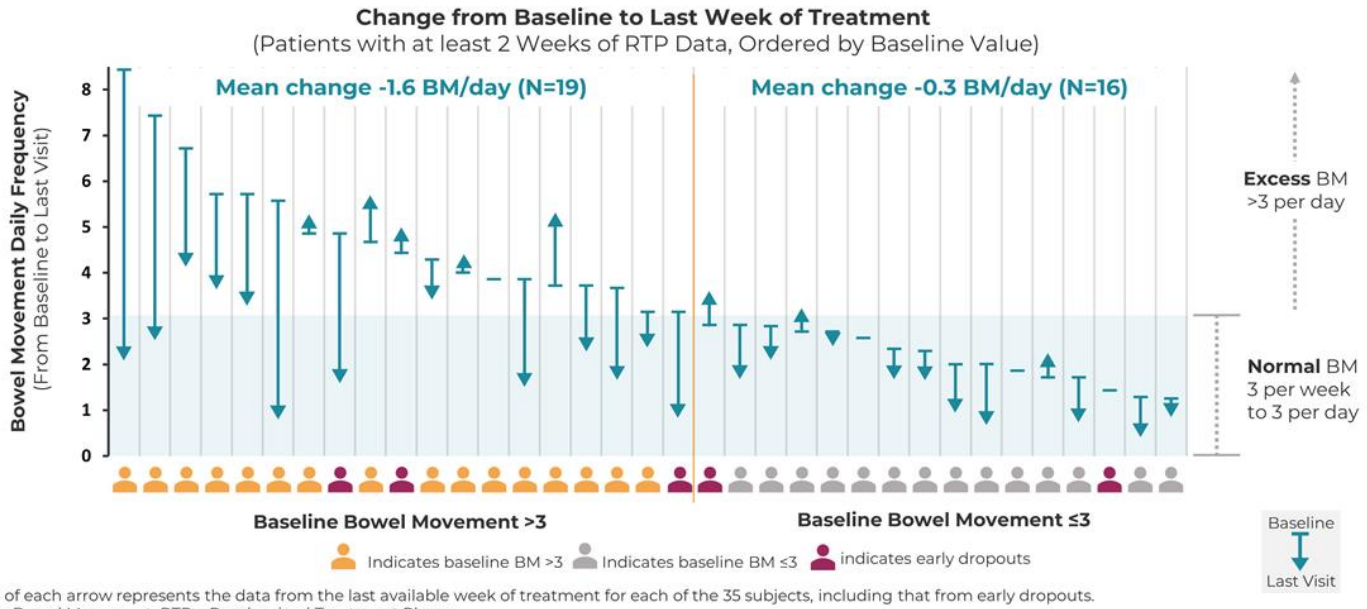
Paltusotine Reduced Frequency of Key Carcinoid Syndrome Symptoms: Excess BM and Flushing





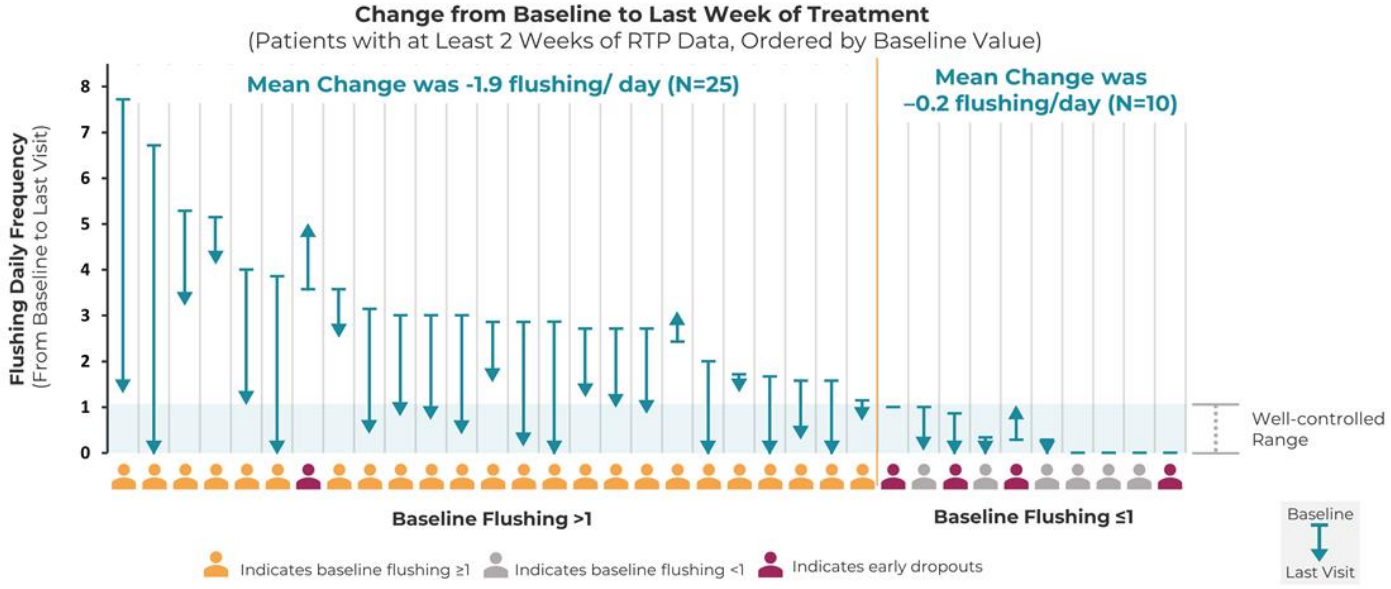
*Excess bowel movements (BM) were defined as daily bowel movements above the upper limit of normal (3 per day).

Paltusotine Showed Improvements in Subjects with Elevated Bowel Movement Frequency



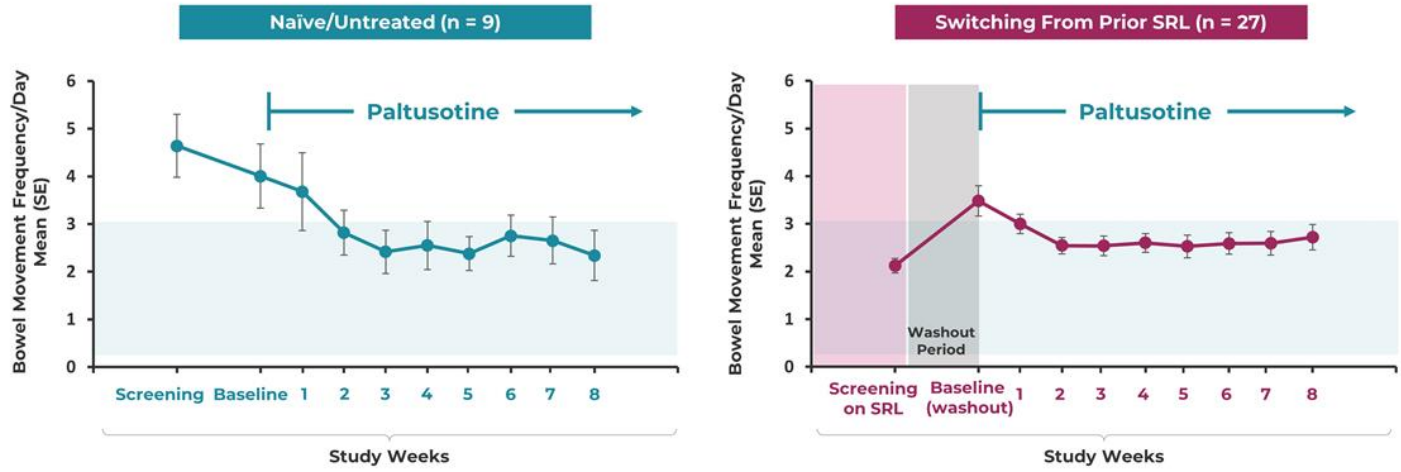
End of each arrow represents the data from the last available week of treatment for each of the 35 subjects, including that from early dropouts.
BM = Bowel Movement; RTP = Randomized Treatment Phase.

Paltusotine Showed Improvements in Flushing Frequency in Majority of Subjects



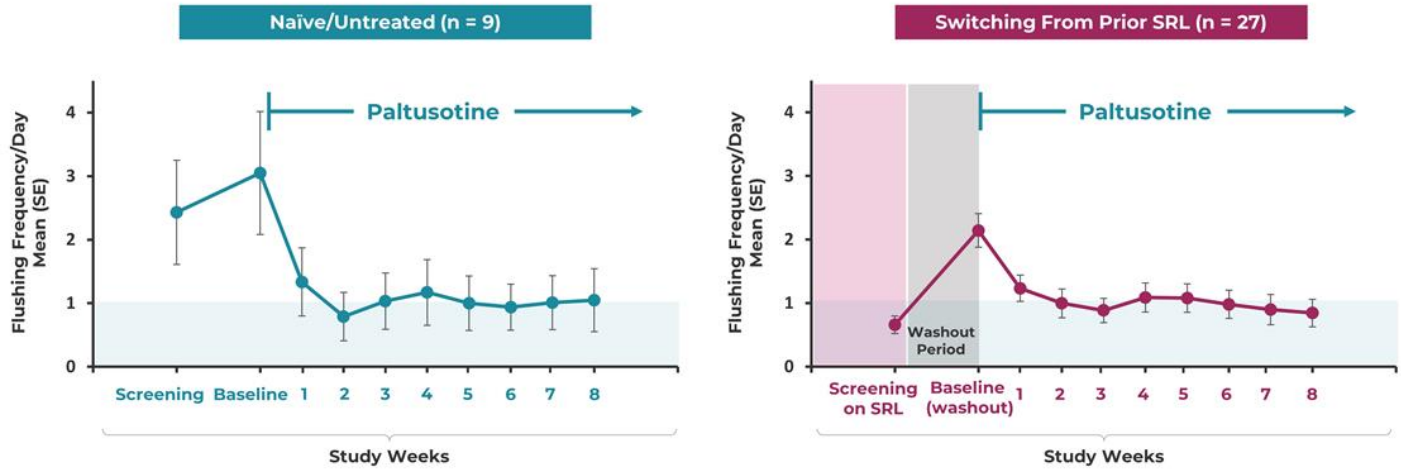
End of each arrow represents the data from the last available week of treatment for each of the 35 subjects, including that from early dropouts. RTP = Randomized Treatment Phase.

Rapid Improvements in Bowel Movement Frequency Were Observed Within 2 Weeks of Treatment and Were Sustained Through Week 8



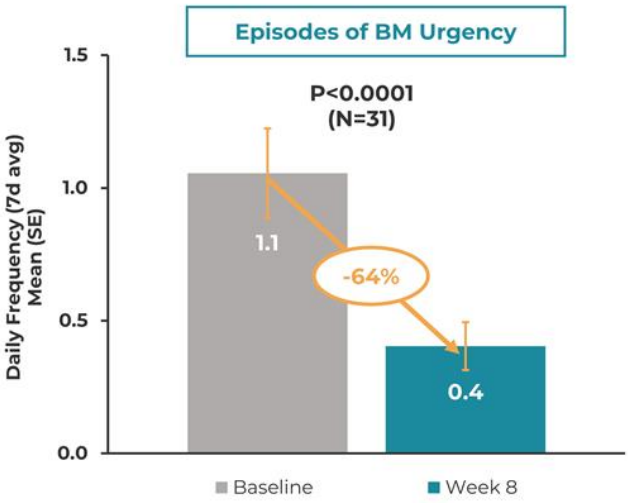
Frequency measure is based on the 14-day average during the screening period and 7-day average prior to baseline on all other timepoints.
SRL = somatostatin receptor ligand.

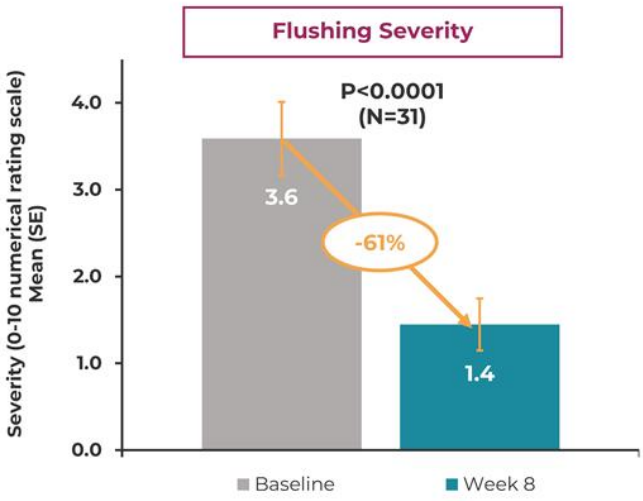
Rapid Improvements in Flushing Frequency Were Observed Within 2 Weeks of Treatment and Were Sustained Through Week 8



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.

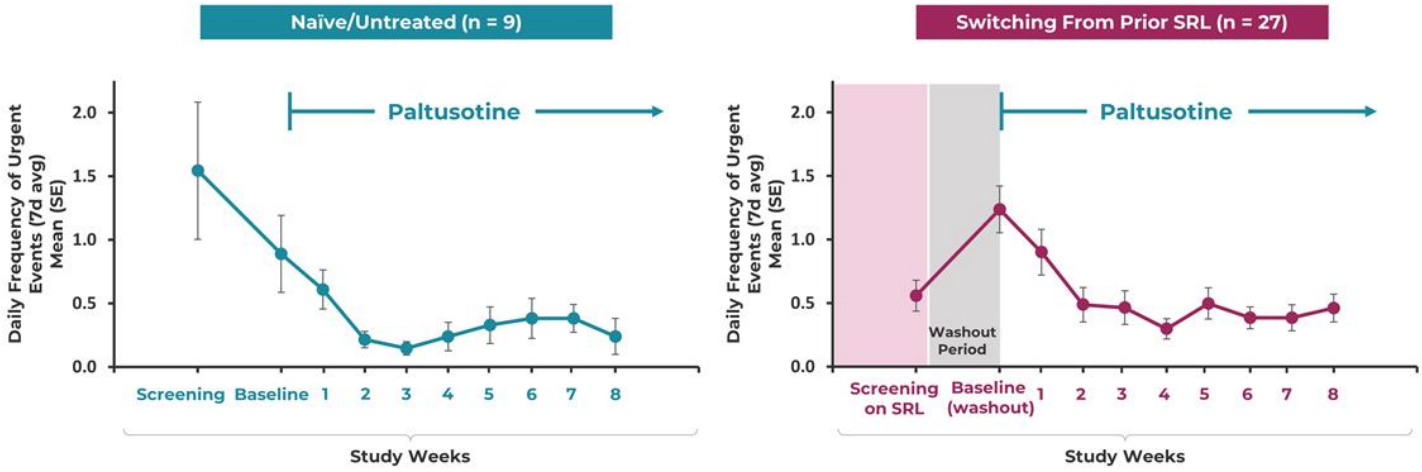
Paltusotine Also Reduced the Severity of Key Carcinoid Syndrome Symptoms





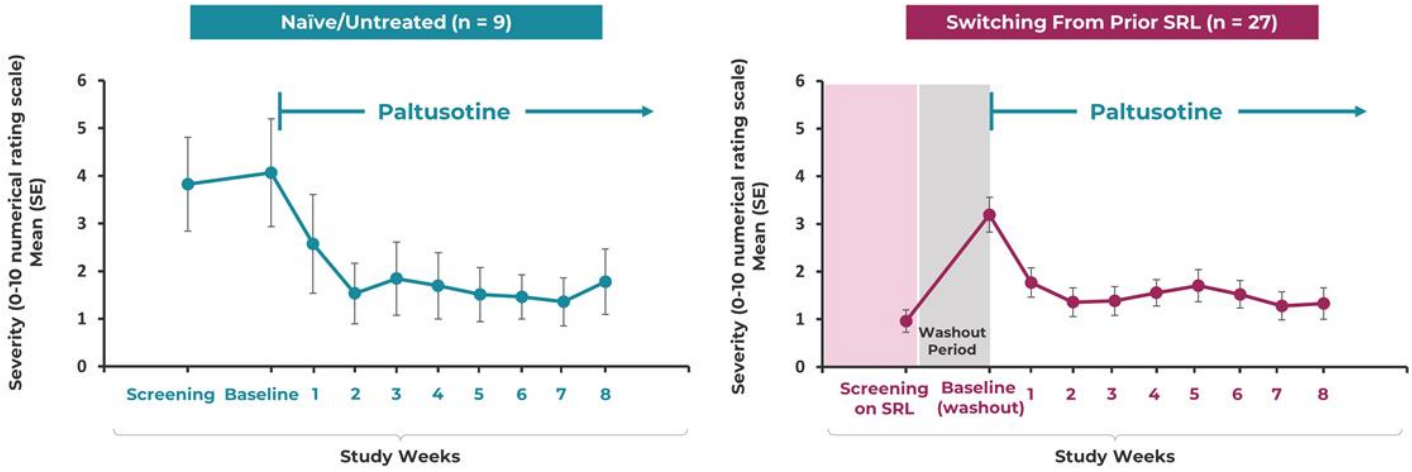
N=31 subjects with data through the Randomized Treatment Period; one subject who discontinued in the RTP dosed with paltusotine and had diary data through week 8 of the RTP; BM = bowel movement.

Rapid Improvements in Episodes of BM Urgency Were Observed Within 2 Weeks of Treatment and Were Sustained Through Week 8



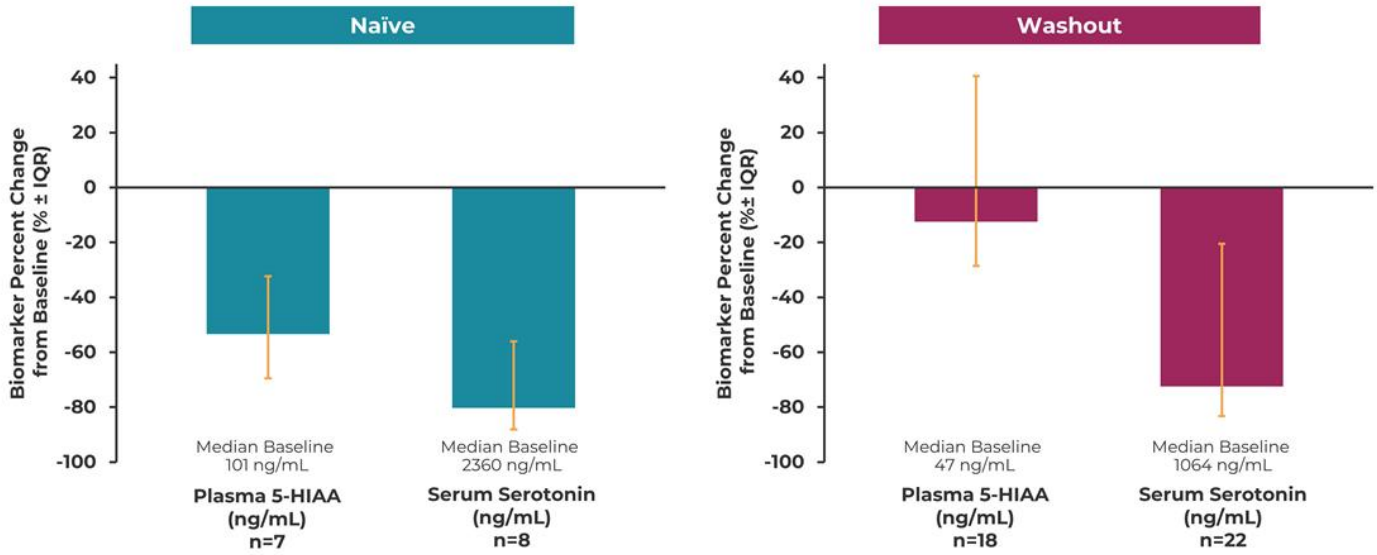
Frequency measure is based on the 14-day average during the screening period and 7-day average prior to baseline on all other timepoints.
BM = bowel movement; SRL = somatostatin receptor ligand.

Rapid Improvements in Flushing Severity Were Observed Within 2 Weeks of Treatment and Were Sustained Through Week 8



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 Suppressed Serotonin Levels, a Key Biomarker in Carcinoid Syndrome Patients



Baseline is last value prior to start of randomized treatment, i.e., Week 1, or Screening 1 for naïve subjects if Week 1 was missing; IQR = Interquartile range is the spread of the middle half of a data set; The upper limit of normal for Plasma 5-HIAA is 22 ng/mL. The upper limit of normal for Serum Serotonin is 541 ng/mL.

Once Daily Oral Paltusotine Showed Positive Results in Carcinoid Syndrome Patients

Summary: Phase 2 Results Support Proceeding to a Phase 3 Program

- Rapid and sustained reductions were observed in frequency and severity of bowel movements and flushing episodes with 40 mg and 80 mg
- Paltusotine was generally well-tolerated with no severe or serious treatment related adverse events
- Overall PK profile was consistent with prior studies
- Serotonin and 5HIAA levels provided additional evidence for activity of paltusotine in carcinoid syndrome

Next Steps: Engage with FDA and Prepare for Phase 3 Start

- Plan to discuss the results and align on a Phase 3 study design
- Begin preparations to enable the initiation of Phase 3 by the end of the year

Paltusotine is an investigational drug in clinical studies for the treatment of acromegaly and carcinoid syndrome.

Market Research Supports that Paltusotine's Emerging Profile can Address Unmet Needs for Carcinoid Syndrome

Oral Alternative

- HCPs note the **extensive training** required for nurses to correctly prepare and administer injectable SRLs and would welcome an **oral SRL with easier prep and administration**
- If SRLs are not administered properly, **patients may not receive the full dose,** missing the full benefit of the medication
- The **SRL injections can lead to significant injection site pain and granulomas**

*"Sometimes they don't thaw [the medication] long enough, they'll pinch the skin instead of flattening. And you get **injection granulomas** because the treatment wasn't delivered correctly, and the **patient doesn't get the maximum benefit of the treatment.**"*

- Med Onc, Academic

Symptom Control

- HCPs say **the level of symptom control demonstrated by paltusotine in phase 2 study was comparable** with their clinical experience with injectable SRLs
- Physicians appreciate that paltusotine **targeted both flushing and diarrhea** symptoms **without added safety concerns**

*"The **two main symptoms, the diarrhea and flushing, if that's getting better, that is a pretty good sign.** The flushing is the main one for me. There is not enough available therapy for that."*

- Med Onc, Community

Patient Preference

- HCPs predict they would offer paltusotine to all patients, and anticipate **most would prefer oral SRLs over injectables**
- Many patients are **injection averse,** or **live far away,** making it difficult to get to monthly appointments (especially elderly patients)

*"Patients who live far from the clinic, and **they want to come to the clinic less frequently**. Or if they said, 'I can't take this injection' or **'I don't want to get injections,'** we can consider [Paltusotine]."*

- Med Onc, Community

Source: *Primary qualitative market research conducted with US Oncologists*

Paltusotine is an investigational drug in clinical studies for the treatment of acromegaly and carcinoid syndrome.

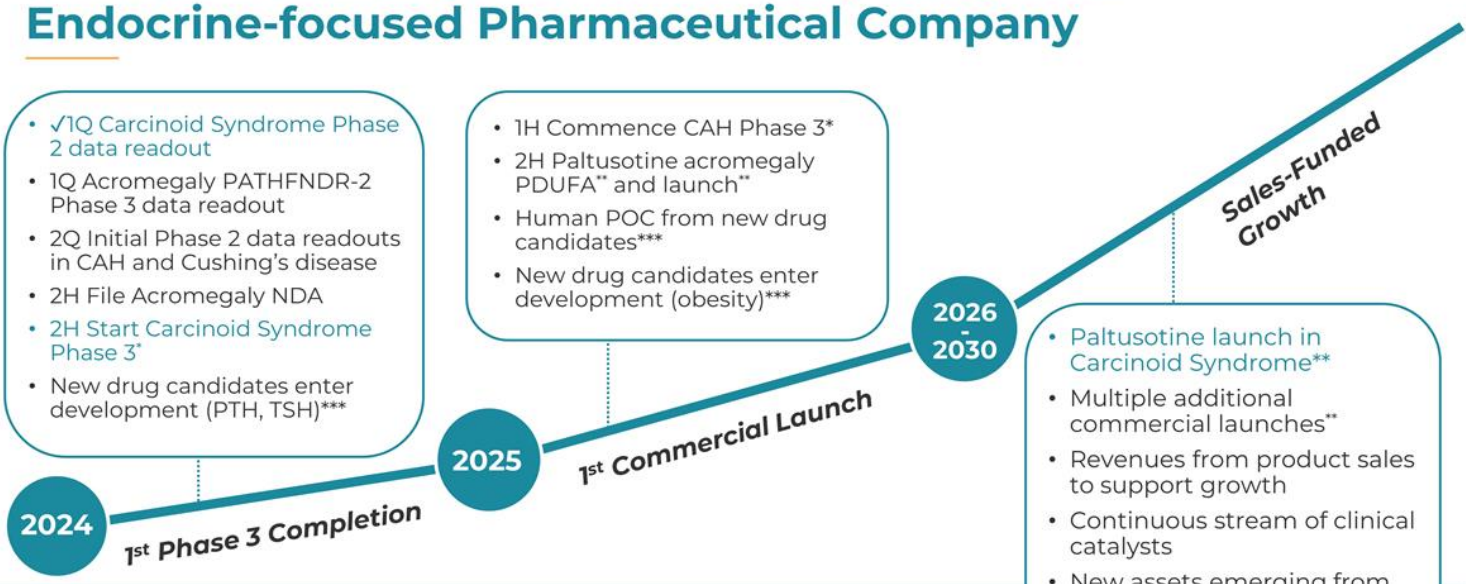
Strategy to Enable Paltusotine to Serve a Greater Number of Patients

Paltusotine Strategic Objectives:

- Build HCP Experience with Acromegaly
- Phase 3 Study Design Supporting Both Switching and Untreated Carcinoid Syndrome Patients
- Build HCP Experience in Carcinoid Syndrome

Paltusotine is an investigational drug in clinical studies for the treatment of acromegaly and carcinoid syndrome.

Crinetics is Building the Premier **Fully Integrated Endocrine-focused Pharmaceutical Company**



Strategic Approach to **Growing Long-term Value**

*Pending alignment with FDA **Pending NDA submission, acceptance and regulatory approval
***Pending identification, creation and clinical development of new drug candidates for additional diseases

CAH: congenital adrenal hyperplasia; PTH: parathyroid hormone; TSH: thyroid stimulating hormone; POC: proof of concept

Q&A

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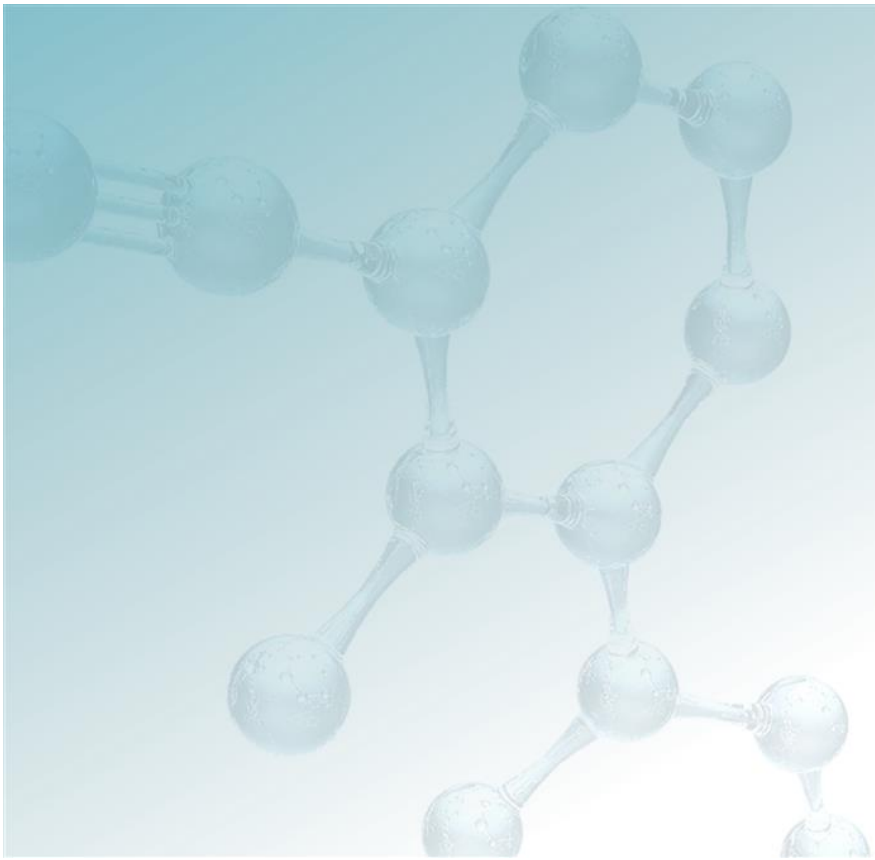
Founder and Chief Executive Officer

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

Alan Krasner, M.D.
Chief Endocrinologist

Jim Hassard
Chief Commercial Officer

Crinetics
Pharmaceuticals



Crinetics Pharmaceuticals

Thank You