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): October 26, 2020

Crinetics Pharmaceuticals, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-38583**	**26-3744114**
(State or Other Jurisdiction of Incorporation or Organization)	**(Commission File Number)**	**(I.R.S. Employer Identification Number)**

10222 Barnes Canyon Road, Bldg #2
San Diego, California 92121
(858) 450-6464
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

N/A
(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 obligations 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 (17 CFR § 230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR § 240.12b-2).

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.

The slides attached as Exhibit 99.1 to this Current Report contain certain additional information related to the clinical data results discussed in Item 8.01 below. Crinetics Pharmaceuticals, Inc. (the "Company" or "Crinetics") intends to present the slides during a conference call and live webcast with the investment community on October 26, 2020, at 8:00 a.m. EDT.

The information contained in this Item 7.01, including in Exhibit 99.1 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 October 26, 2020, the Company announced positive topline results from the Company's Phase 2 ACROBAT Edge and ACROBAT Evolve studies of paltusotine (formerly CRN00808), the Company's lead candidate for the treatment of acromegaly. The prespecified primary endpoint in Edge was achieved, showing that once daily oral paltusotine maintained insulin-like growth factor-1 ("IGF-1") levels at Week 13 in acromegaly patients who were switched from an injected somatostatin receptor ligand ("SRL") depot of either octreotide or lanreotide monotherapy [change in IGF-1 = -0.034 (-0.107, 0.107), median (IQR)]. There were 25 patients enrolled in this prespecified primary analysis population (Group 1). During the four-week washout period after the 13-week treatment period, Group 1 patients showed a meaningful (>20%) and prompt (within two weeks) rise in IGF-1 levels from baseline, which characterized the magnitude of therapeutic activity of oral paltusotine in acromegaly patients. Edge also enrolled an additional 22 patients into four different exploratory populations (Groups 2-5).

Paltusotine was generally well tolerated among the 60 ACROBAT participants (including both Edge and Evolve), which is consistent with prior clinical findings in healthy volunteers. There were no discontinuations due to drug-related adverse events, no safety signals seen in clinical laboratory analyses, no treatment-related serious adverse events ("SAEs"), and no patients required rescue treatments with standard acromegaly medications during treatment. The most common treatment-emergent adverse events (>10%) included: headache, arthralgia, fatigue, peripheral swelling, paresthesia and hyperhidrosis. The Company plans to meet with the U.S. Food and Drug Administration ("FDA") to share these results and finalize the protocol for its planned Phase 3 program, which remains on track to begin in the first half of 2021.

Findings from ACROBAT Edge

Edge enrolled a total of 47 patients with confirmed diagnoses of acromegaly at 45 clinical sites in 13 countries. The prespecified primary analysis population (Group 1) included 25 patients who were previously treated with SRL monotherapy (octreotide or lanreotide) and had a baseline IGF-1 of > 1.0x the upper limit of normal ("ULN") and ≤ 2.5x ULN. Groups 2-5 (n=22) were predefined as exploratory populations and are described in the table below.

Group	Pre-Trial Therapy	Baseline IGF-1 (x ULN)	Total Enrolled
1	SRL monotherapy (octreotide or lanreotide)	> 1.0 ≤ 2.5	25
2	SRL + cabergoline	> 1.0 ≤ 2.5	10
3	SRL + cabergoline	≤ 1.0	5
4	Pasireotide	≤ 1.0	4
5	SRL + Pegvisomant	≤ 1.0	3

Three IGF-1 measurements were taken during a four- to six-week screening period, the average of which was defined as the "baseline" value. Following screening and four weeks after the last depot injection, each patient was treated for 13 weeks with paltusotine. All patients were started on 10 mg of paltusotine and then titrated up to 20, 30 and 40 mg at Weeks 4, 7 and 10, respectively, if the study drug was well tolerated and if the previous IGF-1 levels were > 0.9 x ULN at Weeks 2 and 5, and if IGF-1 levels were > 1.0 x ULN at Week 8. At the end of 13 weeks, 18 of the Group 1 patients who completed the dosing period were on 40 mg, two were on 30 mg, two were on 20 mg, and one was on 10 mg.

The primary endpoint in the primary analysis population prespecified in the Statistical Analysis Plan (Group 1) showed that at the end of the 13 week treatment period, the median IGF-1 was 1.343, compared to the median IGF-1 of 1.335 at baseline (p>0.6 for change from baseline), indicating there was no statistically significant difference in IGF-1 control after patients had switched from pre-trial

injected therapy to oral paltusotine monotherapy. Furthermore, the statistically significant rise in IGF-1 levels during the four-week washout period ($p<0.0001$) compared to the end of treatment time point at Week 13, shows the magnitude of the therapeutic activity of paltusotine in these patients and is shown in the table below. At every timepoint throughout the 13-week dose titration treatment period, median IGF-1 levels were maintained similar to baseline levels.

			Withdrawal Period	
Parameter (units)	**Baseline**	**End of Treatment**	**2 Weeks**	**4 Weeks**
Number of patients	n=25	n=25	n=23	n=22
IGF-1 (xULN)				
Mean (95% CI)	1.337 (1.217, 1.456)	1.327 (1.205, 1.449)	1.983 (1.729, 2.237)	2.031 (1.785, 2.277)
Median (IQR)	1.335 (1.078, 1.471)	1.343 (1.169, 1.448)	1.795 (1.512, 2.382)	2.053 (1.689, 2.511)
Change in IGF-1 (xULN)	**Change from Baseline**		**Change from End of Treatment**	
Mean (95%CI)	-0.010 (-0.093, 0.074)		0.614 (0.394, 0.834)	0.676 (0.469, 0.882)
Median (IQR)	-0.034 (-0.107, 0.107)		0.477 (0.181, 1.068)	0.552 (0.408, 1.024)
p-value^	>0.6		<0.0001	<0.0001

Switching patients in the exploratory Edge populations in Groups 2 and 3 (n=15), who were treated with a combination of cabergoline and an SRL at baseline, to paltusotine monotherapy showed that cabergoline contributed to IGF-1 lowering. However, after withdrawal of paltusotine therapy in the washout period, it appeared that the magnitude of therapeutic activity of paltusotine was greater than that of cabergoline.

Although the small sample sizes in Group 4 (n=4) and Group 5 (n=3) were too low to assess paltusotine's activity in the smaller patient populations represented by these groups, these data will contribute to the broader paltusotine safety database. Patients represented by Groups 2-5 will not be included in the Phase 3 program but are included in the safety analysis.

Findings from ACROBAT Evolve

Evolve was designed as a double-blind, placebo-controlled, randomized withdrawal study conducted at 44 clinical sites in 13 countries. As previously announced, the enrollment was terminated early, enabling data to be available for the end of Phase 2 regulatory interactions on the Edge study. The thirteen patients enrolled in the study with confirmed diagnoses of acromegaly whose levels of IGF-1 were biochemically controlled (<1.0x ULN) on standard-of-care SRL depot injections and completed participation in the study, were included in the safety analysis and provided additional response data at the low end of the dose range.

All patients were switched to 10 mg of paltusotine once daily, four weeks after receiving the last injection of depot SRL during the screening period. At predetermined timepoints, IGF levels and tolerability were assessed and doses were increased in 10 mg increments as dictated by the protocol up to a maximum of 30 mg. After this dose titration phase, participants were randomized to receive paltusotine or placebo for four additional weeks if their week eight IGF-1 was $\leq$ 1.0x ULN. Prior to randomization, only three patients advanced to the 30 mg dose, six were on 20 mg and three on 10 mg (one patient discontinued prior to randomization). Seven patients met the criteria for randomization (n=3 paltusotine and n=4 placebo); the other five patients remained on paltusotine. As in Edge, paltusotine was withdrawn for four weeks following the conclusion of the 13-week treatment period.

The reduced sample size did not allow for meaningful statistical comparisons between groups in the randomized withdrawal period. Data from these patients on lower doses of paltusotine were included in the post-hoc dose response analyses in combination with data from patients in the Edge study, most of whom received the higher doses.

Dose Response Analyses

Post-hoc analyses of patients in Edge (Group 1; n=25) and Evolve (n=13) were conducted in order to explore the effect of paltusotine dose on IGF-1 suppression. These analyses provided evidence of a dose response across the dose range of 10 to 40 mg. Dose-dependent results were observed when evaluating the effect on IGF-1 levels from: 1) switching from injectable SRL to paltusotine, and 2) withdrawing paltusotine during the washout phase. These data and ongoing exposure response analysis will inform the selection of doses to be included the Phase 3 program that will be finalized after consultation with the FDA.

Patient Reported Outcome Measures

Several different patient-reported outcome instruments were evaluated in the ACROBAT studies. Analyses of the performance of these tools are still being conducted, and Crinetics plans to present these findings at an upcoming medical conference.

Forward-Looking Statements

Crinetics cautions you that statements contained in this Current Report on Form 8-K 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 potential benefits of paltusotine for acromegaly patients; the potential to initiate a Phase 3 program of paltusotine in acromegaly based on the Edge and Evolve topline results and the timing thereof; and Crinetics' plans to meet with the FDA to finalize the protocol for a Phase 3 program for paltusotine. The inclusion of forward-looking statements should not be regarded as a representation by Crinetics that any of its plans will be achieved. Actual results may differ from those set forth in this Current Report on Form 8-K due to the risks and uncertainties inherent in Crinetics' business, including, without limitation: topline data that Crinetics reports is based on a preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the clinical trials and such topline data may not accurately reflect the complete results of a clinical trial, and the FDA and other regulatory authorities may not agree with Crinetics' interpretation of such results; advancement of paltusotine into a Phase 3 program is dependent on and subject to the receipt of further feedback from the FDA; the COVID-19 pandemic may disrupt Crinetics' business and that of the third parties on which it depends, including delaying or otherwise disrupting its clinical trials and preclinical studies, manufacturing and supply chain, or impairing employee productivity; the Company's dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of Crinetics' clinical trials and nonclinical studies for paltusotine and its other product candidates; regulatory developments in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of the Company's product candidates that may limit their development, regulatory approval and/or commercialization; Crinetics may use its capital resources sooner than it expects; and other risks described under the heading "Risk Factors" in documents the company files from time to time with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Crinetics undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No	Description
99.1	Slide Presentation entitled "Topline Results from the ACROBAT Phase 2 Program in Acromegaly"
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: October 26, 2020

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

Exhibit 99.1

Crinetics Pharmaceuticals

TOPLINE RESULTS FROM THE ACROBAT PHASE 2 PROGRAM IN ACROMEGALY

October 26, 2020

Safe Harbor Statement

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation are forward-looking statements, including statements regarding: the potential benefits of paltusotine for acromegaly patients; the planned improvement of the paltusotine formulation and the timing thereof; the potential to initiate a Phase 3 program of paltusotine in acromegaly with our to-be-marketed formulation based on the Edge and Evolve results and the timing thereof; our plans to meet with the FDA and the timing of such meeting; the planned expansion of the paltusotine development program to include the treatment of carcinoid syndrome in patients with NETs and the expected timing thereof, including the initiation of a Phase 2 trial in these patients; the potential to initiate a Phase 1 trial of our lead ACTH antagonist and the timing thereof; and the potential to initiate a Phase 1 trial of CRN04777 and the timing thereof. In some cases, you can identify forward-looking statements by terms such as "may," "believe," "anticipate," "could," "should," "estimate," "expect," "intend," "plan," "project," "will," "forecast" and similar terms. These statements involve known and unknown risks, uncertainties 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 data that we report is based on a preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the clinical trials and such topline data may not accurately reflect the complete results of a clinical trial, and the FDA and other regulatory authorities may not agree with our interpretation of such results; advancement of paltusotine into a Phase 3 program and our lead ACTH antagonist and CRN04777 into Phase 1 trials are dependent on and subject to the receipt of further feedback from the FDA; we may not be able to obtain, maintain and enforce our patents and other intellectual property rights, and it may be prohibitively difficult or costly to protect such rights; the COVID-19 pandemic may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our clinical trials 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 trials and nonclinical studies for paltusotine and our other product candidates; regulatory developments 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; 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. 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 and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight 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.

Summary of ACROBAT Phase 2 Results

- *Primary endpoint achieved in Edge:* Once daily oral paltusotine maintained insulin-like growth factor-1 (IGF-1) levels at week 13 after switching from injected somatostatin receptor ligand (SRL) depots of octreotide or lanreotide [ΔIGF-1 =-0.034 (-0.107, 0.107), median (IQR[1])]
- Both IGF-1 and growth hormone (GH) levels promptly rose after withdrawing paltusotine which characterized the magnitude of therapeutic activity of oral paltusotine
- Paltusotine contributed to IGF-1 lowering in patients previously treated with injected SRLs + oral cabergoline combination therapy
- Post-hoc analysis of patients from both Edge (Group 1) and Evolve[2] provided evidence of a dose response with higher doses being more effective
- Paltusotine was well tolerated

[1]Interquartile Range: 25th , 75th percentile
[2]Enrollment in ACROBAT Evolve was discontinued in April 2020. Previously enrolled patients continued in the study. Data from the Evolve patients (N=13) are included safety and dose-response analysis.

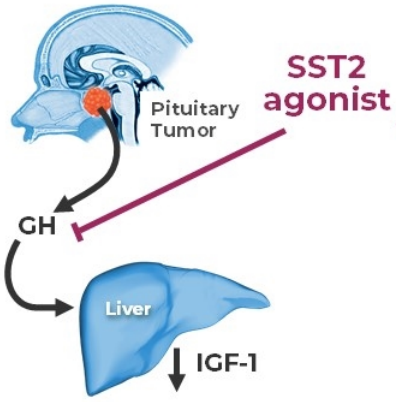
Acromegaly and NETS are Currently Treated with Injected Somatostatin Receptor Ligand (SRL) Depots

Acromegaly

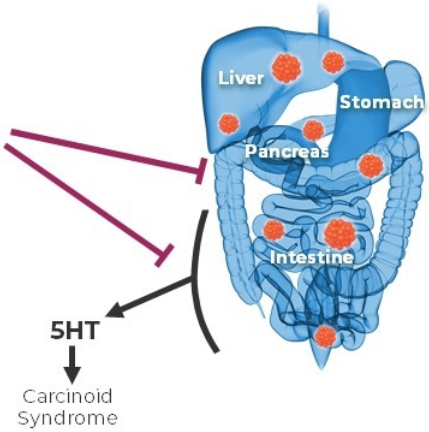
- Benign pituitary tumor
- Secretes excess growth hormone (GH)
- Excess GH causes excess secretion of insulin-like growth factor-1 (IGF-1)

Results in:

1. Bone and cartilage overgrowth
2. Organ enlargement
3. Changes in glucose and lipid metabolism
4. Abnormal growth of hands and feet
5. Alteration of facial features



SST2 agonist



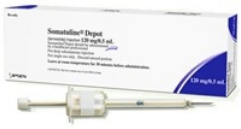
Neuroendocrine Tumors (NETs)

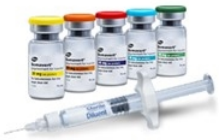
- NETs arise from aberrant enteroendocrine cells
- In ~10% of cases, tumors are associated with excess secretion of serotonin and other hormones resulting in carcinoid syndrome
- Patients with grade 1 and 2 NETs and distant metastases have a 5-year survival ranging from 30-70%

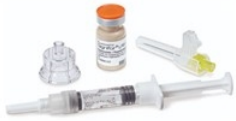
Prevalence: >25,000 in the U.S.

Prevalence: ~171,000 in the U.S.

~$3.1B (2019) Market, Despite Limitations of Injectables



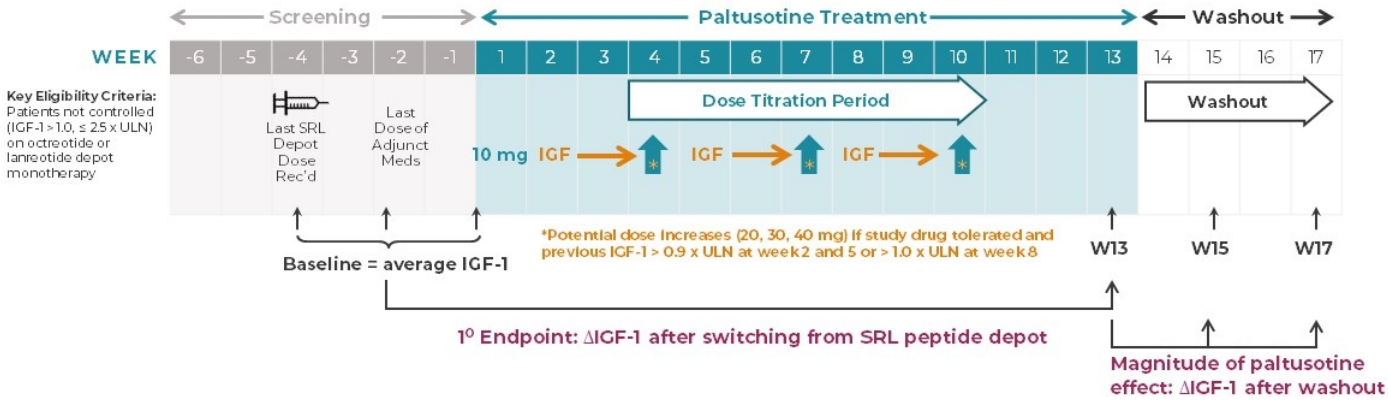




Sandostatin (octreotide)	Somatuline (lanreotide)	Somavert (pegvisomant)	Signifor (pasireotide)
NOVARTIS $1.6B	IPSEN $1.2B	Pfizer $264M	RECORDATI $75M
Monthly intramuscular 5-mL vial; 1½" 19-gauge needle	Monthly deep subcutaneous .2-.5ml; 18-gauge needle	Daily injections 1 ml; 28 – 31-gauge needle not supplied	Monthly intramuscular 1 ml; 20-gauge needle
Painful injections. Injection site reactions **Inconvenient monthly visits** to physician's office interrupts normal life **Limited Efficacy** as many patients experience return of symptoms near end of month	**Painful injections.** Injection site reactions **Inconvenient monthly visits** to physician's office interrupts normal life **Limited Efficacy** as many patients experience return of symptoms near end of month	Patients buy a second refrigerator for storage. Travel is difficult.	Impaired glucose control and risk of diabetes.
Approval date: 1988, 1998(LAR)	**Approval date:** 2007	**Approval date:** 2003	**Approval date:** 2014

ACROBAT Edge Study Design

A global clinical trial conducted at 45 clinical sites in 13 countries



Primary Endpoint: Change in IGF-1 at Week 13 vs. baseline (average of three IGF-1 screening values)
Primary Hypothesis was: No change in the median IGF-1 at Week 13 versus baseline
Primary Analysis Population: Group 1 patients (those previously on octreotide or lanreotide depot monotherapy)

ACROBAT Edge Patient Groups

Group	Pre-Trial Therapy	Baseline IGF-1 (x ULN)	Total Enrolled
1	SRL monotherapy (octreotide or lanreotide)	> 1.0 ≤ 2.5	25
2	SRL + cabergoline	> 1.0 ≤ 2.5	10
3	SRL + cabergoline	≤ 1.0	5
4	Pasireotide	≤ 1.0	4
5	SRL + Pegvisomant	≤ 1.0	3

Prespecified Primary Analysis Population

Exploratory Populations

Prespecified Primary Analysis Population (Group 1)[1]

- Patients treated with SRL (octreotide or lanreotide) with elevated IGF-1 at baseline—representing the majority of patients in clinical practice
- The primary hypothesis was that the group would show no change in the median IGF-1 at Week 13 versus baseline

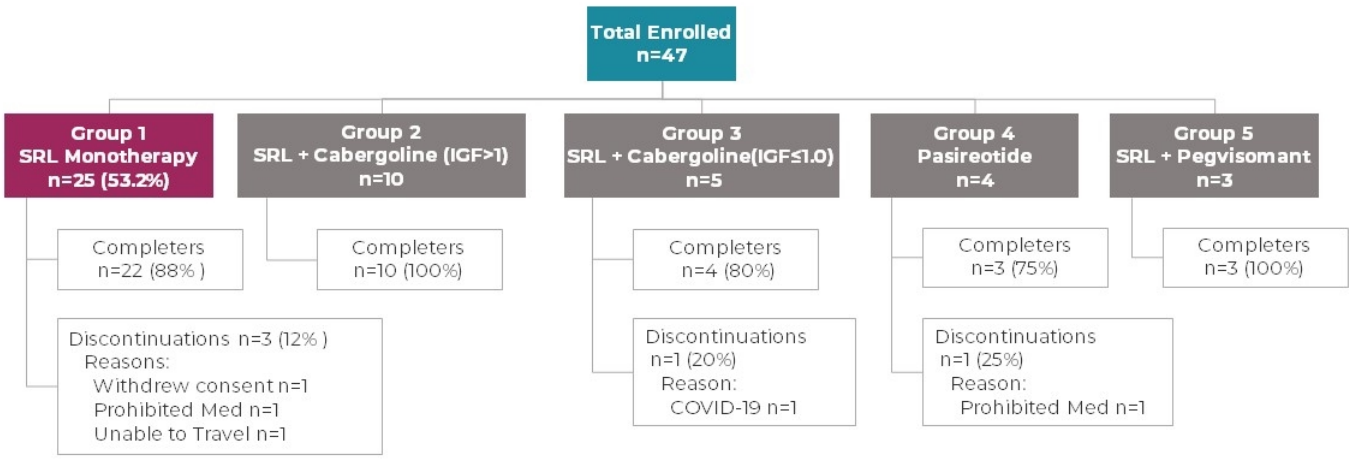
Exploratory populations (Groups 2-5)

The study also evaluated whether paltusotine can contribute to the care of patients treated with more intensive treatment regimens

[1]Prespecified in Edge Statistical Analysis Plan

ACROBAT Edge Patient Disposition

89% of patients completed the study

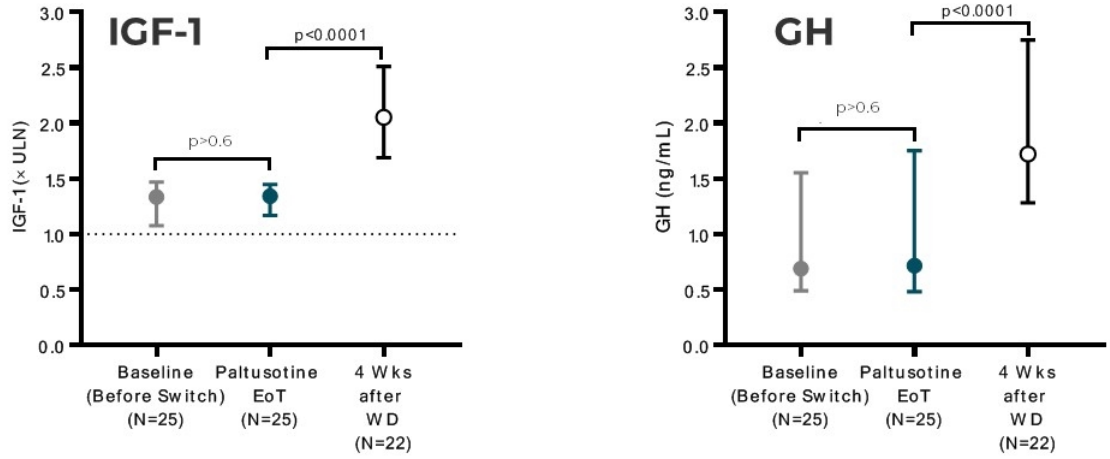


ACROBAT Edge Patient Characteristics

	Group 1 (N=25)	Group 2 (N=10)	Group 3 (N=5)	Group 4 (N=4)	Group 5 (N=3)	Total (N=47)
Demographics						
Median Age, years (Min, Max)	52 (31, 71)	53 (31, 70)	51 (43, 69)	56 (46, 67)	38 (35, 66)	51 (31, 71)
Median Weight, kg (Min, Max)	91 (61, 155)	85 (56, 136)	87 (57, 91)	107 (73, 120)	78 (59, 82)	87 (56, 155)
Sex						
Female	11 (44%)	7 (70%)	3 (60%)	3 (75%)	3 (100%)	27 (57%)
Male	14 (56%)	3 (30%)	2 (40%)	1 (25%)	0	20 (43%)
Prior Therapies						
Lanreotide depot Dose, mg/mo	n=12	n=3	n=2	NA	n=2	n=19
# patients on 60/90/120 mg/mo	1 / 4 / 7	0 / 0 / 3	0 / 0 / 2	--	1 / 1 / 0	2 / 5 / 12
Octreotide LAR Dose, mg/mo	n=13	n=7	n=3	NA	n=1	n=24
# patients on 10/20/30/40 mg/mo	1 / 0 / 9 / 3	0 / 0 / 7 / 0	0 / 1 / 1 / 1	--	0 / 0 / 0 / 1	1 / 1 / 17 / 5
Pasireotide dose, mg/mo	NA	NA	NA	n=4	NA	n=4
# patients on 40/60 mg/mo	--	--	--	2 / 2	--	2 / 2
Cabergoline dose, mg/week	NA	n=10	n=5	NA	NA	n=15
Median (Min, Max)	--	2.3 (0.5, 3.5)	1.5 (0.5, 2.0)	--	--	2 (0.5, 3.5)
Pegvisomant dose, mg/week	NA	NA	NA	NA	n=3	n=3
Median (Min, Max)	--	--	--	--	60 (20, 70)	60 (20, 70)

Paltusotine Maintained IGF-1 and GH Levels After Switching From Injected SRL Peptide Depots

Hormone levels observed in primary analysis population (Group 1)



Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile). EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF). Wks after WD is defined as Week 17 or result at least 22 days after last dose.
Note: p-values are based on non-parametric Wilcoxon Sign Rank test of whether the median change is different from zero.

Paltusotine Maintained IGF-1 Levels After Switching From Injected SRL Peptide Depots

Conclusions

1. IGF-1 levels after 13 weeks of paltusotine treatment did not significantly change from baseline in patients previously treated with injected SRL depots (Group 1)
2. Rise in IGF-1 after withdrawal (within 2 weeks) which characterized the magnitude of therapeutic activity for oral paltusotine

Parameter (units)	Baseline	End of Treatment	Withdrawal Period	
			2 Weeks	4 Weeks
Number of patients	n=25	n=25	n=23	n=22
IGF-1 (xULN)				
Mean (95% CI)	1.337 (1.217, 1.456)	1.327 (1.205, 1.449)	1.983 (1.729, 2.237)	2.031 (1.785, 2.277)
Median (IQR)	1.335 (1.078, 1.471)	1.343 (1.169, 1.448)	1.795 (1.512, 2.382)	2.053 (1.689, 2.511)
Change in IGF-1 (xULN)*		Change from Baseline	Change from End of Treatment	
Mean (95%CI)		-0.010 (-0.093, 0.074)	0.614 (0.394, 0.834)	0.676 (0.469, 0.882)
Median (IQR)		-0.034 (-0.107, 0.107)	0.477 (0.181, 1.068)	0.552 (0.408, 1.024)
p-value^		>0.6	<0.0001	<0.0001

^ p-values based on non-parametric Wilcoxon Signed Rank test of whether the median change is different from zero.
*Calculated as mean and median of individual changes in IGF-1
IQR: Interquartile Range: 25th , 75th percentile

Paltusotine Maintained GH Levels After Switching From Injected SRL Peptide Depots

Conclusions

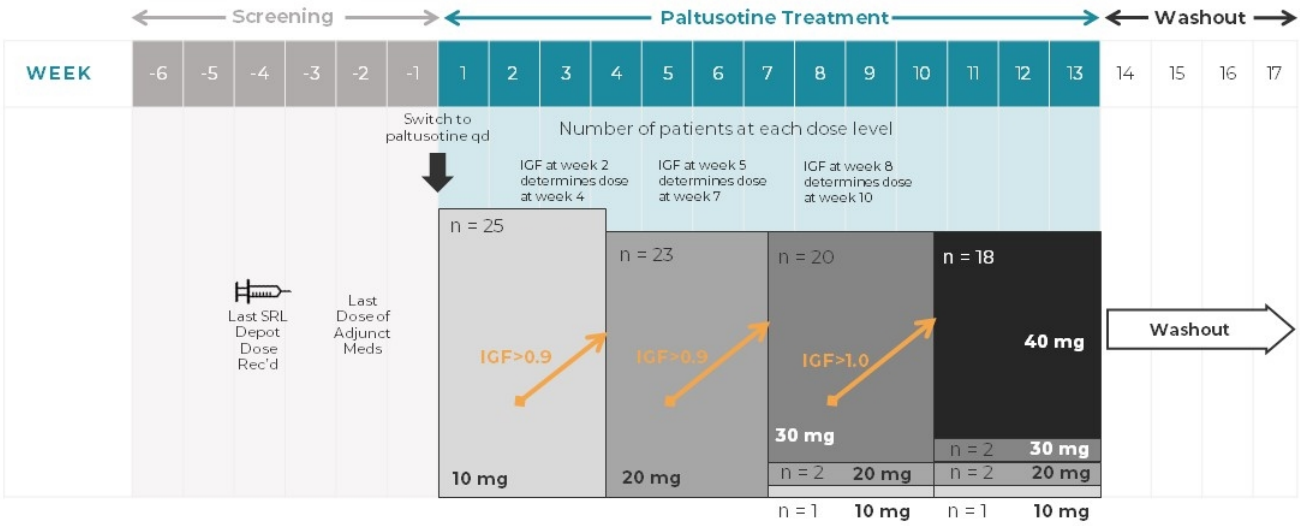
1. GH levels after 13 weeks of paltusotine treatment did not significantly change from baseline levels when patients were previously treated with injected SRL depots (Group 1)
2. Rise in GH after withdrawal characterized the magnitude of therapeutic activity of oral paltusotine

Parameter (units)	Baseline	End of Treatment	Withdrawal (4 Weeks)
Number of patients	n=25	n=25	n=22
GH (ng/mL)			
Mean (95% CI)	1.314 (0.813, 1.815)	1.213 (0.803, 1.624)	2.754 (1.646, 3.861)
Median (IQR)	0.691 (0.491, 1.555)	0.717 (0.483, 1.753)	1.722 (1.283, 2.749)
Change in GH (ng/mL)*		**Change from Baseline**	**Change from End of Treatment**
Mean (95%CI)		-0.100 (-0.486, 0.285)	1.511 (0.600, 2.422)
Median (IQR)		-0.049 (-0.289, 0.199)	0.721 (0.205, 1.915)
p-value^		>0.6	<0.0001

^ p-values based on non-parametric Wilcoxon Signed Rank test of whether the median change is different from zero.
*Calculated as mean and median of individual changes in integrated GH
IQR: Interquartile Range: 25th , 75th percentile

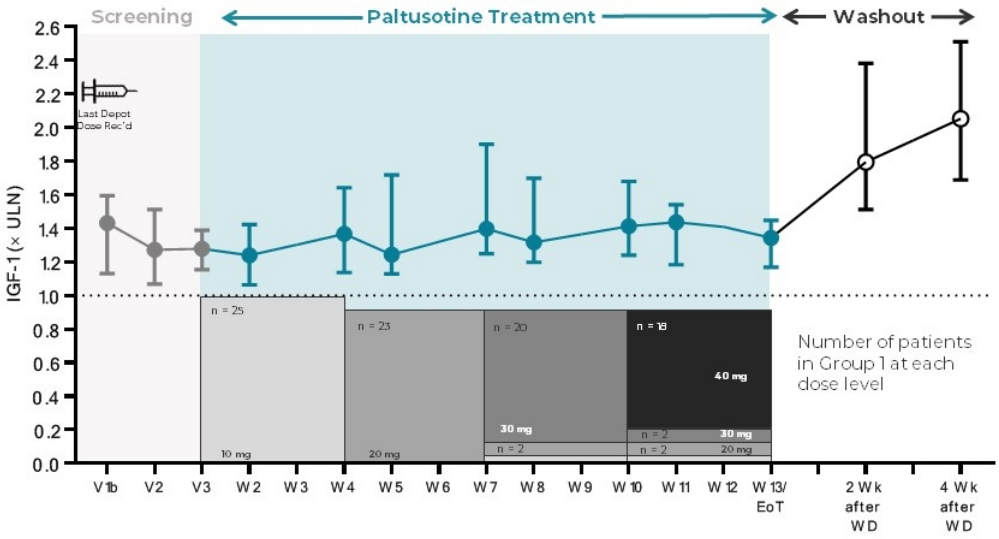
ACROBAT Edge Dose Titration

Most Group 1 patients up-titrated to the highest dose (40 mg)



Dose escalation determined by central reader based on tolerability and IGF-1 (Site staff, patient, sponsor blinded to dose)

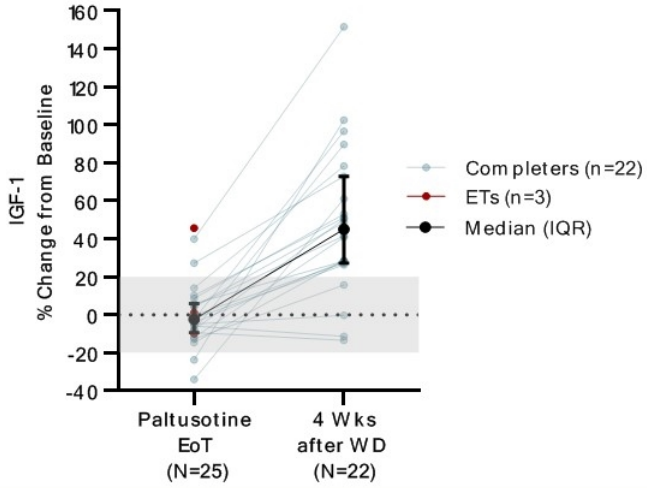
IGF-1 Levels Were Maintained After Switching to Paltusotine from Injected SRL Depots



Potential dose increases (20, 30, 40 mg) if study drug tolerated and previous IGF-1 > 0.9 x ULN at week 2 and 5 or > 1.0 x ULN at week 8
Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile) from Group 1 patients in Acrobat Edge; Screening Period could range from 4-6 weeks.
WD = Withdrawal, where 2 Wks after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks after WD is defined as Week 17 or result at least 22 days after last dose.

Switching to Once Daily Oral Paltusotine Maintained IGF-1 Levels in 87% of Group 1 Patients

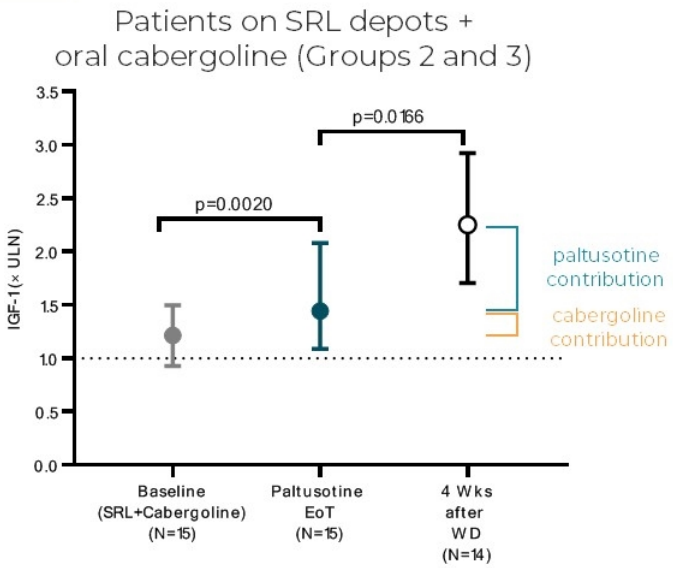
Individual patient percent change in IGF-1 at end of treatment vs. baseline and change at 4 weeks after withdrawal of paltusotine



- 20/23[1] patients (87%) who completed the dosing period achieved IGF-1 levels at EoT that were within 20% of baseline or lower
- 18/22[2] (82%) patients who completed the study showed a meaningful (>20%) rise from baseline in IGF-1 four weeks after withdrawal of paltusotine

[1]Two patients discontinued prior to the completion of the dosing period
[2]One patient discontinued during the washout period

Paltusotine Suppressed IGF-1 in Patients Previously Receiving Combination Therapy with Cabergoline

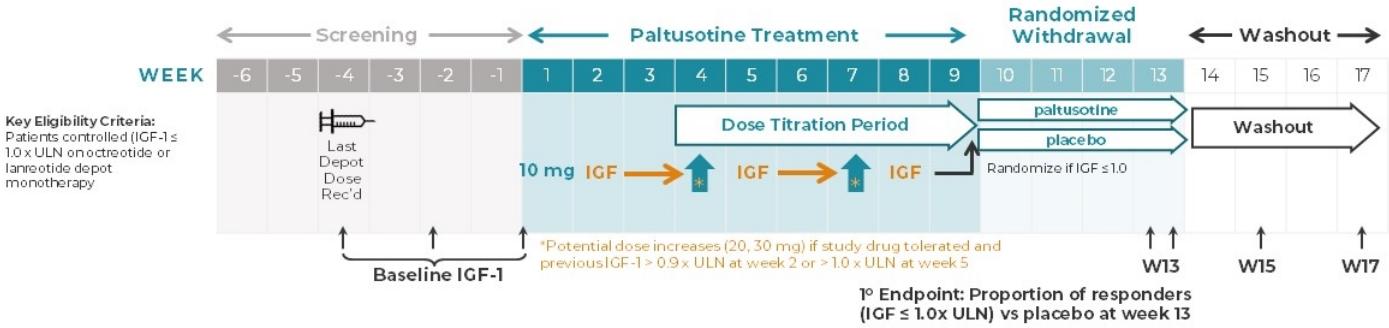


- Paltusotine contributed to IGF-1 lowering in patients previously treated with injected SRL peptide depots + oral cabergoline combination therapy
- Variable IGF-1 results were observed in Group 4 (n=4) and Group 5 (n=3)
- Patients represented by Groups 2-5 will not be included in Phase 3 program

Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile). EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF). WD = Withdrawal, where 2 Wks after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks after WD is defined as Week 17 or result at least 22 days after last dose. Note: p-values are based on non-parametric Wilcoxon Signed Rank test of whether the median change is different from zero.

ACROBAT Evolve Trial Design

Randomized, double-blind global clinical trial conducted at 44 clinical sites in 13 countries

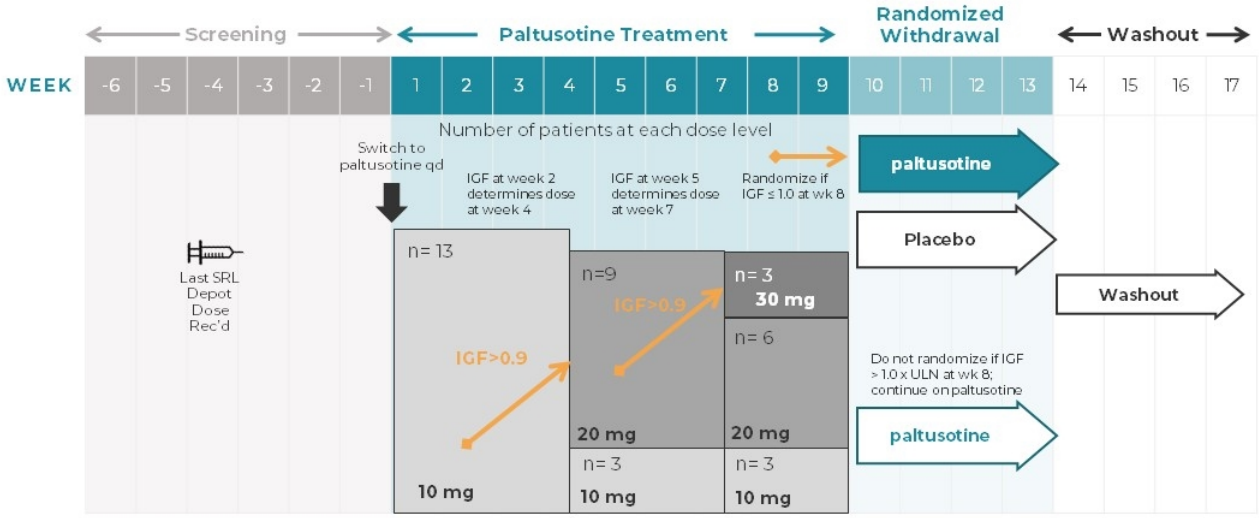


Evolve Enrollment discontinued April 2020

- Edge enrollment was complete at the time and interim results were positive
- Discontinuing Evolve enabled data to be available for end of Phase 2 regulatory interactions on Edge timeline
- 13 previously enrolled patients were allowed to complete participation in the study
- Reduced sample size did not allow for meaningful statistical comparisons between groups in the randomized withdrawal period
- Exposure response data were analyzed in conjunction with Edge Group 1 patients

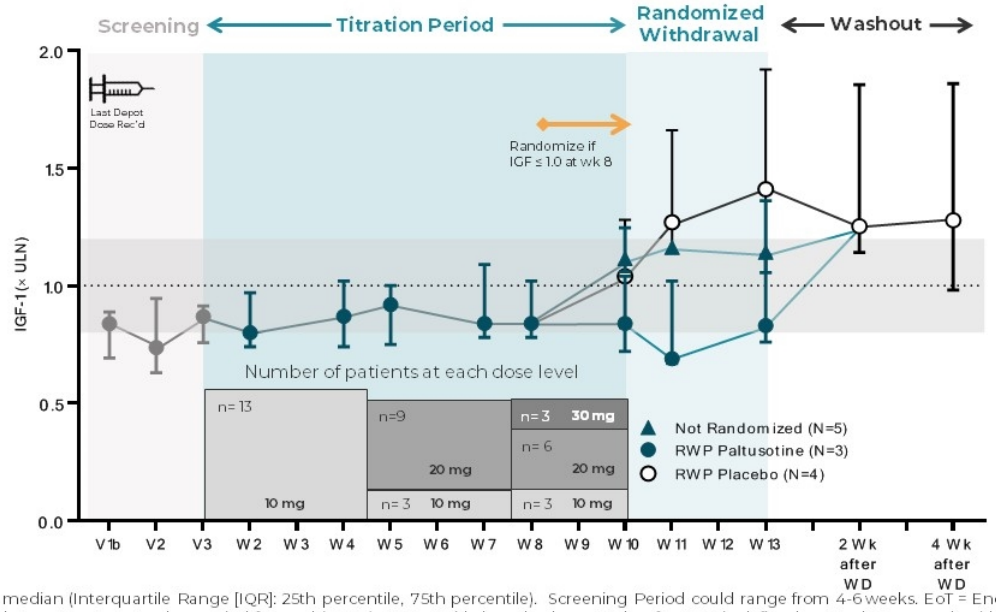
ACROBAT Evolve Dose Titration

Most patients did not reach the highest dose (30 mg)



Dose escalation determined by central reader based on tolerability and IGF-1 (site staff, patient, and sponsor blinded to dose)

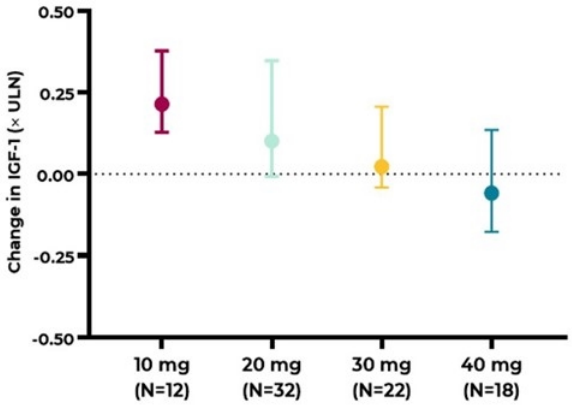
Evolve Results Provided Additional Response Data at the Low End of the Dose Range



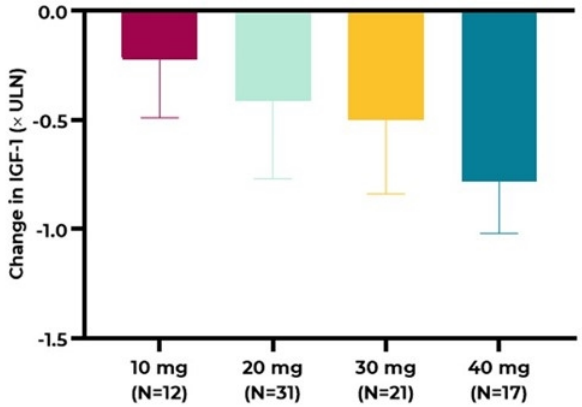
Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile). Screening Period could range from 4-6 weeks. EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF). WD = Withdrawal, where 2 Wks after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks after WD is defined as Week 17 or result at least 22 days after last dose.

Post-Hoc Analysis of Edge (Group 1) and Evolve Provide Evidence of a Dose Response

Results from Switching to Paltusotine: Change in IGF-1 from Baseline to Steady State at Indicated Dose



Magnitude of Paltusotine Activity: Change in IGF-1 from Steady State to 4 Weeks After Withdrawal



Steady state IGF-1 at the indicated dose: Patients were on the indicated dose for at least 12 days. Data prior to Week 7 were excluded because of insufficient washout of depot injection during this window. Data are shown from Week 7, Week 10, and Week 13.
Data presented are median +/- IQR. EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF).
WD = Withdrawal, where 2 Wks after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks after WD is defined as Week 17 or result at least 22 days after last dose. One subject is missing 4 Weeks after withdrawal observation.
Octreotide and lanreotide concentrations were measured 17 weeks after depot dose (W13 of the treatment period). Octreotide was completely washed out. Lanreotide concentrations were >75% reduced from baseline.

Paltusotine was Generally Well Tolerated Across Clinical Trials

Treatment Emergent Adverse Events ≥ 5%*	Edge/Evolve Patients (N=60) n (%)	Healthy volunteers (N=128^) n (%)
Common Acromegaly Symptoms		
Headache	19 (32%)	23 (18%)
Arthralgia	15 (25%)	0
Fatigue	13 (22%)	6 (5%)
Peripheral swelling	11 (18%)	0
Paraesthesia	10 (17%)	1 (1%)
Hyperhidrosis	10 (17%)	0
Sleep apnoea syndrome	4 (7%)	0
Common SRL Side Effects		
Diarrhoea	5 (8%)	27 (21%)
Abd pain/Abd pain upper	5 (8%)/2 (3%)	25 (20%)/6(5%)
Abdominal discomfort	4 (7%)	12 (9%)
Abdominal distension	3 (5%)	7 (6%)
Other		
Catheter site pain	0	9 (7%)
Nausea	0	9 (7%)
Back pain	5 (8%)	2 (2%)
Dyspepsia	3 (5%)	0
Urinary tract infection	3 (5%)	0

Acrobat Edge and Evolve

- No study discontinuations due to adverse events
- No patients required rescue treatments with standard acromegaly medications during treatment
- No safety signals seen with vital signs
- No safety signals seen in clinical laboratories, including no amylase/lipase elevations > 3x ULN, HbA1c, LFTs, ECGs
- No treatment related SAEs; 2 non-treatment related SAEs:
  1. Nephrolithiasis: lithotripsy for pre-existing kidney stone
  2. Headache: admission for diagnostic evaluation

*TEAEs include any AE that newly appears, increases in frequency, or worsens in severity following initiation of study drug through 28 days after last dose.
^ Treated with 1 or more doses of CRN00808.HCl as of 31 August 2020

Summary of ACROBAT Phase 2 Results

- *Primary endpoint achieved in Edge:* Once daily oral paltusotine maintained IGF-1 levels at week 13 after switching from injected somatostatin receptor ligand (SRL) depots of octreotide or lanreotide [ΔIGF-1 =-0.034 (-0.107, 0.107), median (IQR[1])]
- Both IGF-1 and GH levels promptly rose after withdrawing paltusotine which characterized the magnitude of therapeutic activity of oral paltusotine
- Paltusotine contributed to IGF-1 lowering in patients previously treated with injected SRLs + oral cabergoline combination therapy
- Post-hoc analysis of patients from both Edge (Group 1) and Evolve[2] provided evidence of a dose response with higher doses being more effective
- Paltusotine was well tolerated

[1]Interquartile Range: 25th , 75th percentile
[2]Enrollment in ACROBAT Evolve was discontinued in April 2020. Previously enrolled patients continued in the study. Data from the Evolve patients (N=13) are included safety and dose-response analysis.

Paltusotine Development Program Plans

- KOL webinar on November 20th to discuss acromegaly and ACROBAT results
- Update on improved formulation of paltusotine planned for use in Phase 3
- Additional analysis of ACROBAT data including exposure/response and patient reported outcome (PRO) instruments to be presented at future medical meetings
- End-of-phase 2 meeting with FDA in 1Q 2021
- Planned initiation of Phase 3 acromegaly program in 1H 2021 with to-be-marketed formulation
- Planned initiation of NETs trial in carcinoid syndrome in 2021

Paltusotine is Protected by a Strong IP Portfolio

Multiple U.S. patents granted; national stage applications filed in 2017

Additional intellectual property protection

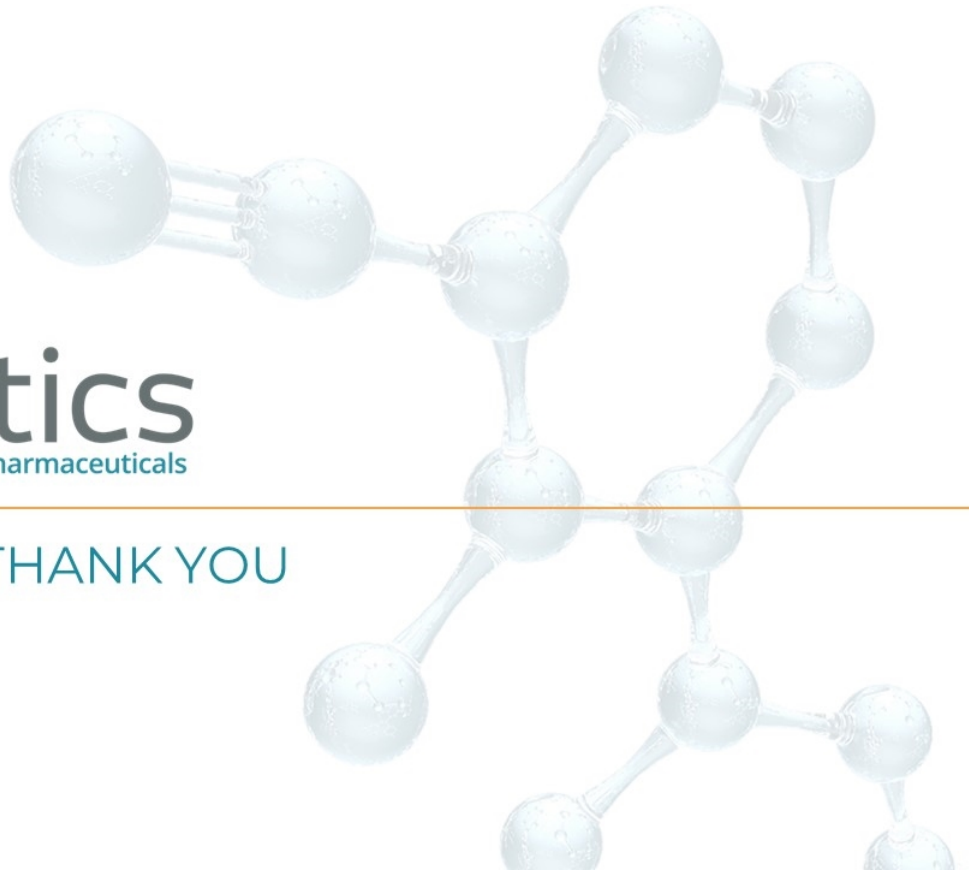
- Crinetics holds U.S. composition of matter patents for 3 additional classes of nonpeptide SST2 agonists
- Paltusotine is eligible for 7 years of market exclusivity upon approval (independent of patents)

Pipeline: Rare Disease Franchise in Endocrinology

PROGRAM	DISCOVERY	PRECLIN	PHASE 1	PHASE 2	PHASE 3	ANTICIPATED NEXT MILESTONE
Paltusotine Acromegaly						End-of-Phase 2 meeting with FDA 1Q2021 Initiate Phase 3 acromegaly 1H 2021
Neuroendocrine Tumors (NETs)						Initiate Phase 2 in 2021
Oral ACTH Antagonist Cushing's Disease, Congenital Adrenal Hyperplasia (CAH)						Initiate Phase 1 late 2020/early 2021
CRN04777 Congenital Hyperinsulinism (CHI)						Initiate Phase 1 early 2021

All product candidates discovered and developed internally. Global rights retained and no licensing obligations.


Crinetics
Pharmaceuticals



Crinetics
Pharmaceuticals

THANK YOU