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.

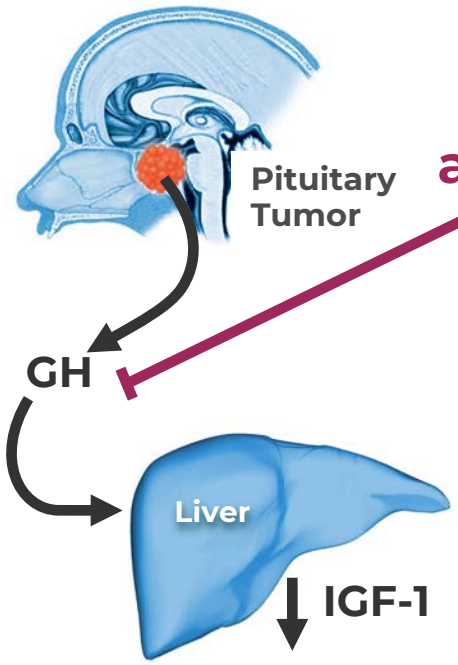
Acromegaly and NETS are Currently Treated with Injected Somatostatin Receptor Ligand (SRL) Depots

Acromegaly

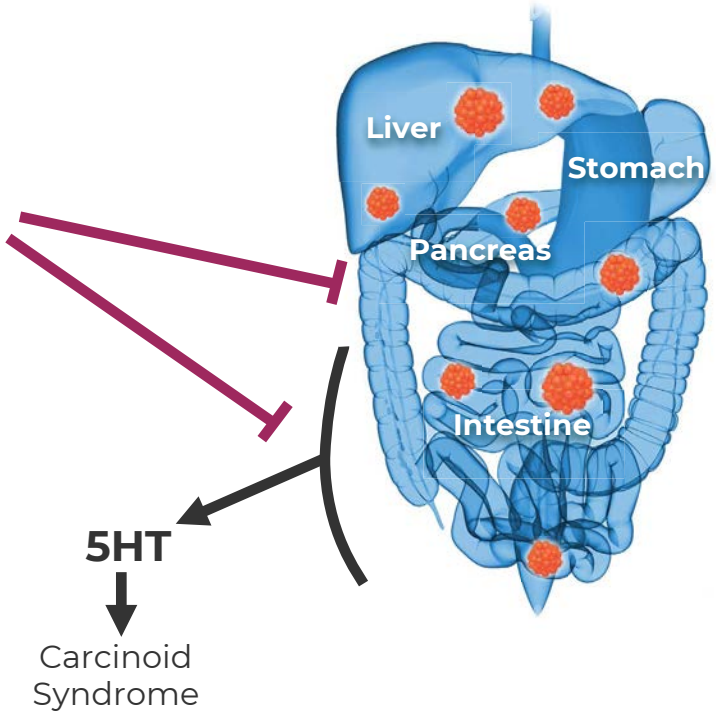
- Benign pituitary tumor
- Secretes excess growth hormone (GH)
- Excess GH causes excess secretion of insulin-like growth factor-1 (IGF-1)

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



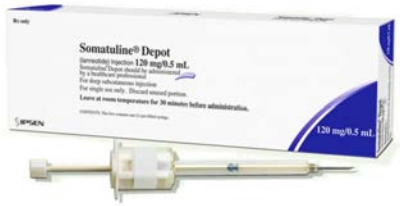
Neuroendocrine Tumors (NETs)

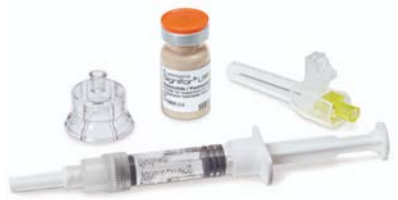
- NETs arise from aberrant enteroendocrine cells
- In ~10% of cases, tumors are associated with excess secretion of serotonin and other hormones resulting in carcinoid syndrome
- Patients with grade 1 and 2 NETs and distant metastases have a 5-year survival ranging from 30-70%

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

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

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

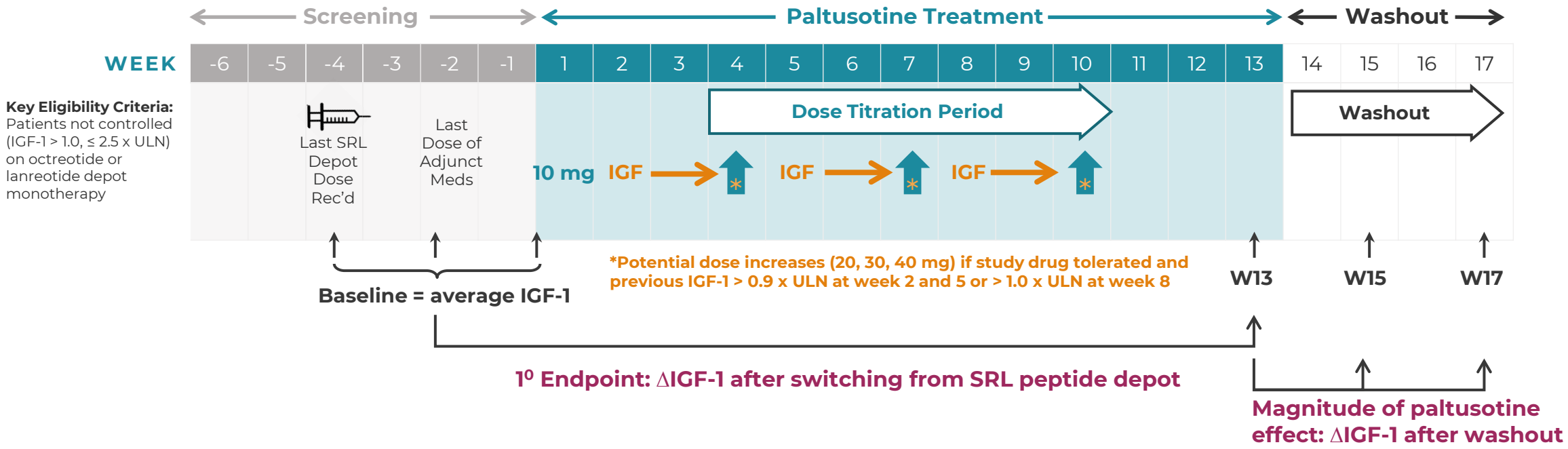




Sandostatin (octreotide)	Somatuline (lanreotide)	Somavert (pegvisomant)	Signifor (pasireotide)
NOVARTIS $1.6B	IPSEN Innovation for patient care $1.2B	Pfizer $264M	RECORDATI $75M
Monthly intramuscular 5-mL vial; 1½" 19-gauge needle	Monthly deep subcutaneous .2-.5ml; 18-gauge needle	Daily injections 1 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

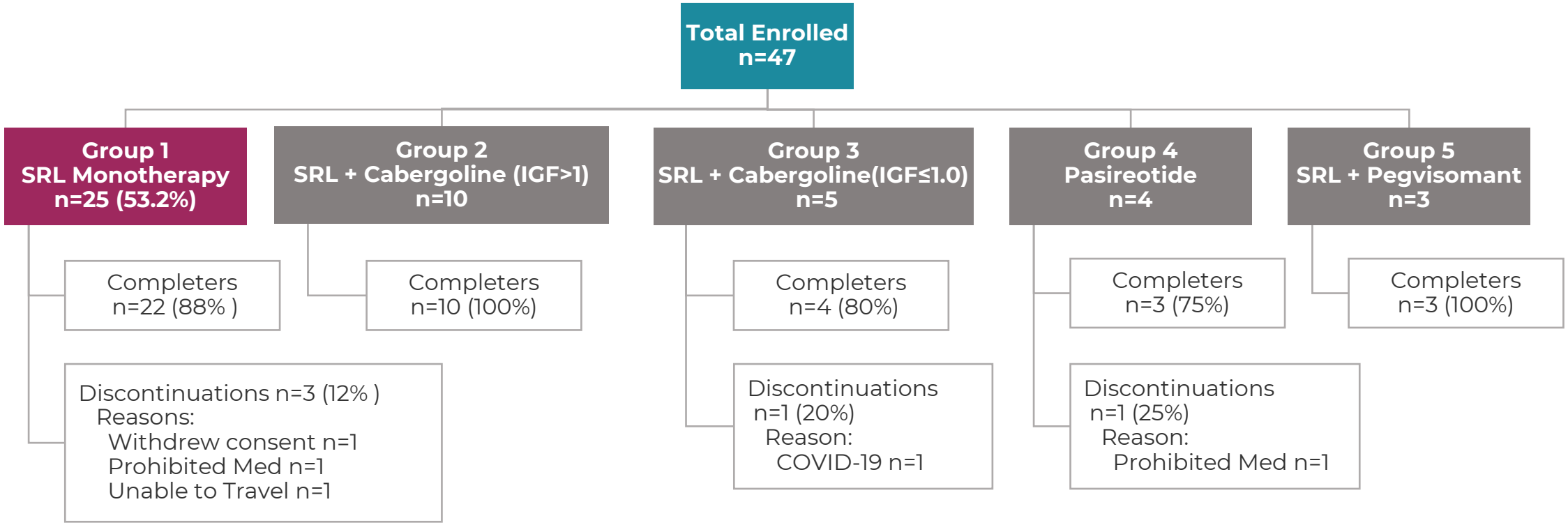
Exploratory populations (Groups 2-5)

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

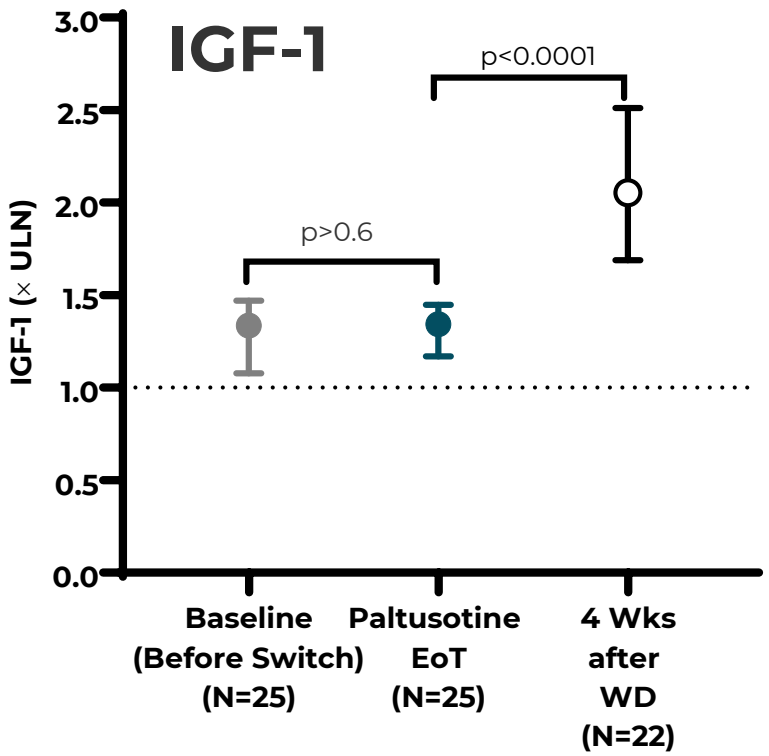


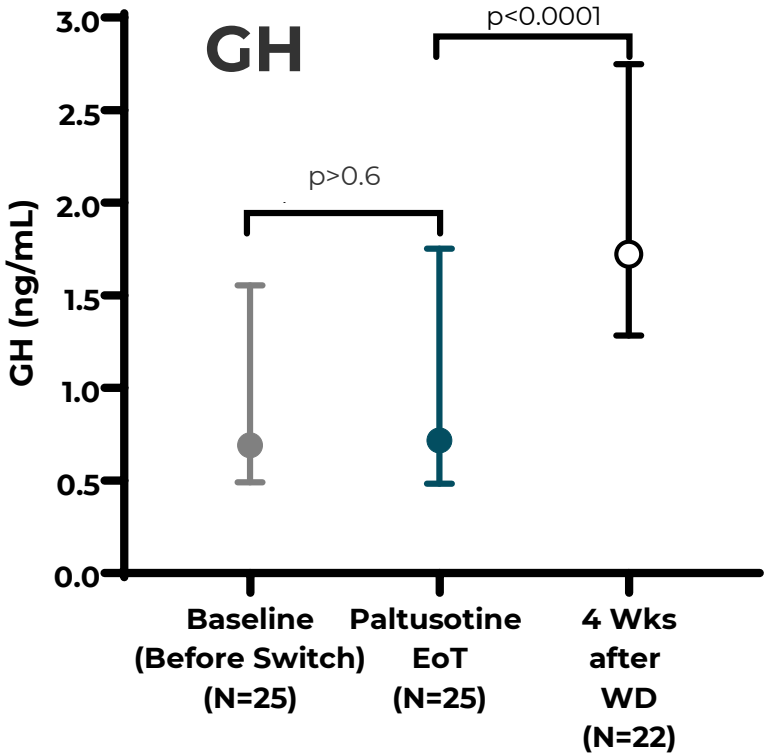
ACROBAT Edge Patient Characteristics

	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

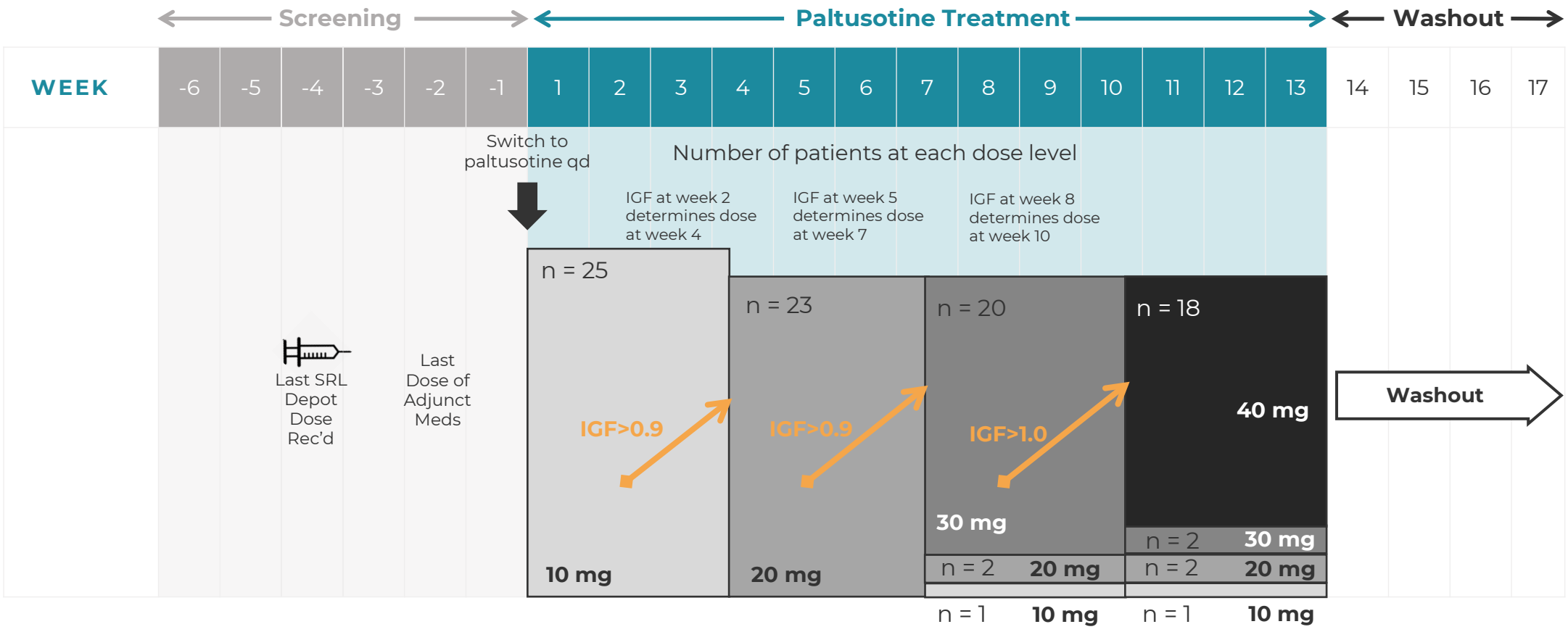
1. GH levels after 13 weeks of paltusotine treatment did not significantly change from baseline levels when patients were previously treated with injected SRL depots (Group 1)
2. Rise in GH after withdrawal characterized the magnitude of therapeutic activity of oral paltusotine

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

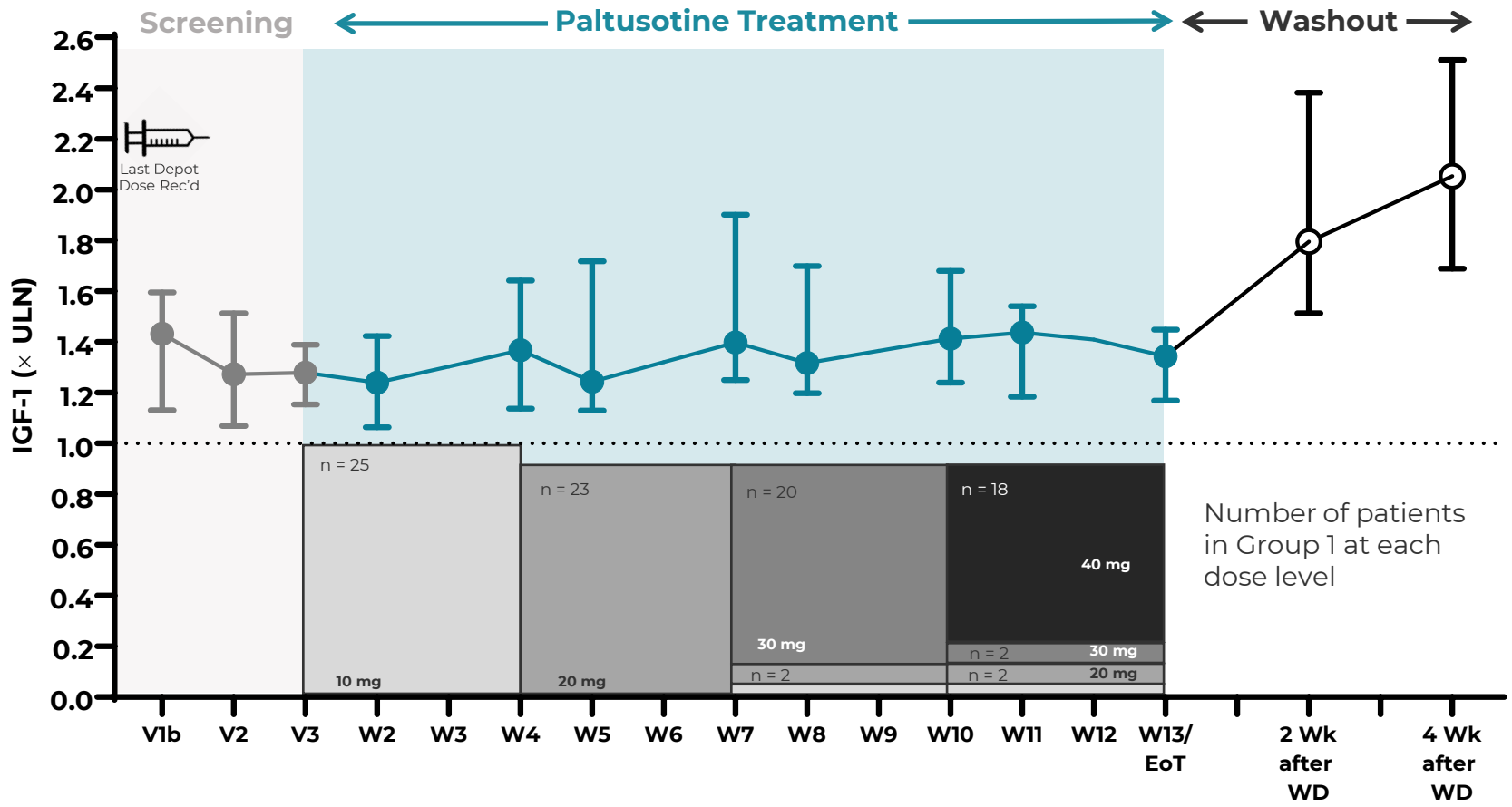
ACROBAT Edge Dose Titration

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)

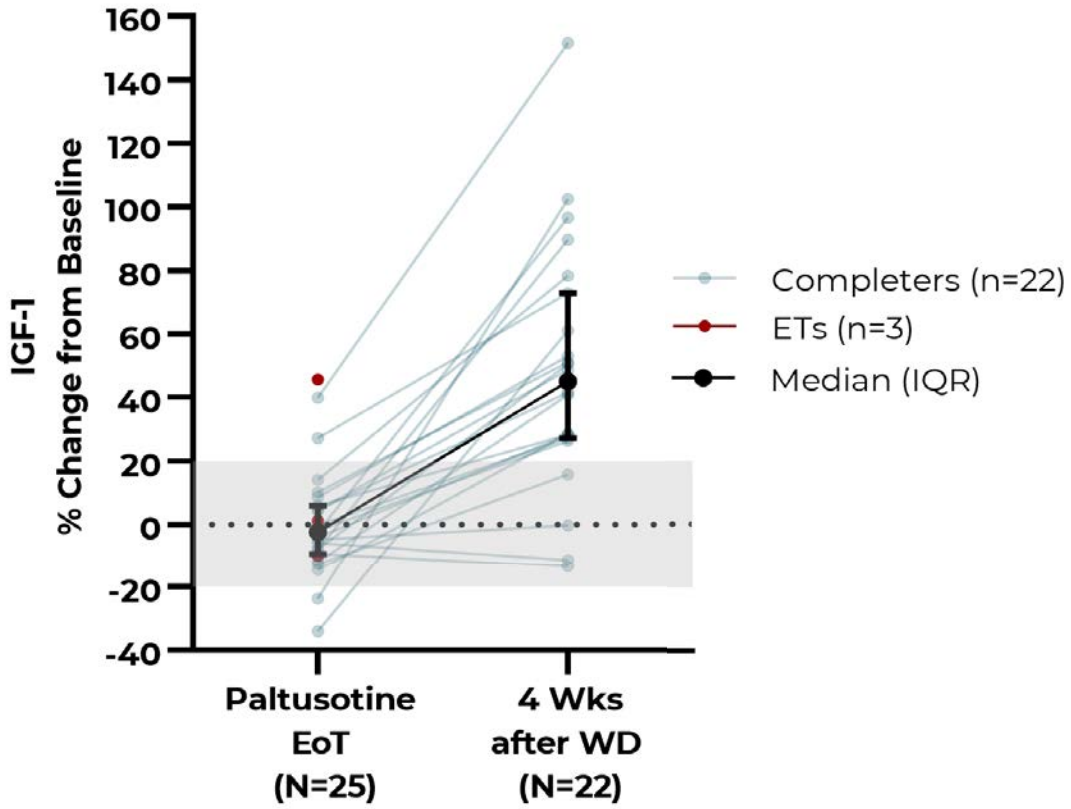
IGF-1 Levels Were Maintained After Switching to Paltusotine from Injected SRL Depots



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

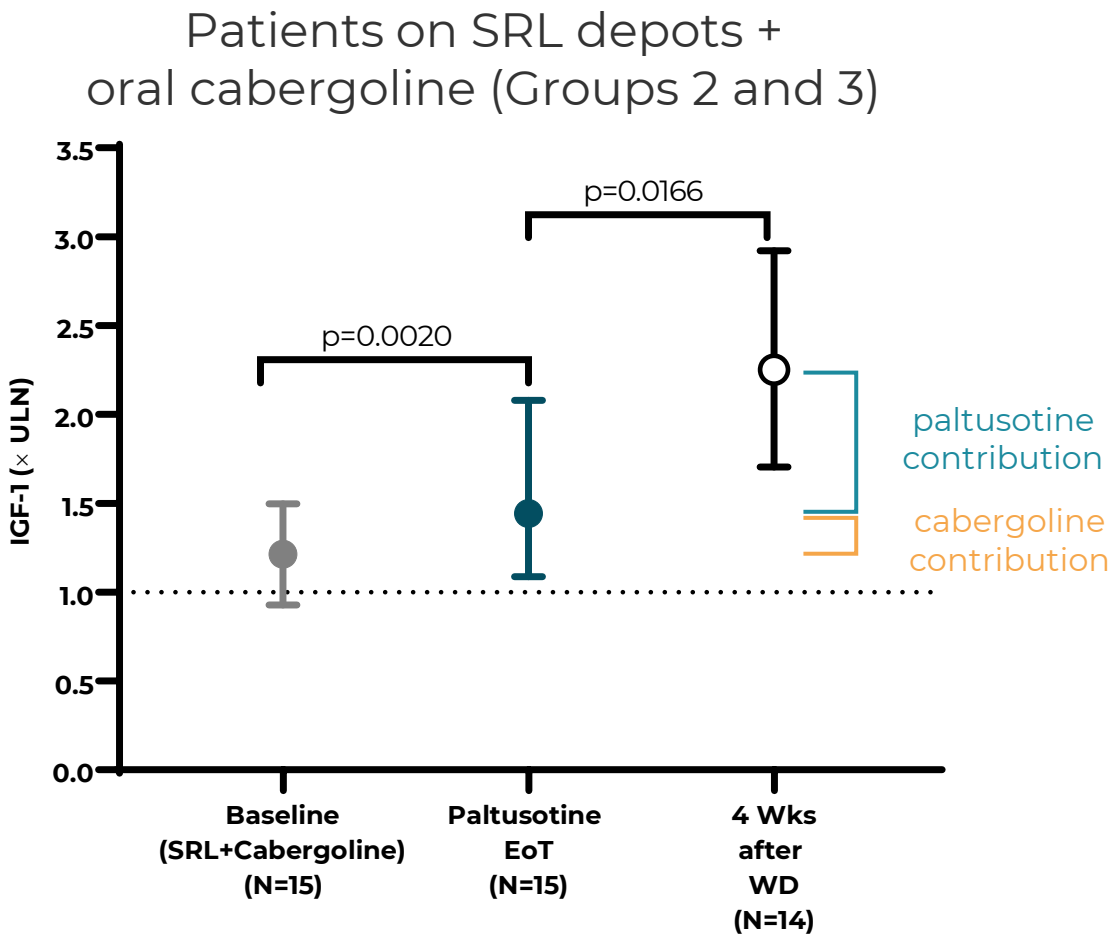
Individual patient percent change in IGF-1 at end of treatment vs. baseline and change at 4 weeks after withdrawal of paltusotine



- 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

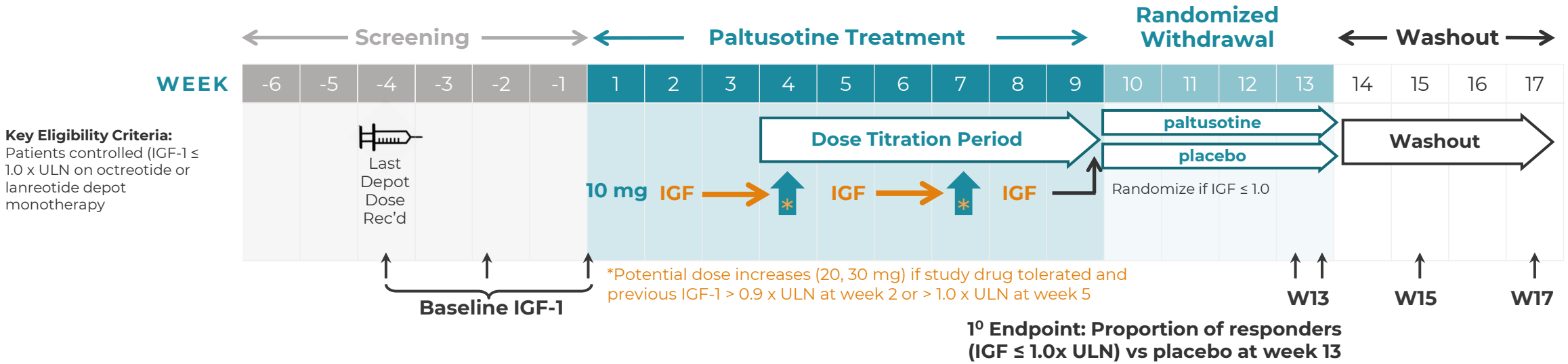


- Paltusotine contributed to IGF-1 lowering in patients previously treated with injected SRL peptide depots + oral cabergoline combination therapy
- Variable IGF-1 results were observed in Group 4 (n=4) and Group 5 (n=3)
- Patients represented by Groups 2-5 will not be included in Phase 3 program

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



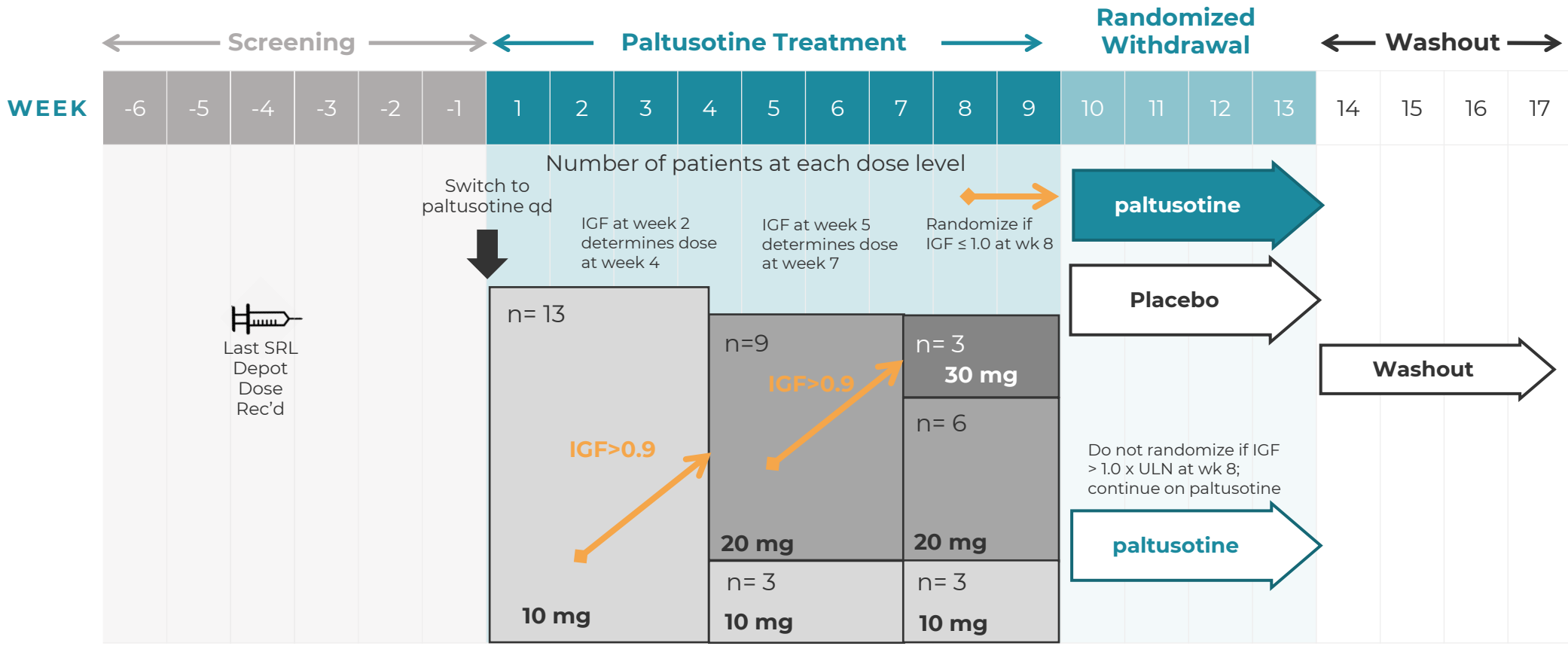
1⁰ Endpoint: Proportion of responders (IGF ≤ 1.0x ULN) vs placebo at week 13

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

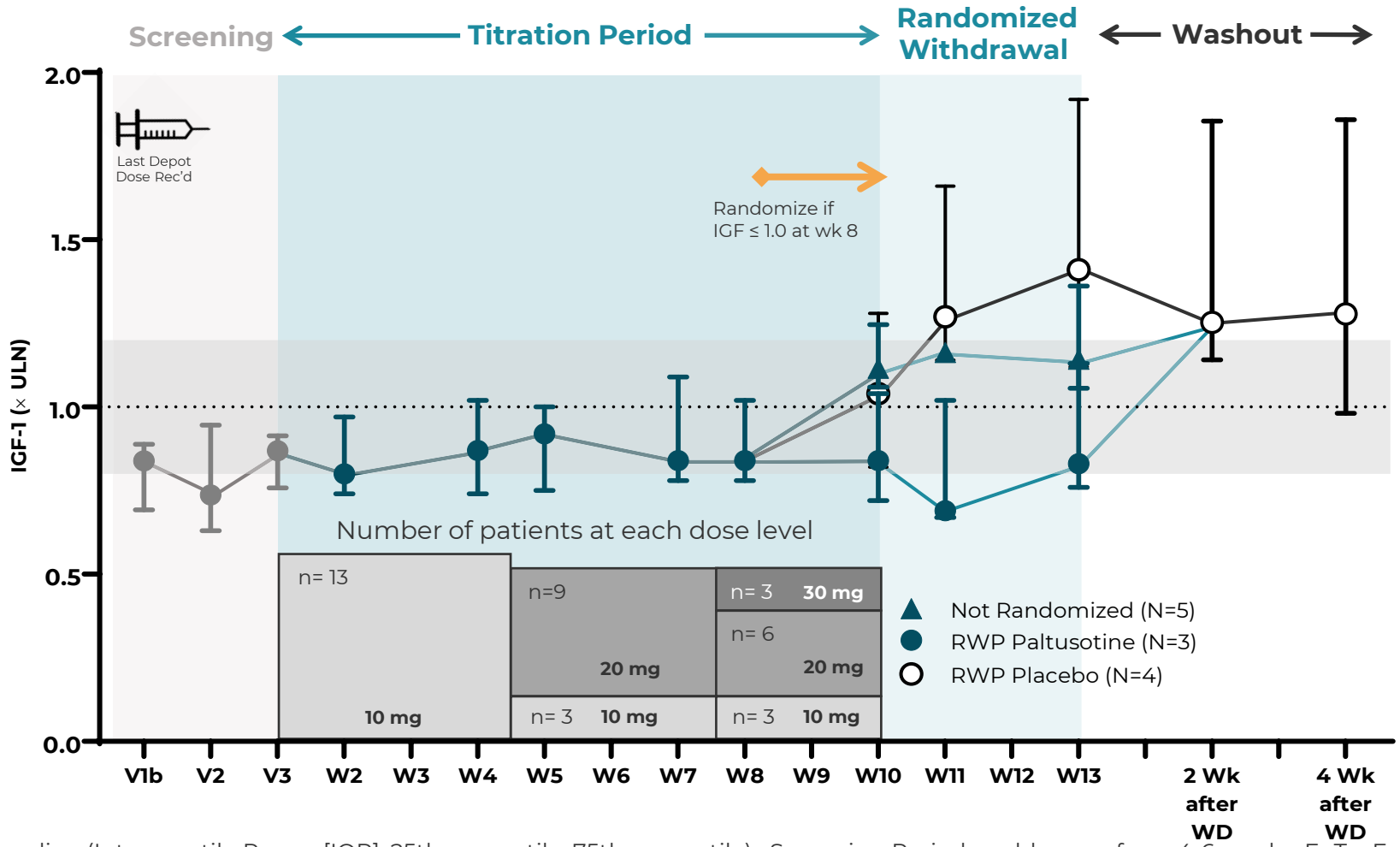
ACROBAT Evolve Dose Titration

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



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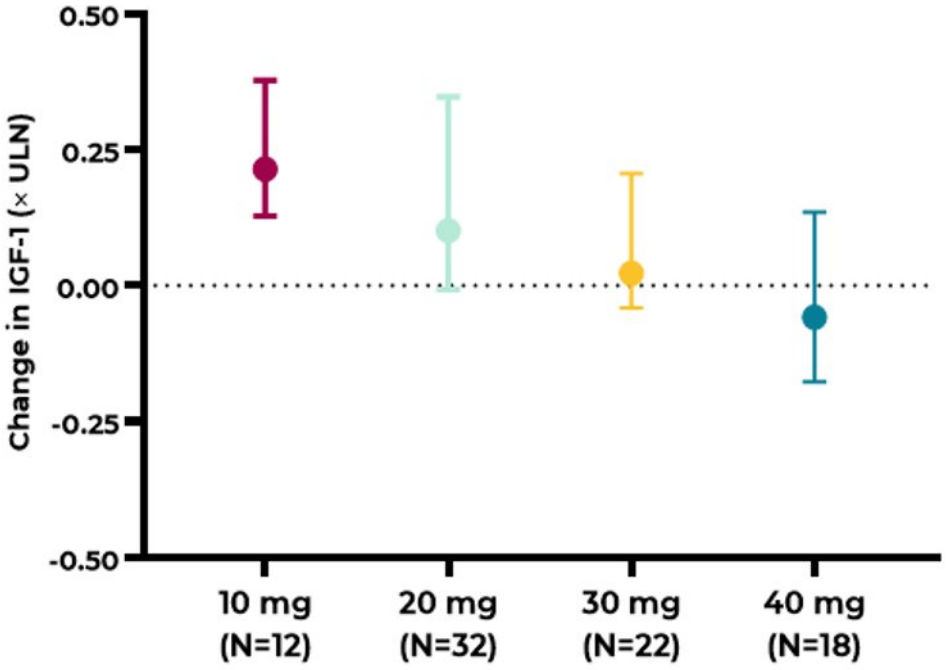
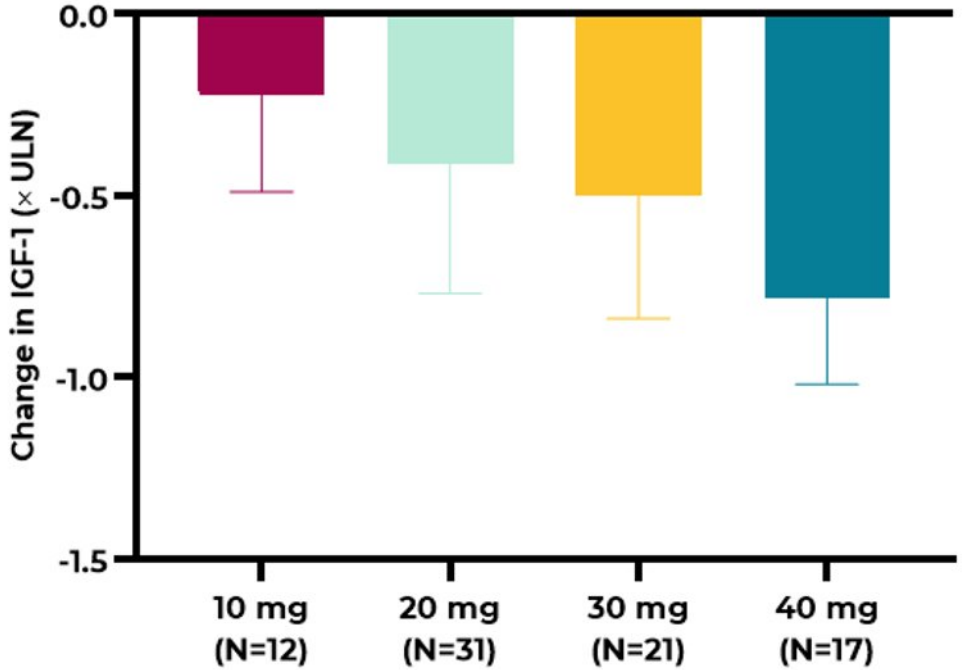
Post-Hoc Analysis of Edge (Group 1) and Evolve Provide Evidence of a Dose Response

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

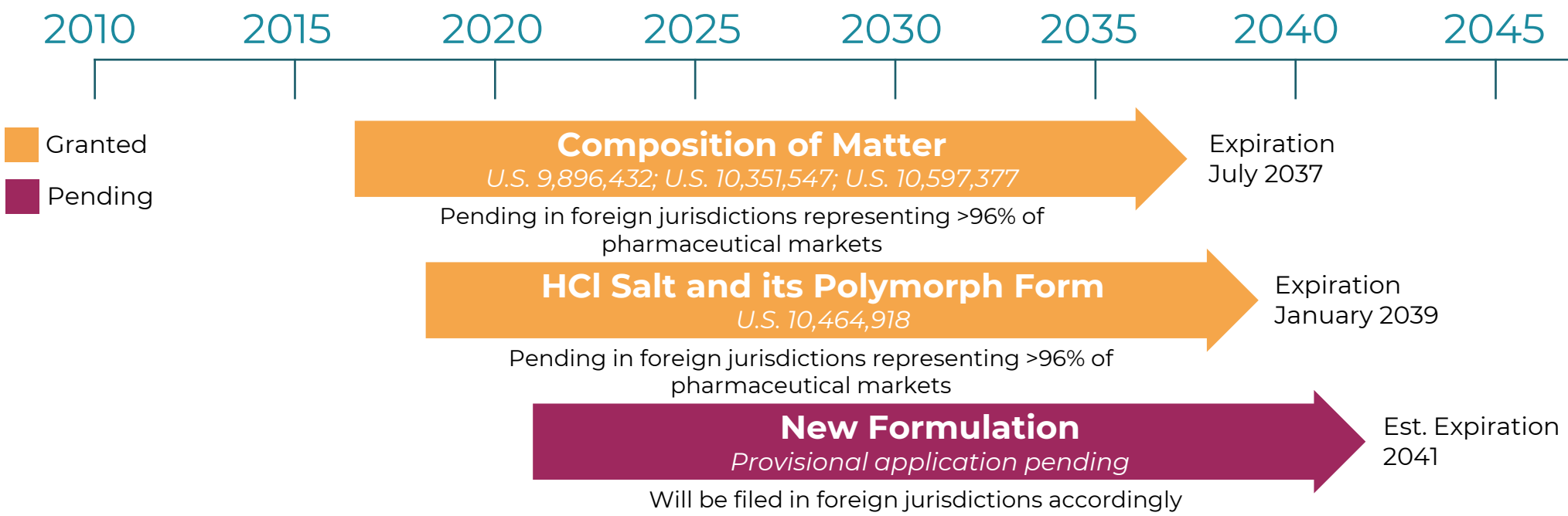
[1]Interquartile Range: 25th , 75th percentile
[2]Enrollment in ACROBAT Evolve was discontinued in April 2020. Previously enrolled patients continued in the study. Data from the Evolve patients (N=13) are included safety and dose-response analysis.

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